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# Clarke, Modet & C<sup>o</sup>

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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO  
DIVISION DE NUEVAS CREACIONES  
E. S. D.

Re: Expediente No. **05.050.160**

Solicitud de patente a nombre de **THE PROCTER & GAMBLE COMPANY.**

Yo, DILIA MARIA RODRIGUEZ D'ALEMAN, actuando como apoderada sustituta de acuerdo con la sustitución adjunta, identificada como aparece al pie de mi firma, domiciliada en la carrera 11 A No. 86-53, piso 6, obrando como apoderada de la sociedad **THE PROCTER & GAMBLE COMPANY**, domiciliada en Ohio, Estados Unidos de América, solicitante de la patente de la referencia, en respuesta al oficio No. 4491 notificado por fijación en lista el 17 de abril de 2009 relacionado con el concepto técnico de fondo No. 626, me permito presentar ante ese despacho el siguiente documento que fue requerido con fundamento en el artículo 46 de la Decisión 486.

GH POSNER ET AL: "Diels-Alder cycloadditions using nucleophilic 2-pyridones. Regiocontrolled and stereocontrolled synthesis of unsaturates, bridged, bicyclic lactams". Journal of Organic Chemistry., vol, 57, no. 15, 1992, páginas 4088 a 4097, XP002277661 American Chemical Society. Easton., US ISSN: 0022-3263.

Sobre este particular, nos permitimos manifestar que con la presentación de este documento queda totalmente atendido el requerimiento de ese despacho fundamentado en el artículo 46 de la Decisión 486.

Señor Superintendente,

DILIA RODRIGUEZ D' ALEMAN  
C.C. 41.654.882 de Bogotá  
T.P. 20824 del C.S.J.

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DIVISION DE NUEVAS TECNICAS  
SUBSECRETARIA DE INDUSTRIA Y COMERCIO

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MEMO A REPORT THE

Yo, DILIA MARIA RODRIGUEZ DALLEMAN, actuando como apoderada de acuerdo con la resolución abogada, identificada como la No. 11-A No. 10-22, emitida en la ciudad de Nueva York, Nueva York, por la abogada de la sociedad THE PROCTOR & KATHLEEN COMPANY, actuando en Ohio, Estados Unidos de América, solicitante de la patente de invención en el caso No. 1491 nominado por la ley en la ley de 17 de agosto de 1900 relacionado con el concepto técnico de fondo No. 626, me permito presentar ante este despacho el siguiente documento que he requerido con

1. *Journal of Organic Chemistry*, vol. 57, no. 12, pages 4108-4109, 1992. American Chemical Society.

documentos que se encuentran en el archivo de la Dirección de la  
Comisión de la Verdad, en el momento de la redacción de este

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# The Journal of Organic Chemistry

VOLUME 57, NUMBER 15

JULY 17, 1992

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## Communications

### Substituent Effects on One-Bond $^{13}\text{C}$ - $^{13}\text{C}$ NMR Coupling Constants between the Carbonyl Carbon and $\text{C}_1$ in Methyl Benzoates. Is There a Dependence on $\pi$ -Bond-Order Changes?

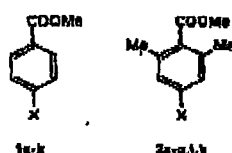
Carlo Dell'Erba,<sup>a,\*</sup> Andrea Mela,<sup>a,†</sup> Roberta Musio,<sup>a</sup> Marino Novi,<sup>a</sup> Giovanni Petrillo,<sup>a</sup> Fernando Sancassan,<sup>a</sup> Oronzo Sciacovelli,<sup>a</sup> and Domenico Spinelli<sup>a</sup>

*Istituto di Chimica Organica dell'Università e CNR, Centro di Studio sui Diariloidi e loro Applicazioni, Corso Europa 28, I-16132 Genova, Italy, Dipartimento di Chimica dell'Università e CNR, Centro di Studio sulle Metodologie Innovative di Sintesi Organiche, Via Amendola 137, I-70126 Bari, Italy, and Dipartimento di Chimica Organica "A. Mangini", Via San Donato 15, I-40127 Bologna, Italy*

Received November 13, 1991 (Revised Manuscript Received April 22, 1992)

**Summary:** Substituent effects on  $^1J_{\text{CO},\text{C}_1}$  in methyl 4-X-benzoates 1 and 2,6-dimethyl-4-X-benzoates 2 appear to be related with chemical-shift variations at the two involved carbon nuclei rather than with  $\pi$ -bond-order changes.

We have recently reported<sup>1a,b</sup> that in both  $\text{CDCl}_3$  and  $(\text{OD})_2\text{SO}$  the responses of the carbonyl carbon chemical shift to the effect of 4-substituents is much the same in methyl 4-X-benzoates and in the corresponding sterically hindered 2,6-dimethyl derivatives. This and other<sup>1c-e</sup> results suggest a minor role for conjugative interactions between the methoxycarbonyl group and the aryl moiety even in 2,6-unsubstituted derivatives.



- a: X =  $\text{NMe}_2$
- b: X =  $\text{NH}_2$
- c: X =  $\text{OMe}$
- d: X = F
- e: X = Br
- f: X =  $\text{Me}$
- g: X = H
- h: X =  $\text{CF}_3$
- i: X = CN
- j: X =  $\text{NO}_2$
- k: X =  $\text{COMe}$

On the other hand, previous work<sup>1a</sup> on one-bond  $^{13}\text{C}$ - $^{13}\text{C}$  coupling constants in some 4-substituted methyl benzoates

in  $\text{CDCl}_3$  mainly attributed the observed substituent effects on  $^1J_{\text{CO},\text{C}_1}$  to changes in the  $\pi$ -bond order between the two carbon atoms. This conclusion was based essentially on the finding that  $^1J_{\text{CO},\text{C}_1}$  increases with electron-donating ( $\text{OMe}$ ,  $\text{Me}$ , F, Cl, and Br) substituents, while a little effect in the opposite direction is exhibited by the only electron-withdrawing group considered ( $\text{CF}_3$ ).

For a better insight into the matter, we have undertaken an investigation aimed at comparing  $^1J_{\text{CO},\text{C}_1}$  values for a more representative set of methyl 4-X-benzoates 1 with those for the corresponding sterically hindered 2,6-dimethyl derivatives 2. Literature on  $^1J$  coupling constants<sup>2</sup>

(1) (a) Dell'Erba, C.; Sancassan, F.; Novi, M.; Petrillo, G.; Magnoli, A.; Spinelli, D.; Consiglio, G.; Gatti, P. *J. Org. Chem.* 1988, 53, 2544. (b) Dell'Erba, C.; Mela, A.; Novi, M.; Petrillo, G.; Sancassan, F.; Spinelli, D. *J. Chem. Soc., Perkin Trans. 2* 1990, 2055. (c) Dell'Erba, C.; Sancassan, F.; Leandri, G.; Novi, M.; Petrillo, G.; Mela, A.; Spinelli, D.; Consiglio, G. *Gazz. Chim. Ital.* 1989, 119, 843. (d) Dell'Erba, C.; Sancassan, F.; Novi, M.; Spinelli, D.; Consiglio, G.; Arnone, C.; Ferzoni, F. *J. Chem. Soc., Perkin Trans. 2* 1989, 1779. (e) Consiglio, G.; Spinelli, D.; Arnone, C.; Sancassan, F.; Dell'Erba, C.; Noto, R.; Tarrler, F. *J. Chem. Soc., Perkin Trans. 2* 1984, 317. (f) Consiglio, G.; Arnone, C.; Spinelli, D.; Sancassan, F.; Dell'Erba, C.; Leandri, G.; Torrici, F. *Gazz. Chim. Ital.* 1987, 117, 287. (g) Dell'Erba, C.; Sancassan, F.; Novi, M.; Spinelli, D.; Consiglio, G. *J. Chem. Soc., Perkin Trans. 2* 1991, 1691.

(2) An X-ray diffraction study of the crystal structure of 2c has evidenced a  $64^\circ$  rotation angle between the  $\text{COOMe}$  and the aryl moieties, together with a residual hindering between the former and the  $\alpha$ -methyl groups.<sup>3</sup> These results, together with the possibility of an even larger torsion angle in solution, allow the conclusion that a marked steric hindrance to conjugation is effective in compounds 2.

(3) Magnoli, A.; Sancassan, F.; Novi, M.; Petrillo, G. *Acta Crystallogr.* 1989, C44, 2149.

(4) (a) Iyer, P. S.; Krishnamurthy, V. V.; Olah, G. A. *J. Org. Chem.* 1985, 50, 3058. (b) Krishnamurthy, V. V.; Surya Prakash, G. K.; Iyer, P. S.; Olah, G. A. *J. Am. Chem. Soc.* 1984, 106, 7058.

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<sup>a</sup> University of Bologna.

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J. Org. Chem. 1992, 57, 4055-4061

benzene under argon. The flask was then immersed in a preheated oil bath and refluxed for 50 min. After the solution was cooled, 20  $\mu$ L of DBU was added and the reaction mixture stirred for 15 min. The solvent was then removed and the mixture purified by flash silica gel chromatography (10–50% EtOAc/hexane) to afford 17.5 mg (0.051 mmol, 84%) of  $\alpha,\beta$ -unsaturated ester 13 as a colorless oil:  $R_f$  = 0.8 (50% EtOAc/hexane);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  7.15 (t,  $J$  = 4.1 Hz, 1 H), 4.52–4.47 (m, 1 H), 4.35–4.28 (m, 2 H), 3.74 (s, 3 H), 2.59–2.48 (m, 3 H), 2.29 (ddd,  $J$  = 19.3, 4.3, 1.1 Hz, 1 H), 2.04–1.91 (m, 2 H), 0.87 (s, 9 H), 0.07 (s, 3 H), 0.06 (s, 3 H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ) 180.6, 165.8, 141.0, 130.8, 65.9, 63.6, 51.9, 44.0, 39.3, 34.7, 34.2, 25.8, 18.0, –4.8; IR ( $\text{CHCl}_3$ ) 1759, 1709  $\text{cm}^{-1}$ ; HRMS  $m/e$  ( $\text{M}^+ - t\text{-Bu}$ ) calcd for  $\text{C}_{17}\text{H}_{25}\text{O}_5\text{Si}$  283.1002, found 283.1005.

**3-(*tert*-Butyldimethylsiloxy)-2-pyrone.** A 25-mL round-bottomed flask was charged with 125.4 mg (1.12 mmol) of 3-hydroxy-2-pyrone (Aldrich Chemical Co., 2,3-dihydroxypyridine) and dissolved in 3 mL of  $\text{CH}_2\text{Cl}_2$  under argon. To this was added 0.16 mL (1.3 mmol, 1.2 equiv) of 2,6-lutidine followed by 0.81 mL (1.3 mmol, 1.2 equiv) of TBDMS-OTf. This was stirred for 1 h, and then the solvent was removed. Purification by silica gel chromatography (10% EtOAc/hexane) gave 170.2 mg (0.75 mmol, 67%) of the silyl ether as a volatile light yellow oil:  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  7.17 (dd,  $J$  = 8.1, 1.8 Hz, 1 H), 6.61 (dd,  $J$  = 7.0, 1.8 Hz, 1 H), 6.10 (dd,  $J$  = 7.0, 5.1 Hz, 1 H), 0.97 (s, 9 H), 0.24 (s, 6 H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  180.9, 144.0, 142.4, 122.2, 105.0, 25.8, 18.4, –4.6; IR ( $\text{CHCl}_3$ ) 1759, 1709  $\text{cm}^{-1}$ ; HRMS  $m/e$  ( $\text{M}^+ - t\text{-Bu}$ )

calcd for  $\text{C}_{24}\text{H}_{34}\text{O}_5\text{Si}$  405.1192, found 405.1186.

**Acknowledgment.** We thank the NIH (Grant GM 30052) for financial support.

**Registry No.** 1, 98081-54-2; *endo*-2, 141510-29-4; *exo*-2, 141553-87-9; *endo*-3, 141510-30-7; *exo*-3, 141553-88-0; *endo*-4, 141510-31-8; *exo*-4, 141553-89-1; *endo*-5, 141510-32-9; *exo*-5, 141553-90-4; *endo*-6, 141510-33-0; *exo*-6, 141553-91-5; *endo*-7, 141510-34-1; *exo*-7, 141553-92-6; *endo*-8, 141510-35-2; *exo*-8, 141553-93-7; *endo*-9, 141510-36-3; *exo*-9, 141553-94-8; *endo*-10, 141524-86-5; *exo*-10, 141510-37-4; 11, 141510-37-4; 12, 141510-38-5; 13, 141510-39-6;  $\text{Ph}_2\text{SO}$ , 127-63-9;  $\text{PhCO}_2\text{Me}$ , 93-68-3;  $\text{PhBr}$ , 105-85-1;  $\text{Ph}_2\text{S}$ , 129-68-2;  $\text{PhOSi}(\text{Me})_2$ , 1529-17-6;  $\text{PhOH}$ , 108-85-2; dihydro-3-methylsila-2(3H)-furanone, 547-85-9; 3-(*tert*-butyldimethylsiloxy)-2-pyrone, 141510-40-9; 3-hydroxy-2-pyrone, 495-64-0; nitroethylene, 3638-64-0; acrylonitrile, 107-13-1; acrolein, 107-02-8; methacrolein, 78-85-3; methyl vinyl ketone, 78-94-4; methyl acrylate, 96-33-9; benzyl acrylate, 2495-35-4; methyl methacrylate, 80-82-6; 3-(*p*-toluenesulfonyl)-2-pyrone, 99268-87-8; 3-carbomethoxy-2-pyrone, 25991-27-8; 3-bromo-2-pyrone, 19878-32-6; 2-pyrone, 504-91-4; benzene, 71-43-2.

**Supplementary Material Available:** Characterization of new compounds by NMR (12 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

## Diels–Alder Cycloadditions Using Nucleophilic 2-Pyridones. Regiocontrolled and Sterecontrolled Synthesis of Unsaturated, Bridged, Bicyclic Lactams

Gary H. Posner,\* Victoria Vinader, and Kamyar Afarinkia

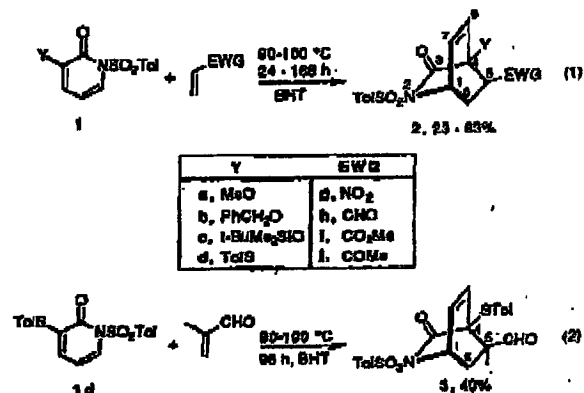
Department of Chemistry, The Johns Hopkins University, Baltimore, Maryland 21218

Received January 28, 1992

Captodative 3-oxo- and 3-(*tert*-butoxy)-1-oxo-2-pyridones 1a–1d are shown to be reactive as nucleophilic dienes undergoing 2 + 4-cycloadditions with various electrophilic alkenes under sufficiently mild thermal conditions (90–100 °C) that the initial bicyclic lactam adducts can be isolated on gram scale in fair to very good yields (23–83%) without loss of an isocyanate from the heteroatom bridge. These bicyclic adducts are formed with complete regiocontrol and stereocontrol. For pyridones sulfide 1d, these Diels–Alder cycloadditions are the first examples of a captodative unsaturated sulfide acting as an enophile. NMR data ( $^{13}\text{C}$ ) are presented correlating the electron density in the pyridone diene systems with their Diels–Alder reactivity, and some transformations of the bicyclic lactam adducts are shown to illustrate the value and versatility of these richly functionalized synthetic intermediates.

### Introduction

A few years ago this laboratory reported the first examples of efficient 2 + 4-cycloadditions of electron-poor 1,3-disulfonyl-2-pyridones with electron-rich dienophiles such as vinylic ethers.<sup>1</sup> To complement such inverse-electron-demand Diels–Alder reactions, we now report normal-electron-demand 2 + 4-cycloadditions of captodative 1,3-disubstituted 2-pyridones under thermal (i.e., not high-pressure) conditions with electron-poor dienophiles such as  $\text{CH}_2=\text{C}(\text{R})\text{EWG}$ , in which the R group is hydrogen or methyl and the electron-withdrawing-group (EWG) is nitro, aldehyde, ester, or ketone (eqs 1 and 2). These successful cycloadditions, stopping at the initial bicyclic lactam stage without extrusion of an isocyanate from the heteroatom bridge,<sup>2</sup> are among the few examples



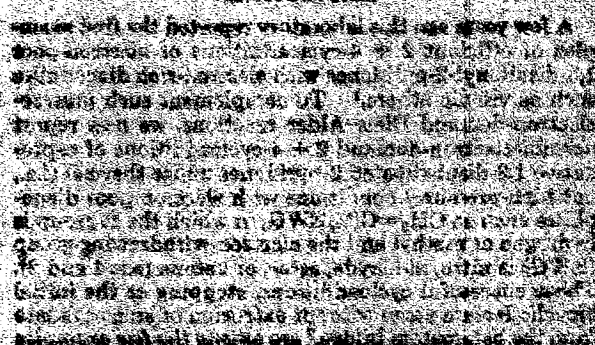
in which normally highly aromatic 2-pyridones (more aromatic than 2-pyrone)<sup>3</sup> have entered as enophiles into

(1) Posner, G. H.; Switzer, C. J. *J. Org. Chem.* 1987, 52, 1644 and references therein to 2 + 4-cycloadditions of 2-pyridones.

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Department of Chemistry, The Johns Hopkins University, Baltimore, Maryland 21218

1998, 1999, 2000, 2001, 2002, 2003, 2004, 2005, 2006, 2007, 2008, 2009, 2010, 2011, 2012, 2013, 2014, 2015, 2016, 2017, 2018, 2019, 2020, 2021, 2022, 2023, 2024, 2025, 2026, 2027, 2028, 2029, 2030, 2031, 2032, 2033, 2034, 2035, 2036, 2037, 2038, 2039, 2040, 2041, 2042, 2043, 2044, 2045, 2046, 2047, 2048, 2049, 2050, 2051, 2052, 2053, 2054, 2055, 2056, 2057, 2058, 2059, 2060, 2061, 2062, 2063, 2064, 2065, 2066, 2067, 2068, 2069, 2070, 2071, 2072, 2073, 2074, 2075, 2076, 2077, 2078, 2079, 2080, 2081, 2082, 2083, 2084, 2085, 2086, 2087, 2088, 2089, 2090, 2091, 2092, 2093, 2094, 2095, 2096, 2097, 2098, 2099, 2100, 2101, 2102, 2103, 2104, 2105, 2106, 2107, 2108, 2109, 2110, 2111, 2112, 2113, 2114, 2115, 2116, 2117, 2118, 2119, 2120, 2121, 2122, 2123, 2124, 2125, 2126, 2127, 2128, 2129, 2130, 2131, 2132, 2133, 2134, 2135, 2136, 2137, 2138, 2139, 2140, 2141, 2142, 2143, 2144, 2145, 2146, 2147, 2148, 2149, 2150, 2151, 2152, 2153, 2154, 2155, 2156, 2157, 2158, 2159, 2160, 2161, 2162, 2163, 2164, 2165, 2166, 2167, 2168, 2169, 2170, 2171, 2172, 2173, 2174, 2175, 2176, 2177, 2178, 2179, 2180, 2181, 2182, 2183, 2184, 2185, 2186, 2187, 2188, 2189, 2190, 2191, 2192, 2193, 2194, 2195, 2196, 2197, 2198, 2199, 2200, 2201, 2202, 2203, 2204, 2205, 2206, 2207, 2208, 2209, 2210, 2211, 2212, 2213, 2214, 2215, 2216, 2217, 2218, 2219, 2220, 2221, 2222, 2223, 2224, 2225, 2226, 2227, 2228, 2229, 2230, 2231, 2232, 2233, 2234, 2235, 2236, 2237, 2238, 2239, 2240, 2241, 2242, 2243, 2244, 2245, 2246, 2247, 2248, 2249, 2250, 2251, 2252, 2253, 2254, 2255, 2256, 2257, 2258, 2259, 2260, 2261, 2262, 2263, 2264, 2265, 2266, 2267, 2268, 2269, 2270, 2271, 2272, 2273, 2274, 2275, 2276, 2277, 2278, 2279, 2280, 2281, 2282, 2283, 2284, 2285, 2286, 2287, 2288, 2289, 2290, 2291, 2292, 2293, 2294, 2295, 2296, 2297, 2298, 2299, 2300, 2301, 2302, 2303, 2304, 2305, 2306, 2307, 2308, 2309, 2310, 2311, 2312, 2313, 2314, 2315, 2316, 2317, 2318, 2319, 2320, 2321, 2322, 2323, 2324, 2325, 2326, 2327, 2328, 2329, 2330, 2331, 2332, 2333, 2334, 2335, 2336, 2337, 2338, 2339, 2340, 2341, 2342, 2343, 2344, 2345, 2346, 2347, 2348, 2349, 2350, 2351, 2352, 2353, 2354, 2355, 2356, 2357, 2358, 2359, 2360, 2361, 2362, 2363, 2364, 2365, 2366, 2367, 2368, 2369, 2370, 2371, 2372, 2373, 2374, 2375, 2376, 2377, 2378, 2379, 2380, 2381, 2382, 2383, 2384, 2385, 2386, 2387, 2388, 2389, 2390, 2391, 2392, 2393, 2394, 2395, 2396, 2397, 2398, 2399, 2400, 2401, 2402, 2403, 2404, 2405, 2406, 2407, 2408, 2409, 2410, 2411, 2412, 2413, 2414, 2415, 2416, 2417, 2418, 2419, 2420, 2421, 2422, 2423, 2424, 2425, 2426, 2427, 2428, 2429, 2430, 2431, 2432, 2433, 2434, 2435, 2436, 2437, 2438, 2439, 2440, 2441, 2442, 2443, 2444, 2445, 2446, 2447, 2448, 2449, 2450, 2451, 2452, 2453, 2454, 2455, 2456, 2457, 2458, 2459, 2460, 2461, 2462, 2463, 2464, 2465, 2466, 2467, 2468, 2469, 2470, 2471, 2472, 2473, 2474, 2475, 2476, 2477, 2478, 2479, 2480, 2481, 2482, 2483, 2484, 2485, 2486, 2487, 2488, 2489, 2490, 2491, 2492, 2493, 2494, 2495, 2496, 2497, 2498, 2499, 2500, 2501, 2502, 2503, 2504, 2505, 2506, 2507, 2508, 2509, 2510, 2511, 2512, 2513, 2514, 2515, 2516, 2517, 2518, 2519, 2520, 2521, 2522, 2523, 2524, 2525, 2526, 2527, 2528, 2529, 2530, 2531, 2532, 2533, 2534, 2535, 2536, 2537, 2538, 2539, 2540, 2541, 2542, 2543, 2544, 2545, 2546, 2547, 2548, 2549, 2550, 2551, 2552, 2553, 2554, 2555, 2556, 2557, 2558, 2559, 2560, 2561, 2562, 2563, 2564, 2565, 2566, 2567, 2568, 2569, 2570, 2571, 2572, 2573, 2574, 2575, 2576, 2577, 2578, 2579, 2580, 2581, 2582, 2583, 2584, 2585, 2586, 2587, 2588, 2589, 2590, 2591, 2592, 2593, 2594, 2595, 2596, 2597, 2598, 2599, 2600, 2601, 2602, 2603, 2604, 2605, 2606, 2607, 2608, 2609, 2610, 2611, 2612, 2613, 2614, 2615, 2616, 2617, 2618, 2619, 2620, 2621, 2622, 2623, 2624, 2625, 2626, 2627, 2628, 2629, 2630, 2631, 2632, 2633, 2634, 2635, 2636, 2637, 2638, 2639, 2640, 2641, 2642, 2643, 2644, 2645, 2646, 2647, 2648, 2649, 2650, 2651, 2652, 2653, 2654, 2655, 2656, 2657, 2658, 2659, 2660, 2661, 2662, 2663, 2664, 2665, 2666, 2667, 2668, 2669, 2670, 2671, 2672, 2673, 2674, 2675, 2676, 2677, 2678, 2679, 26

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Mr. JAMES M. HARRIS, JR., President

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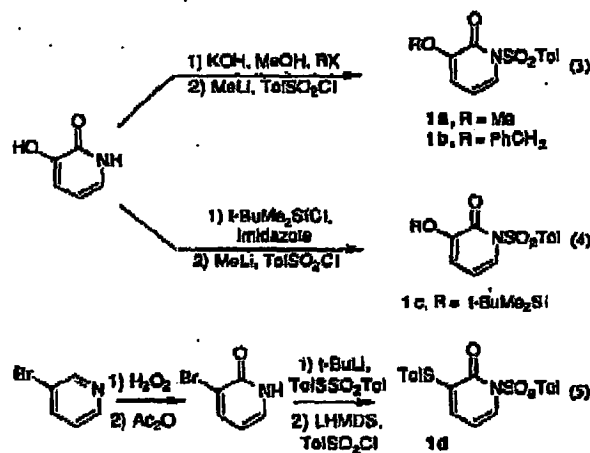
## Cycloadditions Using 2-Pyridones

thermally mild (90–100 °C) and therefore practical 2 + 4 cycloadditions.<sup>4</sup> We report also <sup>13</sup>C NMR chemical shift data for 3-Y-substituted-1-(p-toluenesulfonyl)-2-pyridones correlating electron density in the pyridone diene system with 2 + 4 cycloaddition reactivity toward electron-poor dienophiles. The cycloadducts, formed regioselectively and stereospecifically, are synthetically versatile, unsaturated, bridged, bicyclic lactams. Some transformations of these bicyclic lactams into polyfunctionalized cyclohexenes are presented to illustrate the high value of these synthetic building units.

## Results and Discussion

In Table I are summarized some <sup>13</sup>C NMR chemical shift data for several 3-Y-1-(p-toluenesulfonyl)-2-pyridones; these assignments were made using C–H coupled <sup>13</sup>C NMR spectroscopy.<sup>5</sup> For comparison, <sup>13</sup>C NMR data for similarly Y-substituted benzenes are listed.<sup>6</sup>

The data in Table I deserve comment. First, compared to the corresponding 2-pyrones discussed in the accompanying article,<sup>7</sup> these 2-pyridones are considerably more aromatic as expected,<sup>8</sup> with <sup>13</sup>C NMR chemical shift values differing from those of Y-benzenes by only relatively small amounts. Second, whereas a 3-arenesulfonyl substituent is strongly electron-withdrawing, a 3-oxygen substituent is strongly electron-releasing. Because we already showed that 3-(arenesulfonyl)-2-pyridones cycloadd to nucleophilic alkenes,<sup>4</sup> it was our expectation that 3-oxygen-substituted 1-tosyl-2-pyridones would cycloadd to electrophilic alkenes. The commercial availability of 3-hydroxy-2-pyridone (2,3-dihydroxypyridine) allowed very convenient access to 3-oxygen-substituted 1-tosyl-2-pyridones 1a and 1c, and the commercial availability of 3-bromopyridine enabled easy preparation of 3-(toluenethio)-2-pyridone 1d (eqs 3–6).



- (2) Acheson, R. M.; Tasker, P. A. *J. Chem. Soc. C* 1967, 1542.  
 (3) (a) Eldridge, J. A.; Jackman, L. M. *J. Chem. Soc.* 1961, 859. (b) Adams, J. *J. Am. Chem. Soc.* 1970, 92, 2750. (c) Bird, C. W. *Tetrahedron* 1986, 42, 89.  
 (4) (a) Herdels, C.; Hartke, C. *Heterocycles* 1989, 29, 287. (b) Nakano, H.; Tomisawa, H.; Hongo, H. *J. Chem. Soc., Chem. Commun.* 1990, 1775.  
 (5) Tomisawa, H.; Nakano, H.; Hongo, H. *Heterocycles* 1993, 36, 593. For reviews see: (d) Shusharina, N. F. *Russ. Chem. Rev.* 1974, 43, 551. (e) Katsikis, A. R.; Dennis, N. *Chem. Rev.* 1989, 89, 827.  
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 (7) Breitwieser, E.; Voelter, W. *Carbon-13 NMR Spectroscopy*, 3rd ed.; VCH: Weinheim, FDR, 1987; pp 256–257.  
 (8) Posner, G. H.; Nelson, T. D.; Kintor, C. M.; Johnson, N. *J. Org. Chem.* 1992, 57, accompanying article for a review of cycloadditions of 2-pyrones and 2-pyridones, see: Afaninka, K.; Vinader, V.; Nelson, T. D.; Posner, G. H. *Tetrahedron Rep.*, in press.

Table I. <sup>13</sup>C NMR Chemical Shift Data

| Y                                | <sup>13</sup> C (ppm) | <sup>13</sup> C (ppm) |
|----------------------------------|-----------------------|-----------------------|
| ArSO <sub>2</sub> <sup>-</sup>   | 138.0 <sup>a</sup>    | 139.6 <sup>b</sup>    |
| H <sup>-</sup>                   | 131.7                 | 128.6                 |
| Br <sup>-</sup>                  | 131.3                 | 127.0                 |
| ArS <sup>-</sup>                 | 126.2 <sup>a</sup>    | 128.9 <sup>b</sup>    |
| RM <sub>2</sub> SiO <sup>-</sup> | 123.0 <sup>a</sup>    | 121.4 <sup>d</sup>    |
| PhCH <sub>2</sub> O <sup>-</sup> | 123.0                 |                       |
| MeO <sup>-</sup>                 | 122.4                 | 120.7                 |

<sup>a</sup>Ar = Tol. <sup>b</sup>Ar = Ph. <sup>c</sup>R = t-Bu. <sup>d</sup>R = Me.

Table II. Yields (%) of Cycloadduct 2 According to eq 1

| Y                          | EWG               |       |                      |        |
|----------------------------|-------------------|-------|----------------------|--------|
|                            | NO <sub>2</sub> g | CHO h | CO <sub>2</sub> Me i | COMe j |
| a, MeO                     | 80                | 69    | 57                   | 42     |
| b, PhCH <sub>2</sub> O     | 78                | 88    | trace                |        |
| c, t-BuMe <sub>2</sub> SiO | 69                | 70    | 23                   | 56     |
| d, TolS                    | 45                | 42    | trace                |        |

Table II summarizes results of the successful cycloadditions according to eq 1 in which butylated hydroxytoluene (BHT) was used to retard polymerization of the electrophilic alkenes in all cases except with nitroethylene. In every case, bicyclic lactam 2 was formed *exclusively* with the regiochemistry and the stereochemistry shown as determined by 400-MHz <sup>1</sup>H NMR spectroscopy of the crude reaction products. Both regiochemistry and stereochemistry were established in analogy with excellent literature precedent<sup>1,9</sup> by <sup>1</sup>H NMR spectroscopy showing a 4,6-disubstituted (but not a 4,6-disubstituted) bicyclic lactam with *J*<sub>1,2</sub> larger than *J*<sub>1,6</sub> and *J*<sub>5,6</sub> larger than *J*<sub>5,8</sub>. <sup>1</sup>H NMR data for nitro lactam methyl ether 2ag are shown here (in which the nitro group is endo to the 2-carbon olefinic bridge). Furthermore, exposure of this nitro-substituted bicyclic lactam to ammonium formate produced *exclusively* and quantitatively the epimeric nitro compound (*epi*-2ag) with the <sup>1</sup>H NMR characteristics shown. Note that *J*<sub>5,6</sub> is smaller than *J*<sub>5,8</sub> in the epimerized *epi*-2ag. Analogous results and NMR data were obtained also with bicyclic nitro-bearing benzoyloxy lactam 2hg and tolythio lactam 2dg (see Experimental Section). No rationale is obvious at present to explain the unidirectional epimerization of the initially formed *endo*-nitro cycloadducts 2ag, 2hg, and 2dg into the corresponding *exo* epimers. Interestingly, simply on standing at ambient temperature in CDCl<sub>3</sub> for 17 days, *endo*-nitro-substituted bicyclic lactam 2ag underwent clean and almost complete epimerization into *epi*-2ag.<sup>10</sup>

To examine what effect, if any, a smaller-sized but less electron-withdrawing 1-sulfonyl group would have on the cycloadditions, 1-mesyl-3-methoxy-2-pyridone was prepared in the same way as the corresponding 1-tosyl derivative. 1-Mesyl-3-methoxy-2-pyridone, however, underwent an N → O mesyl shift (50% complete) at 90–100 °C for 40 h, whereas the corresponding 1-tosyl system did not rearrange significantly (i.e., <5%) under these conditions.<sup>11</sup> A competition experiment between equimolar

- (8) (a) Hayano, K.; Aoki, T.; Eto, M.; Nishino, T. *Chem. Pharm. Bull.* 1990, 38, 1182. (b) Herdels, C.; Hartke-Karger, C. *Liebigs Ann. Chem.* 1991, 99. (c) Shusharina, N. F.; Filipenko, V. S.; Kiseeva, O. K.; Gellar, B. I.; Stepanovskaya, A. U. *J. Org. Chem. USSR* 1980, 16, 2047.  
 (9) (a) Abramovitch, R. A.; Knatta, G. N. *J. Org. Chem.* 1975, 40, 883. See also: (b) Hazen, M.; Lira, E. P. *J. Heterocycl. Chem.* 1972, 9, 215.  
 (10) See also: *Pyridine and Its Derivatives*, Abramovitch, R. A., Ed.; Interscience: New York, 1974; Supplement part III, p 744.

1000-1000

1000-1000

TABLE I

| Compound | Yield, % | mp, °C |
|----------|----------|--------|
| 1        | 75       | 105    |
| 2        | 65       | 115    |
| 3        | 55       | 125    |
| 4        | 45       | 135    |
| 5        | 35       | 145    |
| 6        | 25       | 155    |

TABLE II

| Compound | Yield, % | mp, °C |
|----------|----------|--------|
| 7        | 70       | 100    |
| 8        | 60       | 110    |
| 9        | 50       | 120    |
| 10       | 40       | 130    |
| 11       | 30       | 140    |
| 12       | 20       | 150    |

The following table shows the results of the experiments conducted in the laboratory of the American Chemical Society. The data are presented in two tables, Table I and Table II, which show the yields and melting points of the various compounds obtained. The compounds are numbered 1 through 12, and the yields are given in percentages. The melting points are given in degrees Celsius. The data are as follows:

Table I:

| Compound | Yield, % | mp, °C |
|----------|----------|--------|
| 1        | 75       | 105    |
| 2        | 65       | 115    |
| 3        | 55       | 125    |
| 4        | 45       | 135    |
| 5        | 35       | 145    |
| 6        | 25       | 155    |

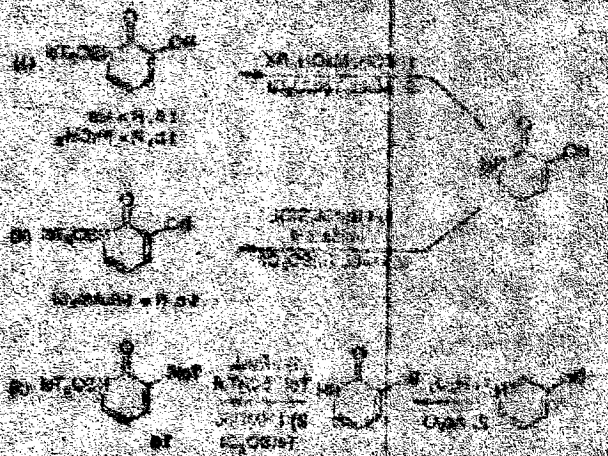
Table II:

| Compound | Yield, % | mp, °C |
|----------|----------|--------|
| 7        | 70       | 100    |
| 8        | 60       | 110    |
| 9        | 50       | 120    |
| 10       | 40       | 130    |
| 11       | 30       | 140    |
| 12       | 20       | 150    |

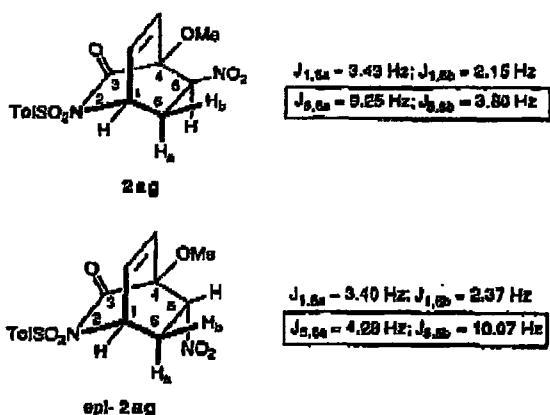
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The following table shows the results of the experiments conducted in the laboratory of the American Chemical Society. The data are presented in two tables, Table I and Table II, which show the yields and melting points of the various compounds obtained. The compounds are numbered 1 through 12, and the yields are given in percentages. The melting points are given in degrees Celsius. The data are as follows:

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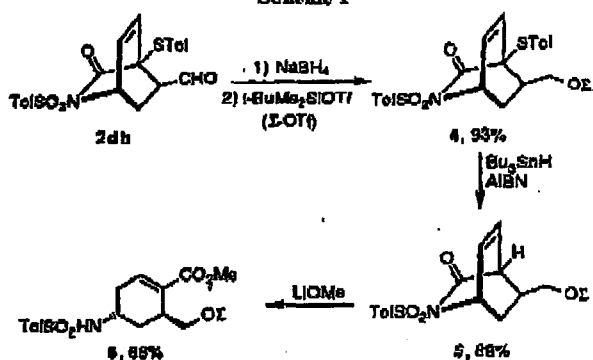
amounts of 1-mesyl- and 1-tosyl-3-methoxy-2-pyridone with excess methyl vinyl ketone showed a 1.5:1 selectivity for 1-mesyl-2-pyridone cycloaddition over 1-tosyl-2-pyridone cycloaddition; this small rate advantage in cycloaddition, however, was substantially outweighed by the large  $N \rightarrow O$  rearrangement rate disadvantage using the 1-mesyl-2-pyridone. Rearrangement of the tosyl group from  $N \rightarrow O$  was even more prominent in 3-unsubstituted 1-tosyl-2-pyridone; for example, at 188 °C for 21 h, 1-tosyl-2-pyridone rearranged 73% to 2-(tosyloxy)pyridine whereas under these conditions 3-methoxy-1-tosyl-2-pyridone (1a) rearranged only 27% to 3-methoxy-2-(tosyloxy)pyridine. Even more striking was the absence of any  $N \rightarrow O$  rearrangement when 3-(tolylthio)- and 3-siloxy-1-tosyl-2-pyridones 1d and 1e were subjected to similar reaction conditions. Thus, a large 3-substituent effectively inhibits  $N \rightarrow O$  tosyl migration in 1-tosyl-2-pyridones. In comparison,  $N$ -acyl-2-pyridones have been reported to undergo rapid  $N \rightarrow O$  rearrangement into 2-acyloxy pyridines even at room temperature.<sup>11</sup>

A separate study of steric and electronic effects on cycloaddition rate was done comparing 3-methoxy- with 3-siloxy-1-tosyl-2-pyridones 1a and 1e. Equimolar amounts of these pyridones reacted at roughly equal rates with an excess of methyl acrylate and separately with an excess of methyl vinyl ketone at 90–100 °C as judged by <sup>1</sup>H NMR determination of the ratios of remaining reactant pyridones as well as ratios of cycloadducts. Interestingly, a similar competition experiment comparing 3-methoxy- with 3-(tolylthio)-2-pyridones 1a with 1d showed 3-(tolylthio)-2-pyridone 1d to react about 1.5 times faster than 3-methoxy-2-pyridone 1a with acrolein. Finally, unlike reactive 3-(tolylthio)pyridone 1d, 3-bromo-1-tosyl-2-pyridone was quite unreactive toward electrophilic acrolein.

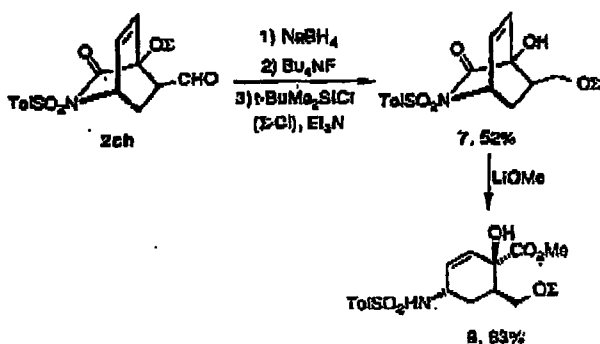
Several electron-poor alkenes failed to cycloadd with one or more of the 2-pyridones 1a–1d even upon prolonged heating at 90–100 °C or, in a few cases, even at 130 °C. Examples of such unreactive alkenes include acrylonitrile, 2-chloroacrylonitrile, phenyl vinyl sulfone,  $\alpha$ -methylene- $\gamma$ -butyrolactone, vinyltriphenylphosphonium bromide, diethyl methylenemalonate, 3,3-dimethylacrolein, and maleic anhydride. Also unreactive were 2-pyridones lacking either a 1-tosyl group or a 3-heteroatom substituent; for example, 1-methyl-3-(tolylthio)-2-pyridone failed to cycloadd with methacrolein whereas the corresponding captodative 1-tosyl-3-(tolylthio)-2-pyridone (1d) did react (eq 2), and 1-tosyl-2-pyridone failed to cycloadd with

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Scheme I



Scheme II



acrolein whereas the corresponding captodative 1-tosyl-3-(tolylthio)-2-pyridone (1d) did react. Even at high pressures (10–11 Kbar)<sup>12</sup> for several days at ambient temperature, 3-(tolylthio)-2-pyridone 1d failed to cycloadd to  $\alpha$ -methylene- $\gamma$ -butyrolactone, and likewise 3-(benzylthio)-2-pyridone 1b failed to cycloadd to methyl acrylate.

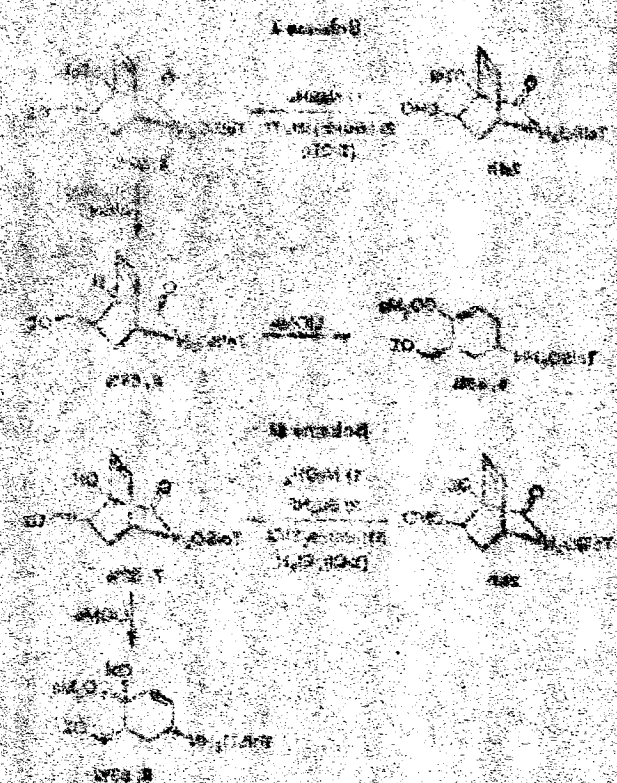
1-Tosyl-3-heteroatom-2-pyridones 1a–1d can be considered as captodative dienes in which C<sub>3</sub> is geminally substituted by an electron-donor heteroatom and also an electron-withdrawing carbonyl (amide) group.<sup>13</sup> The successful 2 + 4-cycloadditions shown in Table II, along with those reported in the accompanying 2-pyrone article,<sup>7</sup> represent the first examples of captodative unsaturated ethers and thioethers acting as enophiles.<sup>13</sup>

To illustrate the high value and versatility of these bicyclic lactams, formed as single regioisomers and exclusively as endo-diastereomers, several ring-opening transformations were performed. Bicyclic lactam aldehyde 2dh was reduced and O-silylated to form bicyclic lactam 4 (Scheme I). Reductive removal of the bridgehead tollythio group under neutral radical conditions was achieved smoothly using tributyltin hydride and azobisisobutyronitrile (AIBN) to form bridgehead-unsubstituted bicyclic lactam 5; this lactam represents a formal regioselective cycloaddition of  $N$ -tosyl-2-pyridone itself to acrolein, a reaction that cannot be achieved thermally because  $N \rightarrow O$  tosyl migration occurs prior to any possible cycloaddition. Thus, 3-(tolylthio)- $N$ -tosyl-2-pyridone (1d) is a highly reactive synthetic equivalent of  $N$ -tosyl-2-pyridone in thermal (i.e., not high-pressure) Diels-Alder

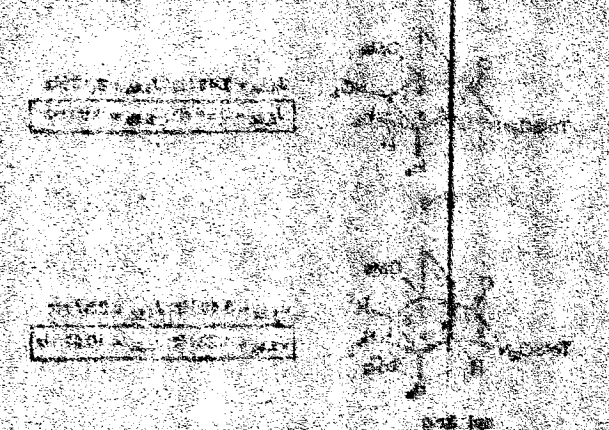
(11) (a) McKillop, A.; Zalesko, M.-T.; Taylor, E. C. *Tetrahedron Lett.* 1988, 4945. See also: (b) Singh, P. A.; Jonsson, M. J. *Ibid.* 1971, 4223. (c) See ref 10c, pp 776–784.

(12) (a) Vieho, H. G.; Janousek, Z.; Merényi, F.; Stella, L. *Acc. Chem. Res.* 1985, 18, 145. (b) Røyer, A.; Aguilera, R.; Muñoz, A. A.; Zwick, J.-C.; Rubio, M.; Escher, J.-L.; Soriano, M.; Toscano, R.; Tomariz, R. *J. Org. Chem.* 1990, 55, 1024.

(13) For an excellent review with leading references, see: De Lucchi, O.; Pasquato, L. *Tetrahedron* 1988, 44, 6755.

[illegible][illegible]

1. The first step is to identify the problem or question that needs to be answered. This involves understanding the context and the specific requirements of the task.



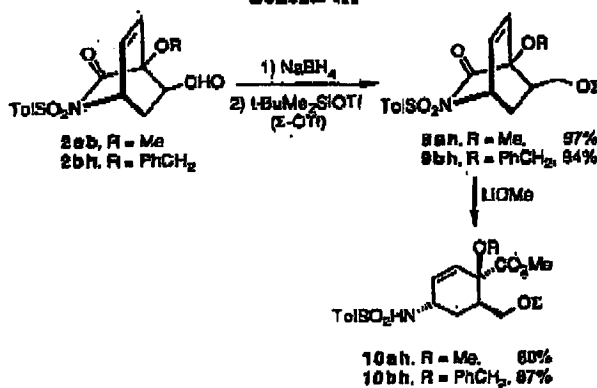
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The first of these is the fact that the  
 data were not collected in a random  
 manner. The data were collected in a  
 manner that was biased in favor of  
 the hypothesis being tested. This is a  
 serious flaw in the study because it  
 introduces a systematic error into the  
 results. The second flaw is that the  
 sample size was too small to detect  
 the effect being tested. The third flaw  
 is that the study did not control for  
 confounding variables. The fourth flaw  
 is that the study did not use a  
 double-blind design. The fifth flaw  
 is that the study did not use a  
 placebo control group. The sixth flaw  
 is that the study did not use a  
 random assignment procedure. The  
 seventh flaw is that the study did  
 not use a standardized protocol. The  
 eighth flaw is that the study did not  
 use a validated measurement instrument.  
 The ninth flaw is that the study did  
 not use a trained research assistant.  
 The tenth flaw is that the study did  
 not use a data management system.  
 The eleventh flaw is that the study  
 did not use a statistical software package.  
 The twelfth flaw is that the study  
 did not use a peer-reviewed journal.  
 The thirteenth flaw is that the study  
 did not use a registered clinical trial.  
 The fourteenth flaw is that the study  
 did not use a pre-registered protocol.  
 The fifteenth flaw is that the study  
 did not use a data sharing policy.  
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Cycloadditions Using 2-Pyridones

Scheme III



cycloadditions with acrolein. Methanolysis of the lactam bridge converted 5 into regioselectively and stereospecifically substituted cyclohexene 6 that we are currently converting into a 1 $\alpha$ -(hydroxymethyl)-3 $\beta$ -amino vitamin D<sub>3</sub> derivative for biological evaluation.<sup>14</sup>

In a similar fashion (Scheme II), bicyclic lactam aldehyde silyl ether 2ah was reduced, desilylated, and protected selectively as the primary alcohol silyl ether 7 using *tert*-butyldimethylsilyl chloride/4-(dimethylamino)pyridine (DMAP). Methanolysis of the lactam bridge produced regioselectively and stereospecifically tetrasubstituted cyclohexene 8. All attempts to deoxygenate tertiary alcohols 7 and 8 were unsuccessful, including, for example, radical reaction of the xanthate derived from bicyclic tertiary alcohol 7. Likewise, bicyclic tertiary alcohol ethers 9ah and 9bh were prepared according to Scheme III. Methanolysis of the bicyclic lactam bridge gave tetrasubstituted cyclohexenes 10ah and 10bh as single diastereomers. All attempts to deoxygenate tertiary alcohol ethers 9 and 10 were unsuccessful, including LiAlH<sub>4</sub>/TiCl<sub>4</sub>,<sup>15</sup> Zn/NH<sub>4</sub>Cl,<sup>16</sup> LiBH<sub>4</sub>,<sup>17</sup> LiEt<sub>3</sub>Al,<sup>18</sup> and HCOONH<sub>4</sub> using a palladium catalyst.<sup>19</sup>

Conclusion

1-Tosyl-3-heteroatom-2-pyridones 1a–1d have been shown for the first time to be reactive captodative dienes that undergo effective thermal 2 + 4-cycloadditions with several unencumbered electron-poor alkenes. Reaction conditions are sufficiently mild so that the bicyclic lactam adducts can be isolated on gram scale in fair to very good yields without loss of an isocyanate from the lactam bridge. These bicycloadducts, formed as single regioisomers and exclusively as endo diastereomers, represent easily prepared, compact, and polyfunctional synthetic intermediates of considerable value.

Experimental Section

General Experimental Data. See ref 7 for details.

A. Preparation of Pyridones. 3-Methoxy-1-(4'-methylbenzenesulfonyl)-2-pyridone (1a). To a stirred solution of

3-methoxy-2-pyridone (165 mg, 1.32 mmol) in dry THF (10 mL), maintained at 0 °C under a dry nitrogen atmosphere, was added MeLi (1.4 M solution in Et<sub>2</sub>O, 1.0 mL, 1.4 mmol). After 20 min, 4-methylbenzenesulfonyl chloride (255 mg, 1.34 mmol) was added as a THF solution (15 mL). After 16 h the solution was poured into water (50 mL) and was extracted with Et<sub>2</sub>O (2 × 100 mL). Drying (Na<sub>2</sub>SO<sub>4</sub>) followed by evaporation of solvent under reduced pressure and flash chromatography (silica gel, Et<sub>2</sub>O) of the residue afforded white solid 1a (285 mg, 78%); mp 146–147 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  2.42 (3 H, s, CH<sub>3</sub>Ar), 3.73 (3 H, s, CH<sub>3</sub>O), 6.18 (1 H, t, *J*<sub>5-6</sub> = *J*<sub>4-5</sub> = 7.4 Hz, pyridone H-5), 6.51 (1 H, dd, *J*<sub>4-5</sub> = 7.4 Hz, *J*<sub>4-3</sub> = 1.0 Hz, pyridone H-4), 7.32 (2 H, d, *J* = 7.9 Hz, tosyl H-3), 7.73 (1 H, dd, *J*<sub>4-5</sub> = 7.4 Hz, *J*<sub>4-3</sub> = 1.0 Hz, pyridone H-6), 8.02 (2 H, d, *J* = 7.9 Hz, tosyl H-2); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  21.51 (CH<sub>3</sub>Ar), 58.20 (CH<sub>3</sub>O), 108.29 (C-5), 112.52 (C-4), 122.36 (C-6), 129.49 (C-2'), 130.11 (C-3'), 133.35 (C-1'), 146.21 (C-3), 150.94 (C-4'), 168.20 (C-2); IR (CHCl<sub>3</sub>) 1673 (C=O), 1620 cm<sup>-1</sup>; MS *m/z* (EI) 279 (M<sup>+</sup>, 13), 215 (39), 214 (20), 124 (27), 96 (26), 82 (22), 91 (100), 65 (24); *m/z* (CI/ammonia) 250 (MH<sup>+</sup>, 100). Anal. Calcd for C<sub>12</sub>H<sub>11</sub>NO<sub>3</sub>S: C, 55.60; H, 4.68; N, 5.01. Found: C, 55.28; H, 4.72; N, 5.00.

1-(4'-Methylbenzenesulfonyl)-2-(phenylmethoxy)-2-pyridone (1b). This compound was prepared in accord with the general procedure described above. Thus, starting from a solution of 3-(benzyloxy)-2-pyridone<sup>20</sup> (1.29 g, 6.41 mmol) in dry THF (75 mL) and using lithium hexamethyldisilazide (LHMDS) (1.0 M solution in hexane, 9.61 mL, 9.61 mmol) and 4-methylbenzenesulfonyl chloride (2.44 g, 12.82 mmol) we obtained after crystallization (CH<sub>2</sub>Cl<sub>2</sub>/Et<sub>2</sub>O (1:2) v/v) white solid 1b (1.72 g, 76%); mp 160–161 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  2.48 (3 H, s, CH<sub>3</sub>Ar), 5.00 (2 H, s, OCH<sub>2</sub>), 6.11 (1 H, t, *J*<sub>5-6</sub> = *J*<sub>4-5</sub> = 7.41 Hz, H-5), 6.55 (1 H, dd, *J*<sub>4-5</sub> = 7.41 Hz, *J*<sub>4-3</sub> = 1.56 Hz, H-4), 7.31–7.34 (7 H, m, H-Ar), 7.72 (1 H, dd, *J*<sub>4-5</sub> = 7.41 Hz, *J*<sub>4-3</sub> = 1.56 Hz, H-6), 8.02 (2 H, d, *J*<sub>3-2</sub> = 8.46 Hz, H-2' and H-6'); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  21.90 (CH<sub>3</sub>Ar), 71.14 (OCH<sub>2</sub>), 105.23 (C-5), 115.33 (C-4), 122.97 (C-6), 127.62, 128.33, 128.72, 129.81, 130.19, 133.45, 135.57, 146.24, 149.86 (C-2); IR (CHCl<sub>3</sub>) 1672 (C=O), 1619 cm<sup>-1</sup>; MS *m/z* (EI) 355 (M<sup>+</sup>, 2), 201 (5), 200 (33), 185 (6), 91 (100), 65 (8); HRMS calcd for C<sub>17</sub>H<sub>15</sub>NO<sub>3</sub>S (M<sup>+</sup>) 355.0578, found 355.0582.

8-[(*tert*-Butyldimethylsilyl)oxy]-2-pyridone. A solution of *tert*-butyldimethylsilyl chloride (TBDMSCl) (305 mg, 2.02 mmol) in anhydrous dimethylformamide (DMF) (5 mL) was delivered to a stirred mixture of 2,3-dihydropyridine (220 mg, 2.00 mmol) and imidazole (340 mg, 5.00 mmol) maintained under a dry nitrogen atmosphere. After 3 h, the mixture was poured into H<sub>2</sub>O (10 mL) and was extracted with Et<sub>2</sub>O (2 × 75 mL). The combined ethereal extracts were washed with water (10 mL) and dried over Na<sub>2</sub>SO<sub>4</sub>. Evaporation of solvent afforded a pale brown solid (435 mg, 67%). The crude product can be used directly for the next step; however, an analytically pure sample may be prepared by crystallization (Et<sub>2</sub>O/hexane (1:10) v/v) as a white solid; mp 117 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  0.25 (8 H, s, CH<sub>3</sub>Si), 0.89 (9 H, s, (CH<sub>3</sub>)<sub>3</sub>Si), 1.86 (1 H, br, NH), 6.13 (1 H, t, *J*<sub>5-6</sub> = *J*<sub>4-5</sub> = 7 Hz, H-5), 6.59 (1 H, dd, *J*<sub>4-5</sub> = 7.0 Hz, *J*<sub>4-3</sub> = 1.7 Hz, H-4), 6.97 (1 H, dd, *J*<sub>4-5</sub> = 7.0 Hz, *J*<sub>4-3</sub> = 1.7 Hz, H-6); IR (CHCl<sub>3</sub>) 1659 (C=O), 1621 cm<sup>-1</sup>; MS *m/z* (CI/ammonia) 228 (5), 227 (17), 228 (MH<sup>+</sup>, 100), 189 (M<sup>+</sup> - *t*-Bu, 19), 129 (4), 118 (3), 112 (62). Anal. Calcd for C<sub>11</sub>H<sub>13</sub>NO<sub>2</sub>Si: C, 58.63; H, 8.50; N, 6.22. Found: C, 58.47; H, 8.52; N, 6.17.

8-[(*tert*-Butyldimethylsilyl)oxy]-1-(4'-methylbenzenesulfonyl)-2-pyridone (1c). This compound was prepared in accord with the general procedure described previously. Thus, starting from a solution of 8-[(*tert*-butyldimethylsilyl)oxy]-2-pyridone (4.66 g, 20.7 mmol) in dry Et<sub>2</sub>O (150 mL) and using MeLi (1.4 M solution in Et<sub>2</sub>O, 15.0 mL, 21.0 mmol) and 4-methylbenzenesulfonyl chloride (3.95 g, 20.7 mmol) we obtained after chromatography (silica gel, 10% v/v Et<sub>2</sub>O in hexane) white solid 1c (7.05 g, 80%); mp 78–79 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  0.11 (8 H, s, CH<sub>3</sub>Si), 0.90 (9 H, s, (CH<sub>3</sub>)<sub>3</sub>Si), 2.43 (3 H, s, CH<sub>3</sub>Ar), 6.09 (1 H, t, *J*<sub>5-6</sub> = *J*<sub>4-5</sub> = 7.3 Hz, pyridone H-5), 6.87 (1 H, dd, *J*<sub>4-5</sub> = 7.3 Hz, *J*<sub>4-3</sub> = 1.7 Hz, pyridone H-4), 7.32 (2 H, d, *J* = 8.4 Hz, tosyl H-3'), 7.73 (1 H, dd, *J*<sub>4-5</sub> = 7.3 Hz, *J*<sub>4-3</sub> = 1.7 Hz, pyridone H-6), 7.98 (2 H, d, *J* = 7.9 Hz, tosyl H-2'); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$

(14) For related work, see: Pomeroy, G. H.; Nelson, T. D.; Guyton, K. Z.; Kanalar, T. W. *J. Med. Chem.*, in press.

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1. The Great Wall of China is a long wall built across the country.

The Great Wall of China is a long wall built across the country. It is one of the most famous landmarks in the world. The wall was built by the Chinese people over many centuries. It is made of stone and brick. The wall is very long and goes through mountains and rivers. It is a symbol of the strength and power of the Chinese people.

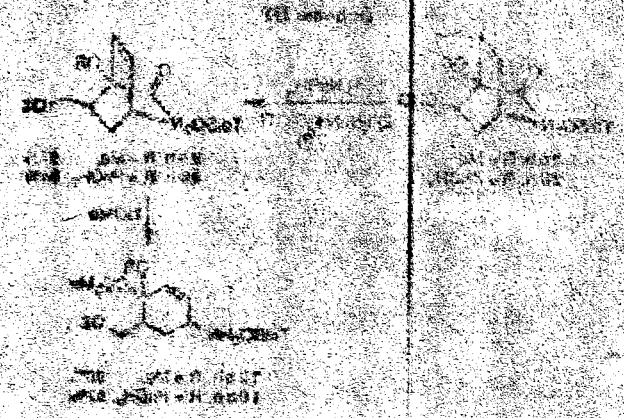
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2. The Great Wall of China is a long wall built across the country.



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Conclusion

The Great Wall of China is a long wall built across the country. It is one of the most famous landmarks in the world. The wall was built by the Chinese people over many centuries. It is made of stone and brick. The wall is very long and goes through mountains and rivers. It is a symbol of the strength and power of the Chinese people.

The Great Wall of China

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-4.59 (2 x CH<sub>3</sub>Si), 18.49 (Me<sub>2</sub>CSi), 21.78 (CH<sub>3</sub>Ar), 25.66 ((C-H<sub>3</sub>)<sub>2</sub>CSi), 105.59 (C-5), 122.39 (C-4), 128.91 (C-8), 129.45 (C-2), 129.77 (C-3), 133.67 (C-1'), 145.97 (C-3), 147.45 (C-4'), 167.90 (C-1); IR (CHCl<sub>3</sub>) 1674 (C=O), 1820 cm<sup>-1</sup>; MS *m/e* (EI) 323 (21), 322 (M<sup>+</sup> - *t*-Bu, 100), 167 (28), 155 (91), 152 (27), 91 (100), 73 (25); *m/e* (CI/ammonia) 380 (M<sup>+</sup>, 100); HRMS calcd for C<sub>14</sub>H<sub>16</sub>N<sub>2</sub>O<sub>2</sub>Si (M<sup>+</sup> - *t*-Bu) 322.0570, found 322.0576.

**3-(4'-Methylbenzenesulfonyl)-1-(4'-methylbenzenesulfonyl)-2-pyridone (1d).** This compound was prepared in accord with the general procedure described above. Thus, starting from a solution of 3-(4-methylbenzenesulfonyl)-2-pyridone<sup>1</sup> (432 mg, 1.99 mmol) in dry THF (20 mL) and using LHMDS (1.0 M solution in hexane, 2.45 mL, 2.45 mmol) and 4-methylbenzenesulfonyl chloride (575 mg, 3.02 mmol) we obtained after crystallization (CH<sub>2</sub>Cl<sub>2</sub>/Et<sub>2</sub>O (1:2) v/v) pale yellow solid 1d (516 mg, 70%); mp 165-166 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 2.37 (3 H, s, CH<sub>3</sub>-C4'), 2.44 (3 H, s, CH<sub>3</sub>-C4'), 6.06 (1 H, t, *J*<sub>4-5</sub> = *J*<sub>5-6</sub> = 7.19 Hz, H-6), 6.46 (1 H, dd, *J*<sub>4-5</sub> = 7.19 Hz, *J*<sub>5-6</sub> = 1.85 Hz, H-4), 7.19 (2 H, d, *J*<sub>7-8</sub> = 7.49 Hz, H-2' and H-8'), 7.38 (4 H, d, *J* = 7.93 Hz, H-3', H-5', H-3'', and H-5''), 7.66 (1 H, dd, *J*<sub>6-7</sub> = 7.19 Hz, *J*<sub>6-8</sub> = 1.85 Hz, H-6), 7.91 (2 H, d, *J*<sub>7-8</sub> = 8.48 Hz, H-2' and H-8'); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 21.43 (CH<sub>3</sub>-C4'), 21.94 (CH<sub>3</sub>-C4'), 106.56 (C-6), 125.21, 128.91 (C-8), 129.73, 130.13, 130.89, 132.62 (C-4), 133.53, 135.56, 137.34, 140.06 (C-3), 146.40, 158.08 (C-2); IR (CHCl<sub>3</sub>) 1660, 1601 cm<sup>-1</sup>; MS *m/e* (EI) 372 (M<sup>+</sup>, 11), 371 (M<sup>+</sup>, 45), 308 (12), 307 (51), 306 (23), 217 (19), 216 (100), 119 (66), 91 (51), 65 (21); HRMS calcd for C<sub>17</sub>H<sub>17</sub>N<sub>2</sub>O<sub>2</sub>S<sub>2</sub> (M<sup>+</sup>) 371.0650, found 371.0647.

**3-Methoxy-1-(methanesulfonyl)-2-pyridone.** This compound was prepared in accord with the general procedure described above. Thus, starting from a solution of 3-methoxy-2-pyridone (541 mg, 4.33 mmol) in dry THF (40 mL) using MeLi (1.0 M solution in Et<sub>2</sub>O, 5.00 mL, 5.0 mmol) and MeCl (0.5 mL, 6.5 mmol) we obtained after crystallization (Et<sub>2</sub>O) a white solid (802 mg, 91%); mp 125 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 3.55 (3 H, s, CH<sub>3</sub>SO<sub>2</sub>), 3.73 (3 H, s, CH<sub>3</sub>O), 6.16 (1 H, t, *J*<sub>4-5</sub> = *J*<sub>5-6</sub> = 7.4 Hz, pyridone H-6), 6.53 (1 H, d, *J*<sub>4-5</sub> = 7.4 Hz, pyridone H-4), 7.42 (1 H, d, *J*<sub>6-7</sub> = 7.4 Hz, pyridone H-8); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 41.77 (CH<sub>3</sub>SO<sub>2</sub>), 56.31 (CH<sub>3</sub>O), 105.53 (C-5), 113.21 (C-4), 121.86 (C-6), 150.71 (C-3), 157.19 (C-2); IR (CHCl<sub>3</sub>) 1671 (C=O), 1619 cm<sup>-1</sup>; MS *m/e* (EI) 203 (M<sup>+</sup>, 86), 125 (100), 124 (99), 109 (22), 96 (94), 85 (24), 82 (21), 55 (87), 54 (23); *m/e* (CI/ammonia) 221 (MNH<sup>+</sup>, 3), 206 (5), 205 (9), 204 (M<sup>+</sup>, 100), 126 (39), 125 (6), 96 (6). Anal. Calcd for C<sub>7</sub>H<sub>7</sub>NO<sub>3</sub>S: C, 41.37; H, 4.46; N, 6.82. Found: C, 41.44; H, 4.49; N, 6.86.

**3-[(*tert*-Butyldimethylsilyl)oxy]-1-(methanesulfonyl)-2-pyridone.** This compound was prepared in accord with the general procedure described above. Thus, starting from a solution of 3-[(*tert*-butyldimethylsilyl)oxy]-2-pyridone (1.89 g, 8.40 mmol) in dry Et<sub>2</sub>O (40 mL) using methyl lithium (1.4 M solution in Et<sub>2</sub>O, 7.00 mL, 9.8 mmol) and MeCl (1.00 mL, 12.9 mmol) we obtained after flash chromatography (silica gel, 20% v/v diethyl ether in hexane) a white solid (1.77 g, 70%); mp 56 °C dec; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 0.24 (9 H, s, CH<sub>3</sub>Si), 0.98 (9 H, s, (CH<sub>3</sub>)<sub>2</sub>CSi), 3.60 (3 H, s, CH<sub>3</sub>SO<sub>2</sub>), 6.14 (1 H, dd, *J*<sub>4-5</sub> = 7.4, *J*<sub>5-6</sub> = 7.2 Hz, pyridone H-6), 6.87 (1 H, dd, *J*<sub>4-5</sub> = 7.2 Hz, *J*<sub>5-6</sub> = 1.6 Hz, pyridone H-4), 7.52 (1 H, dd, *J*<sub>6-7</sub> = 7.4 Hz, *J*<sub>6-8</sub> = 1.6 Hz, pyridone H-8); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ -4.45 (2 x CH<sub>3</sub>Si), 18.89 (Me<sub>2</sub>CSi), 25.82 ((CH<sub>3</sub>)<sub>2</sub>CSi), 41.21 (CH<sub>3</sub>SO<sub>2</sub>), 123.71 (C-6), 125.02 (C-8), 130.27 (C-6), 139.28 (C-4), 142.98 (C-1); IR (CHCl<sub>3</sub>) 1667 (C=O), 1619 cm<sup>-1</sup>; MS *m/e* (EI) 248 (18), 169 (14), 168 (100), 167 (26), 162 (16), 111 (15), 75 (35), 73 (16); *m/e* (CI/ammonia) 305 (10), 304 (82), 207 (28), 192 (5), 191 (8), 190 (100), 168 (7), 112 (34); HRMS calcd for C<sub>17</sub>H<sub>23</sub>NO<sub>3</sub>Si (M<sup>+</sup> - *t*-Bu) 248.0268, found 248.0260.

**1-(Methanesulfonyl)-3-(4'-methylbenzenesulfonyl)-2-pyridone.** This compound was prepared in accord with the general procedure described above. Thus, starting from a solution of 3-(4-methylbenzenesulfonyl)-2-pyridone (500 mg, 2.3 mmol) in dry THF (20 mL) using LHMDS (1.0 M solution in hexane, 2.83 mL, 2.83 mmol) and MeCl (0.270 mL, 3.49 mmol) we obtained after crystallization (CH<sub>2</sub>Cl<sub>2</sub>/Et<sub>2</sub>O (1:2) v/v) a pale yellow solid (480 mg, 70%); mp 170-171 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 2.24 (3 H, s, CH<sub>3</sub>Ar), 3.50 (3 H, s, CH<sub>3</sub>SO<sub>2</sub>), 5.96 (1 H, t, *J*<sub>4-5</sub> = *J*<sub>5-6</sub> = 7.11 Hz, H-6), 6.48 (1 H, dd, *J*<sub>4-5</sub> = 7.11 Hz, *J*<sub>5-6</sub> = 1.52 Hz, H-4), 7.10 (1 H, d, *J*<sub>7-8</sub> = 8.19 Hz, H-2', H-8'), 7.28 (2 H, d, *J*<sub>7-8</sub> = 8.19 Hz, H-3', H-5'), 7.50 (1 H, dd, *J*<sub>6-7</sub> = 7.11 Hz, *J*<sub>6-8</sub> = 1.62 Hz, H-6); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 21.46 (CH<sub>3</sub>-C4'), 42.19 (CH<sub>3</sub>SO<sub>2</sub>), 106.83 (C-5),

125.97, 126.40 (C-6), 131.00, 133.45 (C-4), 135.55, 137.15, 140.22 (C-3), 158.00 (C-2); IR (CHCl<sub>3</sub>) 1654 (C=O), 1595 cm<sup>-1</sup>; MS *m/e* (EI) 295 (M<sup>+</sup>, 29), 218 (13), 217 (100), 216 (64), 184 (17), 119 (17), 91 (12), 48 (70); HRMS calcd for C<sub>15</sub>H<sub>15</sub>N<sub>2</sub>O<sub>2</sub>S<sub>2</sub> (M<sup>+</sup>) 295.0337, found 295.0341.

**B. Thermal Rearrangement of Pyridones.** Typical Procedure. The corresponding pyridones were dissolved in CH<sub>2</sub>Cl<sub>2</sub> and the solutions were heated in a sealed hydrolysis tube at 90-100 °C. Periodically, the tube was cooled and the solvent was removed. Ratios of pyridones/pyridinols were determined on the basis of the <sup>1</sup>H NMR spectra of the crude materials. The residues were then redissolved and subjected to heat again. At the end of the experiment the rearranged products were separated by preparative thin-layer chromatography (TLC) and characterized as follows.

**2-[(4'-Methylbenzenesulfonyl)oxy]pyridine:** gum; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 2.45 (3 H, s, CH<sub>3</sub>Ar), 7.17 (1 H, d, *J*<sub>4-5</sub> = 8.1 Hz, *J*<sub>5-6</sub> = 0.9 Hz, pyridine H-3), 7.21 (1 H, ddd, *J*<sub>4-5</sub> = 8.4 Hz, *J*<sub>5-6</sub> = 5.0 Hz, *J*<sub>6-7</sub> = 0.9 Hz, pyridine H-5), 7.34 (2 H, d, *J* = 8.0 Hz, tosyl H-3'), 7.77 (1 H, ddd, *J*<sub>7-8</sub> = 8.1 Hz, *J*<sub>6-7</sub> = 5.4 Hz, *J*<sub>6-8</sub> = 2.0 Hz, pyridine H-4), 7.89 (2 H, d, *J* = 8.0 Hz, tosyl H-2'), 8.26 (1 H, dd, *J*<sub>6-7</sub> = 6.0 Hz, *J*<sub>6-8</sub> = 2.0 Hz, pyridine H-6); IR (CHCl<sub>3</sub>) 1692, 1672, 1170 cm<sup>-1</sup>; MS *m/e* (EI) 196 (7), 185 (65), 184 (41), 187 (26), 92 (6), 91 (100), 65 (27), 49 (7) and 51 (7); *m/e* (CI/ammonia) 260 (100); HRMS calcd for C<sub>11</sub>H<sub>11</sub>NO (M<sup>+</sup> - SO<sub>2</sub>) 185.0837, found 185.0841.

**3-Methoxy-2-[(4'-methylbenzenesulfonyl)oxy]pyridine:** mp 61-62 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 2.49 (3 H, s, CH<sub>3</sub>Ar), 3.85 (3 H, s, CH<sub>3</sub>O), 7.20 (1 H, dd, *J* = 8.2 Hz, 4.6 Hz, pyridine H-5), 7.27 (1 H, dd, *J* = 8.2, 1.6 Hz, pyridine H-4), 7.34 (2 H, d, *J* = 8.3 Hz, tosyl H-3'), 7.82 (1 H, dd, *J* = 4.8, 1.6 Hz, pyridine H-6), 7.94 (2 H, d, *J* = 8.3 Hz, tosyl H-2'); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 21.69 (CH<sub>3</sub>Ar), 55.93 (CH<sub>3</sub>O), 120.88 (C-4), 123.59 (C-6), 125.59 (C-2), 129.52 (C-3), 134.47 (C-1'), 138.14 (C-8), 144.86 (C-4'), 148.69 (C-3'), 147.09 (C-2'); IR (CHCl<sub>3</sub>) 1688, 1674, 1232, 1194, 1181 cm<sup>-1</sup>; MS *m/e* (EI) 270 (12), 215 (51), 214 (20), 124 (26), 96 (23), 92 (25), 91 (100), 65 (24); *m/e* (CI/ammonia) 230 (100); HRMS calcd for C<sub>15</sub>H<sub>15</sub>NO<sub>3</sub>S (M<sup>+</sup>) 270.0571, found 270.0565.

**3-Methoxy-2-[(methanesulfonyl)oxy]pyridine:** oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 3.49 (3 H, s, CH<sub>3</sub>SO<sub>2</sub>), 3.90 (3 H, s, CH<sub>3</sub>O), 7.25 (1 H, dd, *J* = 8.1, 4.7 Hz, pyridine H-5), 7.33 (1 H, dd, *J* = 8.1, 1.5 Hz, pyridine H-4), 7.88 (1 H, dd, *J* = 4.7, 1.5 Hz, pyridine H-6); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 40.86 (CH<sub>3</sub>SO<sub>2</sub>), 56.08 (CH<sub>3</sub>O), 121.23 (C-4), 123.77 (C-6), 137.32 (C-8), 146.86 (C-3), 147.90 (C-2); IR (film) 1674, 1229, 1153 cm<sup>-1</sup>; HRMS calcd for C<sub>7</sub>H<sub>7</sub>NO<sub>3</sub>S (M<sup>+</sup>) 203.0250, found 203.0254.

**3-[(*tert*-Butyldimethylsilyl)oxy]-2-[(methanesulfonyl)oxy]pyridine:** pale yellow liquid; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 0.26 (9 H, s, CH<sub>3</sub>Si), 1.03 (9 H, s, (CH<sub>3</sub>)<sub>2</sub>CSi), 3.50 (3 H, s, CH<sub>3</sub>SO<sub>2</sub>), 7.16 (1 H, dd, *J* = 8.0, 4.8 Hz, pyridine H-5), 7.29 (1 H, dd, *J* = 8.0, 1.6 Hz, pyridine H-4), 7.90 (1 H, dd, *J* = 4.8, 1.6 Hz, pyridine H-6); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ -4.45 (CH<sub>3</sub>Si), 18.33 ((CH<sub>3</sub>)<sub>2</sub>CSi), 25.62 ((CH<sub>3</sub>)<sub>2</sub>CSi), 41.21 (CH<sub>3</sub>SO<sub>2</sub>), 123.71 (C-4), 125.03 (C-6), 130.27 (C-6), 139.28 (C-2), 142.98 (C-3); IR (CHCl<sub>3</sub>) 1671, 1266, 1168 cm<sup>-1</sup>; MS *m/e* (EI) 248 (17), 210 (39), 189 (12), 168 (100), 167 (24), 162 (13), 73 (19); *m/e* (CI/ammonia) 306 (9), 305 (19), 304 (100), 228 (6), 189 (12), 112 (3), 102 (4), 96 (4).

**C. Cycloadditions of Pyridones.** **4-Methoxy-2-(4'-methylbenzenesulfonyl)-5-endo-nitro-3-oxo-2-azabicyclo[2.2.2]oct-7-ene (2ag).** Nitroethylenes<sup>21</sup> (196 mg and 190 mg after 48 h) was added to a solution of 1a (150 mg, 0.537 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (2.5 mL) in a sealed tube and was heated at 90 °C for 5 days. Chromatography (silica gel, Et<sub>2</sub>O) afforded 2ag as a white solid (151 mg, 80%); mp 155-156 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 2.21 (1 H, ddd, *J*<sub>1-2</sub> = 13.95 Hz, *J*<sub>1-3</sub> = 3.86 Hz, *J*<sub>2-3</sub> = 2.15 Hz, H-6<sub>endo</sub>), 2.44 (3 H, s, CH<sub>3</sub>Ar), 2.75 (1 H, ddd, *J*<sub>1-2</sub> = 13.98 Hz, *J*<sub>1-3</sub> = 2.25 Hz, *J*<sub>2-3</sub> = 3.45 Hz, H-6<sub>exo</sub>), 3.65 (3 H, s, CH<sub>3</sub>O), 6.02 (1 H, ddd, *J*<sub>4-5</sub> = 9.25 Hz, *J*<sub>4-6</sub> = 3.88 Hz, *J*<sub>5-6</sub> = 1.26 Hz, H-5), 8.41 (1 H, m, H-1), 8.31 (1 H, dd, *J*<sub>7-8</sub> = 8.15 Hz, *J*<sub>6-7</sub> = 1.50 Hz, H-8), 6.89 (1 H, dd, *J*<sub>7-8</sub> = 8.13 Hz, *J*<sub>7-9</sub> = 6.12 Hz, H-7), 7.33 (2 H, d, *J*<sub>7-8</sub> = 8.43 Hz, H-3' and H-5'), 7.84 (2 H, d, *J*<sub>7-8</sub> = 8.43 Hz, H-2' and H-8'); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 21.09 (CH<sub>3</sub>Ar), 35.47 (C-6), 51.68 (OCH<sub>3</sub>), 55.05 (C-1), 78.67 (C-5), 84.00 (C-4), 123.13, 129.85, 130.04, 130.13 (C-9), 132.14 (C-7), 146.06, 169.00 (C=O); IR

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(CHCl<sub>3</sub>) 1736, 1660, 1366, 1172 cm<sup>-1</sup>; MS *m/e* (EI) 155 (2), 110 (7), 109 (100), 91 (16), 77 (9); (CI/ammonia) 370 (MNH<sup>+</sup>, 100), 353 (MH<sup>+</sup>, 84); HRMS calcd for C<sub>17</sub>H<sub>15</sub>N<sub>2</sub>O<sub>5</sub>S (MH<sup>+</sup>) 353.0807, found 353.0800.

**4-Methoxy-2-(4'-methylbenzenesulfonyl)-3-oxo-2-azabicyclo[2.2.2]oct-7-ene-5-endo-carboxaldehyde (2ah).** A solution of acrolein (0.115 mL and 0.110 mL after 24 h) and pyridone 1a (48 mg, 0.172 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (0.5 mL) was heated in a sealed tube at 90 °C for 6 days. Removal of solvent followed by chromatography (silica gel, 25–50% Et<sub>2</sub>O in hexane) gave 2ah as a white solid (40 mg, 69%); mp 138 °C dec; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 2.11–2.14 (2 H, m, H-6), 2.44 (3 H, s, CH<sub>3</sub>Ar), 2.92 (1 H, m, H-5), 3.68 (3 H, s, OCH<sub>3</sub>), 5.39 (1 H, m, H-1), 6.38 (1 H, dd, *J* = 8.2 Hz, 1.4 Hz, H-8), 6.60 (1 H, dd, *J* = 8.2 Hz, 6.1 Hz, H-7), 7.32 (2 H, d, *J* = 8.2 Hz, tosyl H), 7.58 (2 H, d, *J* = 8.2 Hz, tosyl H), 9.65 (1 H, s, CHO); IR (CHCl<sub>3</sub>) 1728 (C=O), 1598 (C=C), 1188, 1173 cm<sup>-1</sup>; MS *m/e* (EI) 138 (96), 110 (12), 109 (100), 106 (29), 84 (16), 91 (37), 77 (17), 65 (22); *m/e* (CI/ammonia) 354 (MNH<sup>+</sup>, 19), 353 (100), 337 (19), 326 (MH<sup>+</sup>, 98), 280 (41), 182 (21), 138 (37), 126 (29). Anal. Calcd for C<sub>18</sub>H<sub>17</sub>N<sub>2</sub>O<sub>5</sub>S: C, 57.30; H, 5.11; N, 4.18. Found: C, 57.23; H, 5.11; N, 4.16.

**Methyl 4-Methoxy-2-(4'-methylbenzenesulfonyl)-3-oxo-2-azabicyclo[2.2.2]oct-7-ene-5-endo-carboxylate (2ai).** Thermal. A solution of pyridone 1a (38.8 mg, 0.132 mmol), methyl acrylate (0.21 mL, 10 equiv), and BHT (2 mg) in CH<sub>2</sub>Cl<sub>2</sub> (0.5 mL) was heated for 64 h at 130 °C. Chromatography (50% Et<sub>2</sub>O in hexane) afforded an inseparable mixture of 2ai and 3-methoxy-2-[(4-methylbenzenesulfonyl)oxy]pyridine as a pale yellow gum (44 mg, 31 in favor of the cycloadduct as determined by <sup>1</sup>H NMR). **High Pressure.** Methyl acrylate (0.2 mL, 38 equiv) and BaCO<sub>3</sub> (3 mg) were added to a solution of pyridone 1a (17 mg, 61 μmol) in CH<sub>2</sub>Cl<sub>2</sub> (0.5 mL), and the mixture was subjected to 10 kbar pressure for 144 h. The resulting gum was taken up in hot methanol and filtered to remove polymeric impurities. Removal of solvent afforded an oil which was purified by preparative thin-layer chromatography (Et<sub>2</sub>O) to afford 2ai as a gum (8 mg, 35%); <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 1.85 (1 H, ddd, *J* = 12.0, 4.9, 1.9 Hz, H-6<sub>endo</sub>), 2.45 (4 H, m, CH<sub>2</sub>Ar and H-6<sub>endo</sub>), 3.03 (1 H, ddd, *J* = 9.8, 4.2, 1.1 Hz, H-5), 3.65 (3 H, s, ester CH<sub>3</sub>), 3.68 (3 H, s, ester CH<sub>3</sub>), 5.37 (1 H, m, H-1), 6.57 (1 H, dd, *J* = 8.1, 1.4 Hz, H-8), 6.57 (1 H, dd, *J* = 8.1, 4.0 Hz, H-7), 7.31 (2 H, d, *J* = 8.1 Hz, tosyl H), 7.57 (2 H, d, *J* = 8.1 Hz, tosyl H); IR (film) 1733 (C=O), 1598, 1359, 1229, 1172 cm<sup>-1</sup>; MS *m/e* (EI) 366 (M<sup>+</sup>, 8), 168 (77), 109 (100), 108 (22), 94 (8), 91 (21), 77 (8), 65 (18); *m/e* (CI/ammonia) 366 (100); HRMS calcd for C<sub>18</sub>H<sub>19</sub>N<sub>2</sub>O<sub>5</sub>S (M<sup>+</sup> - OMe) 334.0749, found 334.0752.

**Dimethyl 1,5-Methoxy-4a-[(4'-methylbenzenesulfonyl)-amino]cyclohex-5-ene-1,2-dicarboxylate.** *n*-BuLi (0.8 mmol) was added slowly to MeOH (5 mL), and the solution thus obtained was added to the crude mixture of the bicyclic lactam 2ai (44 mg) at room temperature under dry N<sub>2</sub> atmosphere. After 2 h, standard workup procedure followed by purification by flash chromatography (50% Et<sub>2</sub>O in hexane) afforded the ring-opened compound as a gummy solid (30 mg, 57% from pyridone); <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 1.90–2.15 (2 H, m, H-3<sub>ax</sub> and H-3<sub>eq</sub>), 2.42 (3 H, s, CH<sub>3</sub>Ar), 3.22 (1 H, dd, *J* = 12.0, 2.6 Hz, H-2), 3.32 (3 H, s, ester CH<sub>3</sub>O), 3.64 (3 H, s, ester CH<sub>3</sub>O), 3.77 (3 H, s, ester CH<sub>3</sub>O), 3.96 (1 H, m, H-4), 5.80–5.83 (1 H, m, H-7 and H-8), 7.30 (2 H, d, *J* = 8.0 Hz, tosyl H), 7.77 (2 H, d, *J* = 8.0 Hz, tosyl H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 21.56 (CH<sub>3</sub>Ar), 28.79 (C-5), 43.30 (C-6), 46.94 (C-4), 52.05 (ether CH<sub>3</sub>), 52.68 (CO<sub>2</sub>CH<sub>3</sub>), <sup>13</sup>C NMR (CO<sub>2</sub>CH<sub>3</sub>) 76.52 (C-1), 127.03 (C-3'), 127.72 (C-7/C-8), 129.88 (C-2'), 182.04 (C-7/C-8), 187.61 (C-4'), 149.74 (C-1'), 170.69 (CO<sub>2</sub>Me), 170.95 (CO<sub>2</sub>Me); IR (film) 1735 (C=O), 1437, 1161 cm<sup>-1</sup>; HRMS calcd for C<sub>17</sub>H<sub>19</sub>N<sub>2</sub>O<sub>5</sub>S (M<sup>+</sup> - MeOH) 365.0933, found 365.0943.

**5-endo-Acetyl-4-methoxy-2-(4'-methylbenzenesulfonyl)-3-oxo-2-azabicyclo[2.2.2]oct-7-ene (2aj).** A solution of pyridone 1a (146 mg, 0.52 mmol), methyl vinyl ketone (0.75 mL, 17.1 equiv), and BHT (30 mg) in CH<sub>2</sub>Cl<sub>2</sub> (4.0 mL) was heated for 132 h at 90 °C. Chromatography (50% Et<sub>2</sub>O in hexane) afforded the starting pyridone (76 mg) and 2aj as a colorless gum (78 mg, 42%); <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 1.85 (1 H, ddd, *J* = 12.9, 4.8, 2.0 Hz, H-6<sub>endo</sub>), 2.12 (1 H, ddd, *J* = 12.9, 9.4, 3.7 Hz, H-6<sub>endo</sub>), 2.20 (3 H, s, CH<sub>3</sub>CO), 2.43 (3 H, s, CH<sub>3</sub>Ar), 3.01 (1 H, dd, *J* = 9.4, 4.8 Hz, H-5), 5.67 (3 H, s, CH<sub>3</sub>O), 6.35 (1 H, dd, *J* = 8.0, 3.8, 2.0 Hz, H-1), 6.32 (1 H, dm, *J* = 8.2 Hz, H-7), 6.60 (1 H, dd, *J* = 8.2, 6.0 Hz, H-8),

7.32 (2 H, d, *J* = 8.5 Hz, tosyl H), 7.57 (2 H, d, *J* = 8.5 Hz, tosyl H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 21.75 (CH<sub>3</sub>Ar), 32.20 (CH<sub>3</sub>CO), 32.69 (C-8), 47.22 (C-5), 52.83 (C-1), 55.14 (CH<sub>3</sub>O), 84.24 (C-4), 128.03 (C-2'), 129.83 (C-7/C-8), 129.78 (C-3'), 132.41 (C-7/C-8), 135.42 (C-1'), 145.37 (C-4'), 169.42 (C-3), 208.34 (CH<sub>3</sub>CO); IR (CHCl<sub>3</sub>) 1722 (C=O), 1598, 1360, 1171 cm<sup>-1</sup>; MS *m/e* (EI) 152 (16), 137 (20), 110 (9), 109 (100), 84 (8), 91 (29), 77 (8), 65 (13); *m/e* (CI/ammonia) 367 (26), 352 (7), 351 (20), 350 (MH<sup>+</sup>, 100), 281 (6), 230 (41), 189 (36), 152 (9); HRMS calcd for C<sub>17</sub>H<sub>19</sub>N<sub>2</sub>O<sub>5</sub>S (MH<sup>+</sup>) 350.1062, found 350.1068.

**4-(Benzyloxy)-2-(4'-methylbenzenesulfonyl)-5-endo-nitro-3-oxo-2-azabicyclo[2.2.2]oct-7-ene (2bg).** A solution of nitroethylene (409 mg and 400 mg after 48 h) and pyridone 1b (200 mg, 0.561 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (3 mL) was heated in a sealed tube at 90 °C for 5 days. Removal of solvent followed by preparative thin-layer chromatography (silica gel, 60% EtOAc in hexane, three elutions) afforded 2bg as a white solid (190 mg, 79%); mp 172–173 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 2.22 (1 H, d, *J*<sub>6,7</sub> = 14.0 Hz, *J*<sub>6,8</sub> = 3.63 Hz, *J*<sub>7,8</sub> = 2.14 Hz, H-6<sub>endo</sub>), 2.44 (3 H, s, CH<sub>3</sub>Ar), 2.79 (1 H, ddd, *J*<sub>6,7</sub> = 14.0 Hz, *J*<sub>6,8</sub> = 9.35 Hz, *J*<sub>7,8</sub> = 3.52 Hz, H-6<sub>endo</sub>), 4.89 (1 H, d, *J* = 10.92 Hz, PhCH<sub>2</sub>), 5.04 (1 H, d, *J* = 10.93 Hz, PhCH<sub>2</sub>), 5.11 (1 H, ddd, *J*<sub>6,7</sub> = 9.35 Hz, *J*<sub>6,8</sub> = 3.63 Hz, *J*<sub>7,8</sub> = 1.22 Hz, H-5), 5.44 (1 H, ddd, *J*<sub>6,7</sub> = 6.11 Hz, *J*<sub>7,8</sub> = 3.52 Hz, *J*<sub>7,9</sub> = 2.14 Hz, H-1), 6.36 (1 H, d, *J*<sub>7,8</sub> = 8.11 Hz, H-8), 6.69 (1 H, d, *J*<sub>7,8</sub> = 8.11 Hz, *J*<sub>7,9</sub> = 6.11 Hz, H-7), 7.28–7.37 (7 H, m, H-Ar), 7.59 (2 H, d, *J*<sub>7,8</sub> = 8.51 Hz, H-2' and H-8'); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 21.70 (CH<sub>3</sub>Ar), 34.25 (C-8), 50.82 (C-1), 70.00 (CH<sub>2</sub>Ph), 83.90 (C-5), 84.28 (C-4), 127.60, 128.02, 128.55, 128.62, 130.90, 131.60 (C-3), 133.10, 135.60 (C-7), 137.60, 145.78, 150.00; IR (CHCl<sub>3</sub>) 1736, 1568, 1572, 1165 cm<sup>-1</sup>; MS *m/e* (EI) 185 (10), 184 (3), 155 (10), 91 (100), 77 (20), (CI/ammonia) 448 (MNH<sup>+</sup>, 5); HRMS Calcd for C<sub>21</sub>H<sub>21</sub>N<sub>2</sub>O<sub>5</sub>S (MNH<sup>+</sup>) 448.1388, found 448.1388.

**4-(Benzyloxy)-2-(4'-methylbenzenesulfonyl)-3-oxo-2-azabicyclo[2.2.2]oct-7-ene-5-endo-carboxaldehyde (2bh).** A solution of acrolein (0.318 mL and 0.300 mL after 48 h) and pyridone 1b (200 mg, 0.561 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (2 mL) was heated in a sealed tube at 90 °C for 5 days. Chromatography (silica gel, 30% EtOAc in hexane) afforded white solid 2bh (192 mg, 83%). This compound was found to be unstable and was characterized as the corresponding alcohol.

**4-[(*tert*-Butyldimethylsilyl)oxy]-2-(4'-methylbenzenesulfonyl)-5-endo-nitro-3-oxo-2-azabicyclo[2.2.2]oct-7-ene (2cg).** A solution of pyridone 1c (159 mg, 420 μmol) and nitroethylene (170 mg, 5.5 equiv, and 205 mg, 5.6 equiv, after 67 h) in CH<sub>2</sub>Cl<sub>2</sub> (3.0 mL) was heated in a sealed tube for 160 h at 90 °C. Chromatography (50% Et<sub>2</sub>O/hexane) afforded 2cg as a white solid; mp 112–113 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 0.11 (3 H, s, CH<sub>3</sub>Si), 0.23 (3 H, s, CH<sub>3</sub>Si), 0.88 (9 H, s, (CH<sub>3</sub>)<sub>3</sub>CSi), 2.12 (1 H, ddd, *J* = 13.2, 4.3, 1.8 Hz, H-6<sub>endo</sub>), 2.43 (3 H, s, CH<sub>3</sub>Ar), 2.74 (1 H, ddd, *J* = 12.2, 9.8, 3.6 Hz, H-6<sub>endo</sub>), 4.82 (1 H, ddd, *J* = 9.3, 4.3, 1.2 Hz, H-5), 5.36 (1 H, ddd, *J* = 8.1, 3.6, 1.8 Hz, H-1), 6.10 (1 H, dt, *J* = 8.0 Hz, *J*<sub>7,8</sub> = 1.4 Hz, H-8), 6.42 (1 H, dd, *J* = 8.0, 6.1 Hz, H-7), 7.32 (2 H, d, *J* = 8.5 Hz, tosyl H), 7.58 (2 H, d, *J* = 8.5 Hz, tosyl H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 4.09 (CH<sub>3</sub>Si), 3.15 (CH<sub>3</sub>Si), 17.95 (Me<sub>2</sub>CSi), 21.08 (CH<sub>3</sub>Ar), 24.67 ((CH<sub>3</sub>)<sub>3</sub>CSi), 34.18 (C-6), 51.31 (C-1), 61.48 (C-4), 82.55 (C-5), 127.72 (C-2'), 128.60 (C-3'), 130.80 (C-7/C-8), 133.23 (C-7/C-8), 134.67 (C-1'), 145.62 (C-4'), 187.57 (C-3); IR (CHCl<sub>3</sub>) 1745 (C=O), 1598, 1562, 1370, 1265, 1163, 1172 cm<sup>-1</sup>; MS *m/e* (EI) 395 (M<sup>+</sup> - *t*-Bu), 323 (21), 322 (95), 209 (85), 155 (70), 151 (47), 91 (100), 73 (63); *m/e* (CI/ammonia) 453 (MH<sup>+</sup>, 99), 395 (M<sup>+</sup> - *t*-Bu, 51), 380 (47), 322 (100), 209 (70), 155 (55), 91 (39), 73 (37). Anal. Calcd for C<sub>22</sub>H<sub>25</sub>N<sub>2</sub>O<sub>5</sub>SSi: C, 53.08; H, 6.28; N, 8.19. Found: C, 53.08; H, 6.23; N, 8.27.

**4-[(*tert*-Butyldimethylsilyl)oxy]-2-(4'-methylbenzenesulfonyl)-3-oxo-2-azabicyclo[2.2.2]oct-7-ene-5-endo-carboxaldehyde (2ch).** A solution of pyridone 1c (1.075 g, 2.84 mmol) and acrolein (4.00 mL, 21 equiv) and BHT (50 mg) in CH<sub>2</sub>Cl<sub>2</sub> (16 mL) was heated in a sealed tube for 149 h at 90 °C. The desired product 2ch was isolated by chromatography (silica gel, 10–50% Et<sub>2</sub>O in hexane) as a white solid (863 mg, 70%). An analytically pure sample was obtained by crystallization (1:2 v/v Et<sub>2</sub>O/hexane); mp 121 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 0.11 (3 H, s, CH<sub>3</sub>Si), 0.27 (3 H, s, CH<sub>3</sub>Si), 0.88 (9 H, s, (CH<sub>3</sub>)<sub>3</sub>CSi), 2.08 (1 H, ddd, *J* = 13.3, 4.8, 2.4 Hz, H-6<sub>endo</sub>), 2.14 (1 H, ddd, *J* = 13.3, 8.9, 3.5 Hz, H-6<sub>endo</sub>), 2.43 (3 H, s, CH<sub>3</sub>Ar), 2.85 (1 H, ddd, *J* = 8.9, 4.8, 1.0 Hz, H-5),

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5.31 (1 H, m, H-1), 6.06 (1 H, d,  $J = 8.0$  Hz, H-8), 6.43 (1 H, dd,  $J = 8.0, 6.0$  Hz, H-7), 7.33 (2 H, d,  $J = 8.5$  Hz, tosyl H), 7.84 (2 H, d,  $J = 8.5$  Hz, tosyl H), 9.77 (1 H, d,  $J = 1.3$  Hz, CHO);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  -3.93 ( $\text{CH}_3\text{Si}$ ), -2.85 ( $\text{CH}_3\text{Si}$ ), 18.53 ( $\text{Me}_2\text{CSi}$ ), 21.68 ( $\text{CH}_2\text{Ar}$ ), 25.88 ( $(\text{CH}_2)_2\text{CSi}$ ), 28.57 (C-6), 50.37 (C-5), 62.86 (C-1), 81.02 (C-4), 127.86 (C-27), 129.57 (C-3'), 131.94 (C-1' and C-7), 135.21 (C-3), 146.28 (C-4'), 169.87 (C-3), 200.01 (CHO); IR ( $\text{CHCl}_3$ ) 1728 (C=O), 1360, 1168, 1172  $\text{cm}^{-1}$ ; MS  $m/e$  (EI) 378 ( $\text{M}^+ - t\text{-Bu}$ , 11), 322 (86), 167 (26), 155 (82), 152 (24), 151 (26), 91 (100), 78 (38);  $m/e$  (CI/ammonia) 453 ( $\text{MNH}_4^+$ , 1), 437 (23), 436 ( $\text{MH}^+$ , 78), 381 (26), 382 (11), 380 (100), 322 (9), 226 (9). Anal. Calcd for  $\text{C}_{28}\text{H}_{32}\text{NO}_5\text{SSi}$ : C, 57.90; H, 6.71; N, 3.22. Found: C, 57.84; H, 6.67; N, 3.24.

**Methyl 4-[(tert-Butyldimethylsilyloxy)-2-(4'-methylbenzenesulfonyl)-3-oxo-2-azabicyclo[2.2.2]oct-7-ene-5-endo-carboxylate (2ef).** A solution of pyridone 1e (45 mg, 0.12 mmol) and methyl acrylate (0.11 mL, 10 equiv) and BHT (3 mg) in  $\text{CH}_2\text{Cl}_2$  (0.8 mL) was heated in a sealed tube for 110 h at 90 °C. The desired product 2ef was isolated by chromatography (silica gel, 50–100% Et<sub>2</sub>O in hexane) as a white solid (19 mg, 56%); mp 118 °C;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  -0.14 (3 H, s,  $\text{CH}_3\text{Si}$ ), 0.21 (3 H, s,  $\text{CH}_3\text{Si}$ ), 0.94 (9 H, s,  $(\text{CH}_3)_3\text{CSi}$ ), 1.76 (1 H, ddd,  $J = 12.9, 9.7, 3.6$  Hz, H-6<sub>endo</sub>), 1.93 Hz, H-6<sub>endo</sub>), 2.39 (1 H, ddd,  $J = 12.9, 9.7, 3.6$  Hz, H-6<sub>endo</sub>), 2.43 (3 H, s,  $\text{CH}_3\text{Ar}$ ), 2.86 (1 H, ddd,  $J = 9.7, 5.2, 1.1$  Hz, H-5), 3.64 (3 H, s, ester OCH<sub>3</sub>), 6.29 (1 H, ddd,  $J = 8.0, 3.8, 1.9$  Hz, H-1), 6.10 (1 H, dt,  $J = 8.0$  Hz,  $J_d = 1.5$  Hz, H-8), 6.42 (1 H, dd,  $J = 8.0, 6.0$  Hz, H-7), 7.30 (2 H, d,  $J = 8.4$  Hz, tosyl H), 7.84 (2 H, d,  $J = 8.4$  Hz, tosyl H); IR (NaCl) 1736 (C=O), 1598, 1487, 1381, 1172  $\text{cm}^{-1}$ ; MS  $m/e$  (EI) 408 (41), 322 (100), 288 (21), 211 (90), 155 (62), 151 (47), 91 (91), 78 (51);  $m/e$  (CI/ammonia) 468 (18), 467 (30), 468 ( $\text{MH}^+$ , 100), 408 ( $\text{M}^+ - t\text{-Bu}$ , 4), 380 (9), 322 (5), 226 (3), 211 (6). Anal. Calcd for  $\text{C}_{28}\text{H}_{32}\text{NO}_5\text{SSi}$ : C, 56.75; H, 6.71; N, 3.01. Found: C, 56.62; H, 6.67; N, 3.00.

**8-endo-Acetyl-4-[(tert-butyldimethylsilyloxy)-2-(4-methylbenzenesulfonyl)-3-oxo-2-azabicyclo[2.2.2]oct-7-ene-5-endo-vinyl ketone (2ef).** A solution of pyridone 1e (200 mg, 0.528 mmol) and methyl vinyl ketone (0.76 mL, 19.4 equiv) and BHT (10 mg) in  $\text{CH}_2\text{Cl}_2$  (4.0 mL) was heated in a sealed tube for 132 h. The desired product 2ef was isolated by chromatography (silica gel, 10–50% ether in hexane) as a white solid mass (132 mg, 58%); mp 127–129 °C;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  -0.19 (3 H, s,  $\text{CH}_3\text{Si}$ ), 0.19 (3 H, s,  $\text{CH}_3\text{Si}$ ), 0.86 (9 H, s,  $(\text{CH}_3)_3\text{CSi}$ ), 1.79 (1 H, ddd,  $J = 12.8, 5.1, 1.9$  Hz, H-6<sub>endo</sub>), 2.21 (1 H, ddd,  $J = 12.9, 9.2, 3.8$  Hz, H-6<sub>endo</sub>), 2.24 (3 H, s,  $\text{CH}_3\text{CO}$ ), 2.42 (3 H, s,  $\text{CH}_3\text{Ar}$ ), 3.01 (1 H, dd,  $J = 9.2, 5.1$  Hz, H-5), 5.28 (1 H, ddd,  $J = 7.8, 3.8, 1.9$  Hz, H-1), 5.98 (1 H, dm,  $J = 8.0$  Hz, H-8), 6.42 (1 H, dd,  $J = 8.0, 6.0$  Hz, H-7), 7.29 (2 H, d,  $J = 8.0$  Hz, tosyl H), 7.82 (2 H, d,  $J = 8.0$  Hz, tosyl H); IR ( $\text{CHCl}_3$ ) 1738 (C=O), 1721, 1597, 1473, 1380, 1171  $\text{cm}^{-1}$ ; MS  $m/e$  (EI) 392 (30), 322 (87), 209 (46), 195 (23), 167 (23), 155 (72), 151 (46), 91 (100), 78 (58);  $m/e$  (CI/ammonia) 452 (13), 451 (31), 450 ( $\text{MH}^+$ , 100), 381 (19), 380 (74), 322 (12), 226 (16), 168 (8). Anal. Calcd for  $\text{C}_{28}\text{H}_{32}\text{NO}_5\text{SSi}$ : C, 58.77; H, 6.66; N, 3.12. Found: C, 58.68; H, 6.61; N, 3.19.

**4-(4'-Methylbenzenesulfonyl)-2-(4'-methylbenzenesulfonyl)-5-endo-nitro-3-oxo-2-azabicyclo[2.2.2]oct-7-ene (2dg).** A solution of nitroethylene 7g (78 mg and 78 mg after 48 h) and pyridone 1d (74 mg, 0.193 mmol) in  $\text{CH}_2\text{Cl}_2$  (1 mL) was heated in a sealed tube at 90 °C for 5 days. Removal of solvent and purification by preparative thin-layer chromatography (silica gel, 30% EtOAc in hexane, three elutions) afforded 2dg as a white solid (40 mg, 46%); mp 159–160 °C;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  2.35 (3 H, s,  $\text{CH}_3\text{C}_4'$ ), 2.44 (3 H, s,  $\text{CH}_3\text{C}_4'$ ), 4.67 (1 H, dd,  $J_{1,2} = 9.06$  Hz,  $J_{1,3} = 5.15$  Hz, H-5), 6.49 (1 H, ddd,  $J_{1,2} = 6.81$  Hz,  $J_{1,3} = 3.97$  Hz,  $J_{1,4} = 1.90$  Hz, H-1), 6.20 (1 H, d,  $J_{2,3} = 7.40$  Hz, H-8), 6.62 (1 H, dd,  $J_{2,3} = 7.40$  Hz,  $J_{2,4} = 6.81$  Hz, H-7), 7.19 (2 H, d,  $J_{3,4} = 7.90$  Hz, H-2' and H-6'), 7.35 (2 H, d,  $J_{3,4} = 7.90$  Hz, H-2' and H-6'), 7.80 (2 H, d,  $J_{3,4} = 8.31$  Hz, H-3' and H-5'), 7.91 (2 H, d,  $J_{3,4} = 8.31$  Hz, H-3' and H-5'), (H-8<sub>endo</sub> and H-6<sub>endo</sub> are partially overlapped by the methyl groups);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  21.45 ( $\text{CH}_3\text{C}_4'$ ), 21.95 ( $\text{CH}_3\text{C}_4'$ ), 34.02 (C-5), 51.47 (C-1), 61.87 (C-4), 84.26 (C-5), 128.00, 128.64, 129.85, 130.65, 132.27 (C-8), 182.30, 135.80 (C-7), 138.09, 139.00, 145.73, 158.20 (C=O); IR ( $\text{CHCl}_3$ ) 1730, 1582, 1357, 1172  $\text{cm}^{-1}$ ; MS  $m/e$  (EI) 247 (8), 217 (32), 216 (71), 202 (10), 201 (84), 200 (11), 155 (18), 124 (18), 123 (19), 119 (43), 91 (100), 79 (14), 77 (14), 65 (89);  $m/e$  (CI/ammonia) 462 ( $\text{MNH}_4^+$ , 3), 445 ( $\text{MH}^+$ , 3); HRMS calcd for  $\text{C}_{27}\text{H}_{28}\text{N}_2\text{O}_5\text{S}_2$

( $\text{M}^+$ ) 444.0814, found 444.0811.

**4-(4'-Methylbenzenesulfonyl)-2-(4'-methylbenzenesulfonyl)-3-oxo-2-azabicyclo[2.2.2]oct-7-ene-5-endo-carboxaldehyde (2dh).** A solution of acrolein (0.173 mL and 0.173 mL after 48 hours) and pyridone 1d (100 mg, 0.260 mmol) in  $\text{CH}_2\text{Cl}_2$  (1 mL) was heated in a sealed tube at 90 °C for 5 days. Chromatography (silica gel, 30% EtOAc in hexane) afforded 2dh as a white solid (47 mg, 42%); mp 134–135 °C;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  2.03 (1 H, ddd,  $J_{1,2} = 13.29$  Hz,  $J_{1,3} = 3.84$  Hz,  $J_{1,4} = 2.0$  Hz, H-6<sub>endo</sub>), 2.32 (3 H, s,  $\text{CH}_3\text{C}_4'$ ), 2.40 (1 H, m, H-6<sub>endo</sub>), 2.44 (3 H, s,  $\text{CH}_3\text{C}_4'$ ), 2.74 (1 H, ddd,  $J_{2,3} = 9.63$  Hz,  $J_{2,4} = 2.66$  Hz, CHO), 5.39 (1 H, ddd,  $J_{1,2} = 5.97$  Hz,  $J_{1,3} = 3.66$  Hz,  $J_{1,4} = 2.0$  Hz, H-1), 6.01 (1 H, d,  $J_{2,3} = 7.77$  Hz, H-8), 6.64 (1 H, dd,  $J_{2,3} = 7.77$  Hz,  $J_{2,4} = 6.97$  Hz, H-7), 7.09 (2 H, d,  $J_{3,4} = 7.76$  Hz, H-2' and H-6'), 7.31 (2 H, d,  $J_{3,4} = 7.76$  Hz, H-3' and H-5'), 7.48 (2 H, d,  $J_{3,4} = 8.31$  Hz, H-3' and H-5'), 7.68 (2 H, d,  $J_{3,4} = 8.31$  Hz, H-2' and H-6'), 9.70 (1 H, d,  $J_{\text{CHO}} = 2.66$  Hz, CHO);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  21.23 ( $\text{CH}_3\text{C}_4'$ ), 21.71 ( $\text{CH}_3\text{C}_4'$ ), 32.53 (C-5), 47.17 (C-6), 62.61 (C-1), 61.21 (C-4), 125.57, 127.97, 128.14, 129.69, 130.03, 132.38 (C-8), 135.09 (C-7), 135.87, 139.68, 145.38, 167.69 (C-3), 198.38 (CHO); IR ( $\text{CHCl}_3$ ) 1724, 1697, 1172  $\text{cm}^{-1}$ ; MS  $m/e$  (EI) 281 (10), 220 (58), 229 (1), 228 (2), 202 (8), 201 (25), 124 (45), 123 (57), 91 (52), 77 (6), 76 (17), 65 (21), 54 (2), 49 (100), 49 (8);  $m/e$  (CI/ammonia) 446 ( $\text{MNH}_4^+$ , 57), 428 ( $\text{MH}^+$ , 74); HRMS calcd for  $\text{C}_{27}\text{H}_{28}\text{NO}_5\text{S}_2$  ( $\text{M}^+$ ) 427.0912, found 427.0916.

**5-Methyl-4-(4'-methylbenzenesulfonyl)-2-(4'-methylbenzenesulfonyl)-3-oxo-2-azabicyclo[2.2.2]oct-7-ene-5-endo-carboxaldehyde (3).** High Pressure. Methacrolein (0.223 mL, 27 mmol) was added to a solution of 1d (100 mg, 0.260 mmol) in  $\text{CH}_2\text{Cl}_2$  (1 mL) in a Teflon sealed tube and was subjected to high pressure (12 kbar) for 5 days. Solvent was removed from the reaction mixture, and the residue was chromatographed (silica gel, 30% EtOAc in hexane) to afford 3 as a white solid (62 mg, 54%). Thermal. Methacrolein (0.223 mL and 0.223 mL after 48 h) was added to a solution of 1d (100 mg, 0.260 mmol) in  $\text{CH}_2\text{Cl}_2$  (1 mL) in a sealed tube and was heated at 90 °C for 96 h. Chromatography (silica gel, 30% EtOAc in hexane) afforded 3 as a white solid (46 mg, 40%); mp 134–135 °C;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  0.98 (3 H, s,  $\text{CH}_3\text{C}_5$ ), 1.82 (1 H, dd,  $J_{1,2} = 13.26$  Hz,  $J_{1,3} = 3.52$  Hz, H-6<sub>endo</sub>), 2.10 (1 H, dd,  $J_{1,2} = 13.26$  Hz,  $J_{1,3} = 2.07$  Hz, H-6<sub>endo</sub>), 2.31 (3 H, s,  $\text{CH}_3\text{C}_4'$ ), 2.44 (3 H, s,  $\text{CH}_3\text{C}_4'$ ), 5.87 (1 H, m, H-1), 5.97 (1 H, dd,  $J_{1,2} = 7.80$  Hz,  $J_{1,3} = 1.73$  Hz, H-8), 6.80 (1 H, dd,  $J_{2,3} = 7.80$  Hz,  $J_{2,4} = 6.07$  Hz, H-7), 7.05 (2 H, d,  $J_{3,4} = 7.87$  Hz, H-2' and H-6'), 7.34 (4 H, t,  $J = 8.41$  Hz, H-3' and H-5' and H-3' and H-5'), 7.92 (2 H, d,  $J_{3,4} = 8.41$  Hz, H-2' and H-6'), 9.52 (1 H, s, CHO);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  18.87 ( $\text{CH}_3\text{C}_5$ ), 21.21 ( $\text{CH}_3\text{C}_4'$ ), 21.73 ( $\text{CH}_3\text{C}_4'$ ), 40.94 (C-6), 51.96 (C-5), 62.82 (C-1), 65.76 (C-4), 126.19, 128.45, 130.29, 130.37, 132.55, 134.77, 135.88, 136.17, 139.43, 145.44, 167.49 (C-3), 199.39 (CHO); IR ( $\text{CHCl}_3$ ) 1724, 1724, 1697, 1357, 1172  $\text{cm}^{-1}$ ; MS  $m/e$  (EI) 246 (2), 244 (18), 216 (26), 215 (9), 124 (14), 123 (21), 91 (48), 77 (1), 65 (14), 64 (2), 49 (11), 41 (100);  $m/e$  (CI/ammonia) 459 ( $\text{MNH}_4^+$ , 4), 442 ( $\text{MH}^+$ , 23); HRMS calcd for  $\text{C}_{28}\text{H}_{32}\text{NO}_5\text{S}_2$  ( $\text{M}^+$ ) 441.1069, found 441.1073.

**D. Epimerization of Nitro Bicyclic Adducts. 4-Methoxy-2-(4'-methylbenzenesulfonyl)-5-oxo-2-azabicyclo[2.2.2]oct-7-ene (epi-2ag).** To a solution of 2ag (25 mg, 0.07 mmol) in MeOH (1 mL) and  $\text{CH}_2\text{Cl}_2$  (1 mL) was added ammonium formate (8.85 mg, 0.142 mmol) in one portion, and the reaction mixture was stirred for 20 h at room temperature. Removal of the solvent and purification by column chromatography (silica gel, Et<sub>2</sub>O) gave epi-2ag as a white solid (23.6 mg, 94%); mp 213–214 °C;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  2.24 (1 H, ddd,  $J_{1,2} = 14.0$  Hz,  $J_{1,3} = 4.28$  Hz,  $J_{1,4} = 3.40$  Hz, H-6<sub>endo</sub>), 2.36 (1 H, ddd,  $J_{1,2} = 14.0$  Hz,  $J_{1,3} = 10.07$  Hz,  $J_{1,4} = 2.37$  Hz, H-6<sub>endo</sub>), 2.43 (3 H, s,  $\text{CH}_3\text{Ar}$ ), 3.33 (3 H, s, OCH<sub>3</sub>), 4.77 (1 H, dd,  $J_{2,3} = 10.07$  Hz,  $J_{2,4} = 4.28$  Hz, H-5), 5.49 (1 H, m, H-1), 6.52 (1 H, dd,  $J_{2,3} = 8.14$  Hz,  $J_{2,4} = 1.69$  Hz, H-8), 6.76 (1 H, dd,  $J_{2,3} = 8.14$  Hz,  $J_{2,4} = 6.98$  Hz, H-7), 7.33 (2 H, d,  $J_{3,4} = 8.43$  Hz, H-2' and H-6'), 7.95 (2 H, d,  $J_{3,4} = 8.43$  Hz, H-2' and H-6');  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  21.99 ( $\text{CH}_3\text{C}_4'$ ), 34.29 (C-6), 50.68 (OCH<sub>3</sub>), 55.47 (C-1), 63.00 (C-4), 84.65 (C-5), 128.58, 129.31, 129.88, 130.89 (C-8), 135.81 (C-7), 145.83, 165.82 (C-3); IR ( $\text{CHCl}_3$ ) 1741 (C=O), 1565, 1367, 1173  $\text{cm}^{-1}$ ; MS  $m/e$  (EI) 155 (2), 110 (7), 109 (100), 91 (12), 77 (8);  $m/e$  (CI/ammonia) 370 ( $\text{MNH}_4^+$ , 100), 353 ( $\text{MH}^+$ , 30); HRMS

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# Cycloadditions Using 2-Pyridones

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calcd for  $C_{15}H_{20}N_2O_5S$  ( $MNH_4^+$ ) 370.1073, found 370.1080.

**4-(Benzoyloxy)-2-(4'-methylbenzenesulfonyl)-5-oxo-2-azabicyclo[2.2.2]oct-7-ene** (*epi*-2bg). To a solution of 2bg (50 mg, 0.101 mmol) in MeOH (1 mL) and  $CH_2Cl_2$  (1 mL) was added ammonium formate (12.7 mg, 0.202 mmol) in one portion, and the reaction mixture was stirred for 60 h at room temperature. Removal of the solvent and purification by column chromatography (30% EtOAc in hexane) gave 38.5 mg (89%) of *epi*-2bg as a white solid: mp 195–198 °C;  $^1H$  NMR ( $CDCl_3$ )  $\delta$  2.26 (1 H, dt,  $J_{6,7} = 14.0$  Hz,  $J_{6,8} = 4.28$  Hz,  $J_{6,9} = 3.66$  Hz, H-6<sub>ax</sub>), 2.35 (1 H, ddd,  $J_{6,7} = 14.0$  Hz,  $J_{6,8} = 10.07$  Hz,  $J_{6,9} = 2.36$  Hz, H-6<sub>eq</sub>), 2.45 (3 H, s,  $CH_3$ -C4'), 4.73 (1 H, d,  $J = 11.49$  Hz, PhCH<sub>2</sub>), 4.85 (1 H, dd,  $J_{7,8} = 10.07$  Hz,  $J_{7,9} = 4.28$  Hz, H-5), 5.21 (1 H, d,  $J = 11.49$  Hz, PhCH<sub>2</sub>), 5.51 (1 H, m, H-1), 6.49 (1 H, dd,  $J_{9,10} = 8.11$  Hz,  $J_{9,11} = 1.59$  Hz, H-8), 6.76 (1 H, dd,  $J_{9,10} = 8.11$  Hz,  $J_{9,11} = 6.93$  Hz, H-7), 7.27–7.37 (7 H, m, H-Ar), 7.98 (2 H, d,  $J_{2,3} = 8.37$  Hz, H-2' and H-6');  $^{13}C$  NMR ( $CDCl_3$ )  $\delta$  21.84 ( $CH_3$ -C4'), 34.29 (C-8), 50.70 (C-1), 69.83 ( $CH_2$ Ph), 84.28 (C-4), 84.88 (C-5), 127.30, 128.02, 128.51, 128.82, 129.90, 131.57 (C-6), 135.06, 135.74 (C-7), 137.54, 145.80, 167.03 (C-3); IR (CHCl<sub>3</sub>) 1740 (C=O), 1585, 1566, 1354, 1166  $cm^{-1}$ ; MS  $m/e$  (EI) 185 (8), 164 (2), 155 (6), 91 (100), 77 (3);  $m/e$  (CI/ammonia) 446 ( $MNH_4^+$ , 4); HRMS calcd for  $C_{27}H_{34}N_2O_5S$  ( $MNH_4^+$ ) 446.1896, found 446.1892.

**4-(4'-Methylbenzenesulfonyl)-2-(4'-methylbenzenesulfonyl)-5-oxo-2-azabicyclo[2.2.2]oct-7-ene** (*epi*-2dg). To a solution of 2dg (131 mg, 0.295 mmol) in MeOH (1 mL) and  $CH_2Cl_2$  (2 mL) was added ammonium formate (38.38 mg, 0.59 mmol) in one portion, and the reaction mixture was stirred for 20 h at room temperature. Removal of the solvent and purification by flash column chromatography (30% EtOAc in hexane) afforded *epi*-2dg as a white solid (125 mg, 95%): mp 165–168 °C (from  $CH_2Cl_2$ /Et<sub>2</sub>O (1:2) v/v);  $^1H$  NMR ( $CDCl_3$ )  $\delta$  2.36 (3 H, s,  $CH_3$ -C4'), 2.44 (3 H, s,  $CH_3$ -C4'), 4.67 (1 H, dd,  $J_{6,7} = 8.98$  Hz,  $J_{6,8} = 5.15$  Hz, H-5), 5.48 (1 H, m,  $J_{7,8} = 5.93$  Hz,  $J_{7,9} = 4.38$  Hz,  $J_{7,10} = 2.41$  Hz,  $J_{7,11} = 1.80$  Hz, H-1), 6.19 (1 H, dd,  $J_{9,10} = 7.76$  Hz,  $J_{9,11} = 1.80$  Hz, H-8), 6.51 (1 H, dd,  $J_{9,10} = 7.76$  Hz,  $J_{9,11} = 5.93$  Hz, H-7), 7.18 (2 H, d,  $J_{2,3} = 8.0$  Hz, H-2' and H-6'), 7.34 (2 H, d,  $J_{2,3} = 8.0$  Hz, H-2' and H-6'), 7.51 (2 H, d,  $J_{2,3} = 8.34$  Hz, H-2' and H-6'), 7.91 (2 H, d,  $J_{2,3} = 8.34$  Hz, H-2' and H-6');  $^{13}C$  NMR ( $CDCl_3$ )  $\delta$  21.42 ( $CH_3$ -C4'), 21.95 ( $CH_3$ -C4'), 35.00 (C-8), 51.11 (C-1), 61.87 (C-4), 84.82 (C-5), 123.90, 128.62, 129.85, 130.65, 132.72 (C-6), 135.41 (C-7), 139.01, 140.97, 159.58 (C-3); IR (CHCl<sub>3</sub>) 1725 (C=O), 1560, 1354, 1166  $cm^{-1}$ ; MS  $m/e$  (EI) 247 (2), 217 (12), 216 (36), 201 (37), 155 (7), 124 (13), 123 (100), 119 (33), 91 (90), 79 (14), 77 (16), 85 (49);  $m/e$  (CI/ammonia) 462 ( $MNH_4^+$ , 7), 448 ( $MH^+$ , 12); HRMS calcd for  $C_{27}H_{30}N_2O_5S_2$  ( $MH^+$ ) 444.0592, found 444.0588.

**E. Chemical Manipulation of 1-Azabicyclo[2.2.2]octane.** **5-endo-(Hydroxymethyl)-4-(4'-methylbenzenesulfonyl)-2-(4'-methylbenzenesulfonyl)-3-oxo-2-azabicyclo[2.2.2]oct-7-ene.**  $NaBH_4$  (19.35 mg) was added to a solution of 2dh (218.6 mg, 0.511 mmol) in  $CH_2Cl_2$  (3 mL) and methanol (5 mL) at 0 °C, and the reaction mixture was stirred for 15 min and then poured into  $H_2O$  (25 mL) and extracted with  $CH_2Cl_2$  (3  $\times$  50 mL), dried ( $MgSO_4$ ), filtered, and concentrated. Purification of the residue by flash column chromatography (silica gel, EtOAc) afforded *epi*-2dh as a clear oil (203.9 mg, 93%):  $^1H$  NMR ( $CDCl_3$ )  $\delta$  1.59 (1 H, ddd,  $J_{6,7} = 13.0$  Hz,  $J_{6,8} = 4.24$  Hz,  $J_{6,9} = 2.0$  Hz, H-6<sub>ax</sub>), 1.76 (1 H, bs, OH), 2.15 (1 H, m, H-5), 2.32 (3 H, s,  $CH_3$ -C4'), 2.86 (1 H, m, H-6<sub>eq</sub>), 2.44 (3 H, s,  $CH_3$ -C4'), 3.42 (1 H, dd,  $J_{7,8} = 11.34$  Hz,  $J_{7,9} = 6.94$  Hz,  $-CH_2H_{20}OH$ ), 3.92 (1 H, dd,  $J_{9,10} = 11.34$  Hz,  $J_{9,11} = 5.17$  Hz,  $-CH_2H_{20}OH$ ), 5.30 (1 H, ddd,  $J_{1,2} = 6.02$  Hz,  $J_{1,3} = 3.48$  Hz,  $J_{1,4} = 2.0$  Hz, H-1), 5.92 (1 H, d,  $J_{2,3} = 7.80$  Hz, H-8), 6.50 (1 H, ddd,  $J_{7,8} = 7.80$  Hz,  $J_{7,9} = 6.02$  Hz, H-7), 7.05 (2 H, d,  $J_{2,3} = 8.0$  Hz, H-2' and H-6'), 7.30 (2 H, d,  $J_{2,3} = 8.0$  Hz, H-2' and H-6'), 7.39 (2 H, d,  $J_{2,3} = 8.37$  Hz, H-2' and H-6'), 7.89 (2 H, d,  $J_{2,3} = 8.37$  Hz, H-2' and H-6');  $^{13}C$  NMR ( $CDCl_3$ )  $\delta$  21.29 ( $CH_3$ -C4'), 21.81 ( $CH_3$ -C4'), 33.55 (C-8), 38.36 (C-6), 52.43 (C-1), 63.76 (C-4), 84.38 (C-5), 127.07, 128.27, 129.69, 129.92, 132.79, 132.08, 134.81, 135.45, 138.94, 145.19, 169.29 (C-3); IR (CHCl<sub>3</sub>) 3512, 3518, 1713, 1595, 1364, 1172  $cm^{-1}$ ; MS  $m/e$  (EI) 232 ( $M^+$  -  $TeNCO$ , 3), 155 (2), 123 (4), 109 (8), 91 (8), 42 (7), 41 (100);  $m/e$  (CI/ammonia) 447 ( $MNH_4^+$ , 3), 430 ( $MH^+$ , 21); HRMS calcd for  $C_{22}H_{24}NO_5S_2$  ( $MH^+$ ) 430.1147, found 430.1141.

**5-endo-[[[(*tert*-Butyldimethylsilyl)oxy]methyl]-4-(4'-methylbenzenesulfonyl)-2-(4'-methylbenzenesulfonyl)-3-oxo-2-azabicyclo[2.2.2]oct-7-ene** (4). Triethylamine (0.019 mL, 0.151 mmol) was added to the solution of 5-(hydroxymethyl)-4-(4'-methylbenzenesulfonyl)-2-(4'-methylbenzenesulfonyl)-3-oxo-2-azabicyclo[2.2.2]oct-7-ene (54.4 mg, 0.126 mmol) in  $CH_2Cl_2$  (2 mL) at 0 °C. After 5 min, TBDMSOTf (0.034 mL, 0.151 mmol) was added via syringe. After 5 min the reaction mixture was quenched with  $H_2O$  (5 mL) and extracted with Et<sub>2</sub>O (3  $\times$  76 mL), dried ( $MgSO_4$ ), filtered, and concentrated to give a residue which was purified by column chromatography (silica gel, 30% EtOAc in hexane) to give 4 as a clear oil (65 mg, 95%):  $^1H$  NMR ( $CDCl_3$ )  $\delta$  -0.01 (3 H, s,  $CH_3$ -Si), 0.05 (3 H, s,  $CH_3$ -Si), 0.89 (9 H, s,  $(CH_3)_3CSi$ ), 1.92 (1 H, ddd,  $J_{6,7} = 12.92$  Hz,  $J_{6,8} = 4.09$  Hz,  $J_{6,9} = 2.01$  Hz, H-6<sub>ax</sub>), 2.11 (1 H, m, H-5), 2.35 (1 H, m, H-6<sub>eq</sub>), 2.37 (3 H, s,  $CH_3$ -C4'), 2.50 (3 H, s,  $CH_3$ -C4'), 3.46 (1 H, dd,  $J_{7,8} = 10.0$  Hz,  $J_{7,9} = 8.37$  Hz,  $-CH_2H_{20}OSi$ ), 3.97 (1 H, dd,  $J_{9,10} = 10.0$  Hz,  $J_{9,11} = 4.08$  Hz,  $-CH_2H_{20}OSi$ ), 5.35 (1 H, ddd,  $J_{1,2} = 5.97$  Hz,  $J_{1,3} = 4.05$  Hz,  $J_{1,4} = 2.01$  Hz, H-1), 5.92 (1 H, d,  $J_{2,3} = 7.8$  Hz, H-8), 6.51 (1 H, dd,  $J_{7,8} = 7.80$  Hz,  $J_{7,9} = 5.97$  Hz, H-7), 7.09 (2 H, d,  $J_{2,3} = 8.0$  Hz, H-2' and H-6'), 7.35 (2 H, d,  $J_{2,3} = 8.0$  Hz, H-2' and H-6'), 7.44 (2 H, d,  $J_{2,3} = 8.41$  Hz, H-2' and H-6'), 7.49 (2 H, d,  $J_{2,3} = 8.41$  Hz, H-2' and H-6');  $^{13}C$  NMR ( $CDCl_3$ )  $\delta$  -5.34 ( $CH_3$ -Si), -5.25 ( $CH_3$ -Si), 18.20 ( $(CH_3)_3CSi$ ), 21.27 ( $CH_3$ -C4'), 21.82 ( $CH_3$ -C4'), 25.90 ( $(CH_3)_3CSi$ ), 33.02 (C-8), 38.37 (C-6), 52.56 (C-1), 63.22 (C-4), 63.94 (C-5), 127.65, 128.30, 129.63, 129.81, 132.33, 133.29, 134.52, 135.57, 138.43, 145.02, 169.52 (C-3); IR (CHCl<sub>3</sub>) 3038, 2954, 1719 (C=O), 1595, 1354, 1249, 1166, 1096  $cm^{-1}$ ; MS  $m/e$  (EI) 544 ( $MH^+$ , 100), 390 (13), 347 (15), 299 (4), 229 (18), 155 (2), 91 (8), 58 (4);  $m/e$  (CI/ammonia) 486 ( $M^+$  -  $t$ -Bu, 2); HRMS calcd for  $C_{34}H_{44}NO_5Si_2$  ( $M^+$  -  $t$ -Bu) 486.1229, found 486.1232.

**5-endo-[[[(*tert*-Butyldimethylsilyl)oxy]methyl]-2-(4'-methylbenzenesulfonyl)-3-oxo-2-azabicyclo[2.2.2]oct-7-ene** (5).  $Bu_4SnH$  (0.076 mL, 0.283 mmol) and azobisisobutyronitrile (AIBN) (48.4 mg, 0.283 mmol) were added to the solution of compound 4 (70 mg, 0.126 mmol) in anhydrous benzene (3 mL), the mixture was heated at reflux temperature for 2 h, another 0.283 mmol of AIBN was added via syringe in benzene (0.5 mL), after 2 h reflux the reaction mixture was cooled down to room temperature, the solvent was removed under reduced pressure, and the resultant residue was purified by PTLT (silica gel, 20% EtOAc in hexane, three elutions) to give 5 (48 mg, 89%) as a clear oil:  $^1H$  NMR ( $CDCl_3$ )  $\delta$  -0.01 (6 H, s,  $CH_3$ -Si), 0.84 (9 H, s,  $(CH_3)_3CSi$ ), 0.97 (1 H, m, H-5), 1.24–1.38 (2 H, m, H-6<sub>ax</sub> and H-4), 2.18 (1 H, ddd,  $J_{6,7} = 14.0$  Hz,  $J_{6,8} = 9.26$  Hz,  $J_{6,9} = 3.66$  Hz, H-6<sub>eq</sub>), 2.40 (3 H, s,  $CH_3$ -C4'), 3.11 (1 H, d,  $J_{7,8} = 10.0$  Hz,  $J_{7,9} = 10.0$  Hz,  $-CH_2H_{20}OSi$ ), 3.41 (1 H, dd,  $J_{9,10} = 10.0$  Hz,  $J_{9,11} = 5.28$  Hz,  $-CH_2H_{20}OSi$ ), 5.31 (1 H, ddd,  $J_{1,2} = 6.8$  Hz,  $J_{1,3} = 3.68$  Hz,  $J_{1,4} = 1.41$  Hz, H-1), 6.14 (1 H, ddd,  $J_{7,8} = 7.87$  Hz,  $J_{7,9} = 7.82$  Hz,  $J_{7,10} = 1.66$  Hz, H-8), 6.50 (1 H, ddd,  $J_{7,8} = 7.82$  Hz,  $J_{7,9} = 5.8$  Hz,  $J_{7,10} = 1.63$  Hz, H-7), 7.27 (2 H, d,  $J_{2,3} = 8.35$  Hz, H-2' and H-6'), 7.84 (2 H, d,  $J_{2,3} = 8.35$  Hz, H-2' and H-6');  $^{13}C$  NMR ( $CDCl_3$ )  $\delta$  -5.37 ( $CH_3$ -Si), -5.25 ( $CH_3$ -Si), 21.76 ( $CH_3$ -C4'), 25.34 ( $(CH_3)_3CSi$ ), 25.97 ( $(CH_3)_3CSi$ ), 30.37 (C-6), 35.40 (C-8), 47.32 (C-4), 53.86 (C-1), 84.81 (C-5), 128.11, 129.51, 129.72 (C-6), 129.83, 133.35 (C-7), 144.72, 171.27 (C-3); IR (CHCl<sub>3</sub>) 1713 (C=O), 1595, 1354, 1255, 1102, 1090  $cm^{-1}$ ; MS  $m/e$  (EI) 422 ( $MH^+$ , 2), 394 ( $M^+$  -  $t$ -Bu, 24), 167 (46), 155 (21), 152 (41), 115 (7), 100 (5), 81 (72), 59 (15), 57 (4);  $m/e$  (CI/ammonia) 439 ( $MNH_4^+$ , 6), 423 ( $MH^+$ , 100), 394 ( $M^+$  -  $t$ -Bu, 4); HRMS calcd for  $C_{34}H_{42}NO_5Si_2$  ( $MH^+$ ) 422.1821, found 422.1818.

**Methyl 6a-[[[(*tert*-Butyldimethylsilyl)oxy]methyl]-4-(4'-methylbenzenesulfonyl)amino]cyclohexene-1-carboxylate** (6). To a solution of LiOMe (0.32 mL of *n*-BuLi 1.6M in hexanes in 5 mL of anhydrous MeOH) at 0 °C, a solution of compound 5 (11 mg, 0.026 mmol) in  $CH_2Cl_2$  (0.5 mL) was added via cannula. The reaction mixture was warmed to room temperature and stirred for 4 h, quenched with saturated aqueous  $NH_4Cl$  (5 mL), extracted with  $CH_2Cl_2$  (4  $\times$  20 mL), dried ( $MgSO_4$ ), filtered, and concentrated. The resultant residue was purified by pte (30% EtOAc in hexanes) to give 6 as a clear oil (7.7 mg, 66%):  $^1H$  NMR ( $CDCl_3$ )  $\delta$  -0.07 (3 H, s,  $CH_3$ -Si), -0.03 (3 H, s,  $CH_3$ -Si), 0.82 (9 H, s,  $(CH_3)_3CSi$ ), 1.25 (1 H, m, H-5a), 1.44 (1 H, m, H-5b), 1.97–2.04 (1 H, m, H-6), 2.42 (3 H, s,  $CH_3$ -C4'), 2.52 (2 H, m, H-3a,6), 2.76 (1 H, m, H-4), 3.47 (1 H, dd,  $J_{7,8} = 10.0$

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10-11-1964

1. The first step in the process of the investigation is to identify the problem or issue that needs to be addressed. This involves gathering information about the situation and determining the scope of the investigation.

2. Once the problem is identified, the next step is to develop a plan of action. This plan should outline the objectives of the investigation, the methods to be used, and the timeline for completion.

3. The third step is to collect data. This involves gathering information from various sources, including interviews, observations, and documents. The data should be organized and analyzed to identify patterns and trends.

4. The fourth step is to interpret the data. This involves drawing conclusions from the data and identifying the causes of the problem. It is important to consider the limitations of the data and the potential for bias.

5. The final step is to report the findings. This involves writing a report that summarizes the results of the investigation and provides recommendations for action. The report should be clear, concise, and easy to understand.

H<sub>2</sub>,  $J_{7-8} = 7.02$  Hz,  $-\text{CH}_2\text{H}_7\text{OSi}$ , 3.61 (1 H, dd,  $J_{7-8} = 10.0$  Hz,  $J_{7-9} = 8.29$  Hz,  $-\text{CH}_2\text{H}_7\text{OSi}$ ), 3.70 (3 H, s,  $\text{CH}_3\text{O}$ ), 4.47 (1 H, d, NH,  $J = 8.0$  Hz), 6.86 (1 H, t,  $J = 8.35$  Hz, H-2), 7.25 (2 H, d,  $J_{3-4} = 8.31$  Hz, H-3' and H-5'), 7.77 (2 H, d,  $J_{3-4} = 8.31$  Hz, H-2' and H-6');  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  -5.47 ( $\text{CH}_2\text{Si}$ ), -5.37 ( $\text{CH}_2\text{Si}$ ), 17.83 ( $(\text{CH}_3)_2\text{CSi}$ ), 21.72 ( $\text{CH}_3\text{-C-4'}$ ), 28.02 ( $(\text{CH}_3)_2\text{CSi}$ ), 32.90, 34.12, 37.01, 48.04 ( $\text{OCH}_3$ ), 51.83 (C-3), 84.81 (C-7), 127.17, 129.93, 130.13, 128.26 (C-1), 139.27 (C-2), 143.35, 146.98 ( $\text{CO}_2\text{Me}$ ); IR ( $\text{CHCl}_3$ ) 1707, 1648, 1595, 1285, 1186, 1076  $\text{cm}^{-1}$ ; MS  $m/e$  (EI) 397 (24), 396 ( $\text{M}^+ - t\text{-Bu}$ , 100), 226 (18), 225 (99), 155 (7), 115 (6), 91 (40), 89 (84), 59 (14), 58 (5), 57 (4). HRMS calcd for  $\text{C}_{20}\text{H}_{24}\text{N}_2\text{O}_5\text{Si}$  ( $\text{M}^+ - t\text{-Bu}$ ) 398.1301, found 398.1305.

4-[(*tert*-Butyldimethylsilyloxy)-5-*endo*-(hydroxymethyl)-2-(4'-methylbenzenesulfonyl)-3-*oxo*-2-azabicyclo[2.2.2]oct-7-ene. NaBH<sub>4</sub> (49 mg, 1.29 mmol) was added to a solution of 2eh (561 mg, 1.29 mmol) in  $\text{CH}_3\text{OH}$  (10 mL) at room temperature. The reaction mixture was stirred for 15 min and then poured into  $\text{H}_2\text{O}$  (10 mL) and was extracted with  $\text{CH}_2\text{Cl}_2$  (3  $\times$  50 mL) and dried ( $\text{Na}_2\text{SO}_4$ ). Removal of solvent followed by flash column chromatography (silica gel, 50–100% Et<sub>2</sub>O in hexane) afforded a gummy solid (563 mg, 100%):  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  -0.14 (3 H, s,  $\text{CH}_3\text{Si}$ ), 0.24 (3 H, s,  $\text{CH}_3\text{Si}$ ), 0.89 (9 H, s,  $(\text{CH}_3)_2\text{CSi}$ ), 1.09 (1 H, ddd,  $J = 13.0, 4.8, 1.9$  Hz, H-6<sub>ax</sub>), 2.14 (1 H, m, H-5), 2.27 (1 H, ddd,  $J = 13.0, 9.8, 3.6$  Hz, H-8<sub>ax</sub>), 2.42 (3 H, s,  $\text{CH}_3\text{Ar}$ ), 3.39 (1 H, dd,  $J = 11.8, 4.6$  Hz,  $\text{CH}_2\text{OH}$ ), 3.59 (1 H, dd,  $J = 11.3, 8.1$  Hz,  $\text{CH}_2\text{OH}$ ), 5.20 (1 H, m, H-1), 6.07 (1 H, d,  $J = 8.0$  Hz, H-8), 6.39 (1 H, dd,  $J = 8.0, 8.0$  Hz, H-7), 7.29 (2 H, d,  $J = 8.5$  Hz, *tosyl* H), 7.83 (2 H, d,  $J = 8.5$  Hz, *tosyl* H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  -3.98 ( $\text{CH}_3\text{Si}$ ), -2.89 ( $\text{CH}_3\text{Si}$ ), 19.41 ( $\text{Me}_2\text{CSi}$ ), 21.63 ( $\text{CH}_3\text{Ar}$ ), 25.98 ( $(\text{CH}_3)_2\text{CSi}$ ), 30.98 (C-6), 39.71 (C-5), 52.04 (C-1), 64.85 ( $\text{CH}_2\text{OH}$ ), 83.05 (C-4), 127.82 (C-2'), 129.47 (C-3'), 130.68 (C-4' and C-7), 156.04 (C-5), 135.39 (C-1'), 171.02 (C-3); IR ( $\text{CHCl}_3$ ) 1736 (C=O), 1598, 1472, 1381, 1188, 1121, 1030  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{21}\text{H}_{28}\text{N}_2\text{O}_5\text{Si}$ : C, 57.64; H, 7.14; N, 8.20. Found: C, 57.71; H, 7.15; N, 8.16.

4-Hydroxy-5-*endo*-(hydroxymethyl)-2-(4'-methylbenzenesulfonyl)-3-*oxo*-2-azabicyclo[2.2.2]oct-7-ene. The alcohol from the above preparation (73 mg, 0.167 mmol) was dissolved in THF, and tetra-*n*-butylammonium fluoride (TBAF) (1 M solution in THF, 1 mL) was added at room temperature. After 20 min, the solvent was evaporated and the residue was chromatographed directly (Et<sub>2</sub>O) to afford a white solid (32 mg, 60%): mp 174 °C;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  1.10 (1 H, ddd,  $J = 13.0, 4.98, 1.9$  Hz, H-6<sub>ax</sub>), 2.02 (1 H, m, H-5), 2.31 (1 H, ddd,  $J = 13.0, 9.8, 3.6$  Hz, H-8<sub>ax</sub>), 2.44 (3 H, s,  $\text{CH}_3\text{Ar}$ ), 3.45 (1 H, m,  $\text{CH}_2\text{OH}$ ), 3.76 (1 H, dd,  $J = 11.4, 9.4$  Hz,  $\text{CH}_2\text{OH}$ ), 5.28 (1 H, ddd,  $J = 7.6, 3.9, 1.9$  Hz, H-1), 6.20 (1 H, d,  $J = 6.0$  Hz, H-8), 6.43 (1 H, dd,  $J = 7.5, 8.0$  Hz, H-7), 7.32 (2 H, d,  $J = 8.0$  Hz, *tosyl* H), 7.84 (2 H, d,  $J = 8.0$  Hz, *tosyl* H); IR ( $\text{CHCl}_3$ ) 3493, 1723, 1598, 1519, 1174  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{18}\text{H}_{20}\text{N}_2\text{O}_5$ : C, 55.72; H, 5.80; N, 4.33. Found: C, 55.81; H, 5.82; N, 4.28.

This bis-alcohol is sensitive to chromatography. Therefore, for the next step, the crude product obtained after standard aqueous workup was used.

4-Hydroxy-5-*endo*-[(*tert*-butyldimethylsilyloxy)-methyl]-2-(4'-methylbenzenesulfonyl)-3-*oxo*-2-azabicyclo[2.2.2]oct-7-ene (7). To a  $\text{CH}_2\text{Cl}_2$  (5 mL) solution of crude bis-alcohol, prepared as described previously by addition of TBAF (1 M solution in THF, 2 mL) to alcohol (430 mg, 0.98 mmol), was added TBDMSOTf (150 mg, 1.0 mmol) and triethylamine (0.15 mL, 1.05 mmol). After 8 h, the solution was poured into water (10 mL) and was extracted with  $\text{CH}_2\text{Cl}_2$  (3  $\times$  50 mL). Evaporation of solvent followed by chromatography (15–50% Et<sub>2</sub>O in hexane) afforded white solid 7 (380 mg, 90% over two steps): mp 113 °C;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  -0.01 (6 H, s,  $(\text{CH}_3)_2\text{Si}$ ), 0.84 (9 H, s,  $(\text{CH}_3)_3\text{CSi}$ ), 1.48 (1 H, ddd,  $J = 13.1, 4.6, 1.95$  Hz, H-6<sub>ax</sub>), 2.00 (1 H, m, H-5), 2.26 (1 H, ddd,  $J = 13.1, 9.4, 3.7$  Hz, H-8<sub>ax</sub>), 2.42 (3 H, s,  $\text{CH}_3\text{Ar}$ ), 3.49 (1 H, dd,  $J = 9.9, 7.2$  Hz,  $\text{CH}_2\text{OSi}$ ), 3.76 (1 H, dd,  $J = 9.9, 5.6$  Hz,  $\text{CH}_2\text{OSi}$ ), 6.27 (1 H, ddd,  $J = 6.0, 3.7, 1.95$  Hz, H-1), 6.08 (1 H, d,  $J = 8.0$  Hz, H-8), 6.35 (1 H, dd,  $J = 8.0, 6.0$  Hz, H-7), 7.30 (2 H, d,  $J = 8.5$  Hz, *tosyl* H), 7.85 (2 H, d,  $J = 8.5$  Hz, *tosyl* H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  -6.41 ( $\text{CH}_3\text{Si}$ ), -6.40 ( $\text{CH}_3\text{Si}$ ), 18.11 ( $\text{Me}_2\text{CSi}$ ), 21.67 ( $\text{CH}_3\text{Ar}$ ), 25.77 ( $(\text{CH}_3)_2\text{CSi}$ ), 31.38 (C-6), 39.51 (C-5), 52.81 (C-1), 63.87 ( $\text{CH}_2\text{OSi}$ ), 78.63 (C-4), 127.89 (C-2'), 129.63 (C-3'), 129.94 (C-3), 135.37 (C-4'), 135.65 (C-3/C-7), 145.24 (C-1'), 172.43 (C-5); IR ( $\text{CHCl}_3$ ) 1721 (C=O), 1588,

1472, 1361, 1188, 1172, 1089  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{27}\text{H}_{34}\text{N}_2\text{O}_5\text{Si}$ : C, 57.64; H, 7.14; N, 8.20. Found: C, 57.51; H, 7.03; N, 8.18.

Methyl 6-β-[(*tert*-Butyldimethylsilyloxy)methyl]-1-β-hydroxy-4-α-(4'-methylbenzenesulfonylamido)cyclohex-2-ene-carboxylate (8). *n*-BuLi (3.2 mmol) was added slowly to MeOH (10 mL), and the solution thus obtained was added to bicyclic lactam (360 mg, 0.822 mmol) at room temperature under dry N<sub>2</sub> atmosphere. After 2 h, a workup procedure as described above followed by purification by flash chromatography (50% Et<sub>2</sub>O in hexane) afforded 8 as a gummy solid (260 mg, 81%):  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  0.00 (3 H, s,  $\text{CH}_3\text{Si}$ ), 0.01 (3 H, s,  $\text{CH}_3\text{Si}$ ), 0.85 (9 H, s,  $(\text{CH}_3)_2\text{CSi}$ ), 1.25 (1 H, m, H-6), 1.55 (1 H, dm,  $J = 13.0$  Hz, H-5<sub>ax</sub>), 1.67 (1 H, dt,  $J_1 = 4.4$  Hz,  $J_2 = 11.5$  Hz, H-5<sub>ax</sub>), 2.43 (3 H, s,  $\text{CH}_3\text{Ar}$ ), 3.43 (1 H, dd,  $J = 4.7, 9.9$  Hz,  $\text{CH}_2\text{OSi}$ ), 3.61 (1 H, dd,  $J = 8.7, 9.9$  Hz,  $\text{CH}_2\text{OSi}$ ), 3.74 (3 H, s,  $\text{CO}_2\text{CH}_3$ ), 3.87 (1 H, m, H-4), 4.81 (1 H, dd,  $J = 8.0$  Hz, NH), 5.60 (2 H, d,  $J = 10.0$  Hz, H-2), 6.84 (1 H, dd,  $J = 4.0, 10$  Hz, H-3), 7.31 (2 H, d,  $J = 8.0$  Hz, ArH), 7.78 (2 H, d,  $J = 8.0$  Hz, ArH);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  -5.84 ( $\text{CH}_3\text{Si}$ ), 18.31 ( $\text{Me}_2\text{CSi}$ ), 21.48 ( $\text{CH}_3\text{Ar}$ ), 25.85 ( $(\text{CH}_3)_2\text{CSi}$ ), 27.41 (C-6), 37.58 (C-6), 47.12 (C-4), 52.93 (ester  $\text{CH}_2$ ), 62.59 ( $\text{CH}_2\text{O}$ ), 71.45 (C-1), 128.92 (C-2'), 128.51 (C-2/C-3), 129.75 (C-3'), 131.56 (C-2/C-3), 137.90 (C-4'), 143.46 (C-1'), 176.13 ( $\text{CO}_2\text{Me}$ ); IR (film) 3278 (OH and NH), 2928, 1735 (C=O), 1437, 1250, 1086  $\text{cm}^{-1}$ ; HRMS calcd for  $\text{C}_{24}\text{H}_{32}\text{N}_2\text{O}_5\text{Si}$  ( $\text{M}^+ - t\text{-Bu}$ ) 412.1250, found 412.1259.

5-*endo*-(Hydroxymethyl)-4-methoxy-2-(4'-methylbenzenesulfonyl)-3-*oxo*-2-azabicyclo[2.2.2]oct-7-ene. This compound was prepared in accordance with the general procedure described previously. Thus, starting from a solution of aldehyde (357 mg, 1.07 mmol) in MeOH (10 mL) and NaBH<sub>4</sub> (88 mg, 1.0 mmol), we obtained a waxy solid (313 mg, 94%):  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  1.02 (1 H, ddd,  $J = 12.6, 4.4, 1.8$  Hz, H-6<sub>ax</sub>), 2.14 (1 H, m, H-5), 2.22 (1 H, ddd,  $J = 12.6, 9.7, 3.7$  Hz, H-8<sub>ax</sub>), 2.44 (3 H, s,  $\text{CH}_3\text{Ar}$ ), 3.32 (1 H, dd,  $J = 11.4, 4.1$  Hz,  $\text{CH}_2\text{OH}$ ), 3.54 (1 H, dd,  $J = 11.4, 8.5$  Hz,  $\text{CH}_2\text{OH}$ ), 3.65 (3 H, s,  $\text{CH}_3\text{O}$ ), 5.26 (1 H, ddd,  $J = 6.0, 3.7, 1.8$  Hz, H-1), 6.43 (1 H, dd,  $J = 8.2, 1.4$  Hz, H-8), 6.58 (1 H, dd,  $J = 8.2, 8.0$  Hz, H-7), 7.32 (2 H, d,  $J = 8.3$  Hz, *tosyl* H), 7.83 (2 H, d,  $J = 8.3$  Hz, *tosyl* H); IR (film) 3522 (OH), 1726 (C=O), 1597 (C=C), 1355, 1170, 1089  $\text{cm}^{-1}$ ; HRMS calcd for  $\text{C}_{18}\text{H}_{20}\text{N}_2\text{O}_5$  ( $\text{MH}^+$ ) 398.1082, found 398.1069.

4-(Benzyloxy)-5-*endo*-(hydroxymethyl)-2-(4'-methylbenzenesulfonyl)-3-*oxo*-2-azabicyclo[2.2.2]oct-7-ene. NaBH<sub>4</sub> (17.67 mg) was added to a solution of 2eh (192 mg, 0.487 mmol) in  $\text{CH}_2\text{Cl}_2$  (3 mL) and MeOH (5 mL) at 0 °C, and the reaction mixture was stirred at this temperature for 16 min, poured into 25 mL of  $\text{H}_2\text{O}$ , extracted with  $\text{CH}_2\text{Cl}_2$  (3  $\times$  50 mL), dried ( $\text{MgSO}_4$ ), filtered, and concentrated. Purification by column chromatography (silica gel, 50% EtOAc in hexane) gave a white solid (149 mg, 88%): mp 105–106 °C;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  1.11 (1 H, m, H-6<sub>ax</sub>), 2.20–2.28 (2 H m, H-5 and H-8<sub>ax</sub>), 2.44 (3 H, s,  $\text{CH}_3\text{Ar}$ ), 2.78 (1 H, s broad, OH), 3.35 (1 H, t,  $J = 11.36$  Hz,  $-\text{CH}_2\text{H}_2\text{OH}$ ), 3.63 (1 H, dd,  $J_{\text{ax-ax}} = 11.36$  Hz,  $J_{\text{ax-ax}} = 8.0$  Hz,  $-\text{CH}_2\text{H}_2\text{OH}$ ), 4.68 (1 H, d,  $J = 12.03$  Hz,  $\text{PhCH}_2$ ), 5.11 (1 H, d,  $J = 12.03$  Hz,  $\text{PhCH}_2$ ), 5.28 (1 H, ddd,  $J_{1-7} = 6.04$  Hz,  $J_{1-8} = 8.84$  Hz,  $J_{1-9} = 1.76$  Hz, H-1), 6.46 (1 H, d,  $J_{4-5} = 8.21$  Hz, H-8), 6.66 (1 H, dd,  $J_{4-5} = 8.21$  Hz,  $J_{4-6} = 6.04$  Hz, H-7), 7.30–7.40 (7 H, m, H-Ar), 7.90 (2 H, d,  $J_{3-4} = 8.34$  Hz, H-2' and H-6');  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  21.85 ( $\text{CH}_3\text{Ar}$ ), 31.55 (C-6), 38.88 (C-6), 52.39 (C-1), 64.82 ( $\text{PhCH}_2$ ), 69.97 ( $\text{OCH}_2$ ), 88.17 (C-4), 127.80, 128.08, 128.18, 128.75, 129.09, 131.09 (C-8), 132.54 (C-7), 135.64, 137.66, 145.45, 170.37 (C=O); IR ( $\text{CHCl}_3$ ) 3671, 3642, 1725, 1595, 1225, 1173  $\text{cm}^{-1}$ ; MS  $m/e$  (EI) 217 (2), 216 ( $\text{M}^+ - \text{tBuNO}_2$ , 13), 165 (2), 125 (2), 91 (100);  $m/e$  (CI/ammonia) 431 ( $\text{MNH}_4^+$ , 23), 414 ( $\text{MH}^+$ , 100); HRMS calcd for  $\text{C}_{27}\text{H}_{34}\text{N}_2\text{O}_5$  ( $\text{MH}^+$ ) 414.1375, found 414.1378.

5-*endo*-[(*tert*-Butyldimethylsilyloxy)methyl]-4-methoxy-2-(4'-methylbenzenesulfonyl)-3-*oxo*-2-azabicyclo[2.2.2]oct-7-ene (9ah). This compound was prepared in accordance with the general procedure described previously. Thus, starting from a solution of alcohol (313 mg, 0.929 mmol) in  $\text{CH}_2\text{Cl}_2$  (15 mL), TBDMSOTf (0.5 mL), and Et<sub>3</sub>N (0.25 mL), we obtained 9ah as gummy solid (388 mg, 91%):  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  -0.02 (3 H, s,  $\text{CH}_3\text{Si}$ ), 0.00 (3 H, s,  $\text{CH}_3\text{Si}$ ), 0.83 (9 H, s,  $(\text{CH}_3)_2\text{CSi}$ ), 1.63 (1 H, ddd,  $J = 13.1, 4.6, 1.9$  Hz, H-6<sub>ax</sub>), 2.16 (2 H, m, H-5 and H-8<sub>ax</sub>), 2.43 (3 H, s,  $\text{CH}_3\text{Ar}$ ), 3.33 (1 H, dd,  $J = 9.9, 7.5$  Hz,  $\text{CH}_2\text{OSi}$ ), 3.68 (3 H, s,  $\text{CH}_3\text{O}$ ), 3.78 (1 H, dd,  $J = 9.7, 3.9$  Hz,  $\text{CH}_2\text{OSi}$ ), 5.25 (1 H, m, H-1), 6.21 (1 H, dd,  $J = 8.2, 1.8$  Hz, H-8),

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In the second part, the focus shifts to the analysis of the recorded data. It describes how the collected information can be used to identify trends, patterns, and potential areas of concern. The document stresses the need for a thorough review of the records to ensure that all data points are correctly interpreted and that any anomalies are properly investigated.

The third part of the document provides a detailed overview of the reporting process. It explains how the analyzed data should be compiled into a clear and concise report that can be used by management to make informed decisions. This section also discusses the importance of transparency and the need to provide a clear explanation of the findings and the basis for any conclusions drawn.

The final part of the document concludes with a summary of the key points discussed throughout the report. It reiterates the importance of maintaining accurate records and the need for a thorough analysis of the data. The document also provides a final statement on the overall findings and the recommendations for future actions to improve the accuracy and reliability of the financial reporting process.

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3.44 (1 H, dd,  $J = 8.2, 5.9$  Hz, H-7), 7.29 (2 H, d,  $J = 8.6$  Hz, tosyl H), 7.86 (2 H, d,  $J = 8.6$  Hz, tosyl H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  -5.40 ( $\text{CH}_2\text{Si}$ ), 16.16 ( $\text{Me}_2\text{CSi}$ ), 21.78 ( $\text{CH}_2\text{Ar}$ ), 25.85 ( $(\text{CH}_2)_2\text{CSi}$ ), 31.57 (C-8), 39.04 (C-5), 52.58 (C-1), 54.25 ( $\text{CH}_2\text{O}$ ), 62.09 ( $\text{CH}_2\text{OSi}$ ), 83.20 (C-4), 128.02 (C-2'), 129.64 (C-3'), 131.03 (C8/C-7), 135.58 (C-4'), 132.01 (C-8/C-7), 145.04 (C-1'), 172.40 (C-3); IR ( $\text{CHCl}_3$ ) 1728 (C=O) 1598, 1472, 1360, 1262, 1172, 1081  $\text{cm}^{-1}$ ; MS  $m/e$  (EI) 394 ( $\text{M}^+ - t\text{-Bu}$ , 20), 197 (30), 122 (100), 109 (38), 91 (32), 69 (41), 85 (34), 73 (45);  $m/e$  (CI/ammonia) 469 ( $\text{MNH}_4^+$ , 10), 453 (31), 452 ( $\text{MH}^+$ , 100), 355 (14), 339 (50), 140 (10), 122 (22), 79 (20); HRMS calcd for  $\text{C}_{18}\text{H}_{24}\text{NO}_6\text{SSi}$  ( $\text{M}^+ - t\text{-Bu}$ ) 394.1145, found 394.1152.

4-(Benzyloxy)-5-endo-[(*tert*-butyldimethylsilyloxy)-methyl]-2-(4'-methylbenzenesulfonyl)-3-oxo-2-azabicyclo[2.2.2]oct-7-ene (9bb). Triethylamine (0.027 mL, 0.274 mmol) was added to the solution of 4-(benzyloxy)-5-endo-(hydroxymethyl)-2-(4'-methylbenzenesulfonyl)-3-oxo-2-azabicyclo[2.2.2]oct-7-ene (103 mg, 0.249 mmol) in  $\text{CH}_2\text{Cl}_2$  (3 mL) at 0 °C, and after 5 min TBDMSOTf (0.038 mL, 0.259 mmol) was added via syringe. The reaction mixture was quenched with  $\text{H}_2\text{O}$  (5 mL) after 5 min and was extracted with  $\text{Et}_2\text{O}$  (3  $\times$  75 mL), dried ( $\text{MgSO}_4$ ), filtered, and concentrated to give a residue which was purified by column chromatography (silica gel 50%  $\text{EtOAc}$  in hexane) to give the title compound as a clear oil (128 mg, 98%).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  -0.01 (3 H, s,  $\text{CH}_3\text{Si}$ ), 0.03 (3 H, s,  $\text{CH}_3\text{Si}$ ), 0.85 (9 H, s,  $(\text{CH}_3)_3\text{CSi}$ ), 1.67-1.73 (2 H, m, H-6<sub>endo</sub>, H-5), 2.22-2.26 (1 H, m, H-6<sub>endo</sub>), 2.43 (3 H, s,  $\text{CH}_3\text{-C4'}$ ), 3.49 (1 H, dd,  $J_{\text{H-5,6}} = 10.0$  Hz,  $J_{\text{H-5,7}} = 6.84$  Hz,  $-\text{CH}_2\text{H}_6\text{OSi}$ ), 3.80 (1 H, dd,  $J_{\text{H-5,6}} = 10.0$  Hz,  $J_{\text{H-5,7}} = 2.78$  Hz,  $-\text{CH}_2\text{H}_5\text{OSi}$ ), 4.77 (1 H, d,  $J = 11.62$  Hz,  $\text{PhCH}_2$ ), 4.98 (1 H, d,  $J = 11.62$  Hz,  $\text{PhCH}_2$ ), 5.29 (1 H, m, H-1), 5.27 (1 H, d,  $J_{\text{H-1,2}} = 7.59$  Hz, H-8), 6.46 (1 H, dd,  $J_{\text{H-2,3}} = 7.59$  Hz,  $J_{\text{H-2,4}} = 6.16$  Hz, H-7), 7.27-7.43 (7 H, m, ArH), 7.80 (1 H, d,  $J_{\text{H-4,5}} = 8.04$  Hz, H-2' and H-6');  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  -5.38 ( $\text{CH}_2\text{Si}$ ), -5.33 ( $\text{CH}_2\text{Si}$ ), 16.50 ( $(\text{CH}_3)_2\text{CSi}$ ), 21.78 ( $\text{CH}_2\text{-C4'}$ ), 25.92 (C-H<sub>2</sub>CSi), 31.58 (C-5), 39.59 (C-6), 52.62 (C-1), 62.69 (C-9), 83.84 (C-10), 84.41 (C-4), 127.51, 127.89, 128.05, 128.48, 129.76, 131.02 (C-8), 132.49 (C-7), 135.93, 135.58, 145.10, 171.16 (C-3); IR ( $\text{CHCl}_3$ ) 1726 (C=O), 1595, 1472, 1360, 1090  $\text{cm}^{-1}$ ; MS  $m/e$  (EI) 229 (27), 189 (19), 187 (4), 155 (1), 115 (21), 113 (100), 91 (60), 67 (10);  $m/e$  (CI/ammonia) 545 ( $\text{MNH}_4^+$ , 1), 528 ( $\text{MH}^+$ , 28); HRMS calcd for  $\text{C}_{22}\text{H}_{24}\text{N}_2\text{O}_6\text{SSi}$  ( $\text{MNH}_4^+$ ) 545.2605, found 545.2499.

Methyl 6-[(*tert*-Butyldimethylsilyloxy)methyl]-1 $\beta$ -methoxy-4 $\alpha$ -[(4'-methylbenzenesulfonyl)amino]cyclohex-2-ene-1-carboxylate (10ah). *n*-BuLi (4.8 mmol) was added slowly to MeOH (15 mL), and the solution thus obtained was added to bicyclic lactam 9ab (380 mg, 0.842 mmol) at room temperature under dry  $\text{N}_2$  atmosphere. After 2 h, a workup procedure as described above followed by purification by flash chromatography (50%  $\text{Et}_2\text{O}$  in hexane) afforded 10ah as a white solid (368 mg, 90%); mp 106 °C;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  -0.01 (6 H, s, 2  $\times$   $\text{CH}_3\text{Si}$ ), 0.85 (9 H, s,  $(\text{CH}_3)_3\text{CSi}$ ), 1.64 (1 H, dt,  $J = 14.0, 3.1$  Hz, H-6 $\beta$ ), 1.79 (1 H, ddd,  $J = 5.3, 11.5, 6.3$  Hz, H-5 $\beta$ ), 2.25 (1 H, m, H-6 $\alpha$ ), 2.43 (3 H, s,  $\text{CH}_3\text{Ar}$ ), 3.29 (3 H, s,  $\text{CH}_3\text{O}$ ), 3.39 (1 H, dd,  $J = 10.8, 7.9$  Hz,  $\text{CH}_2\text{OSi}$ ), 3.89 (1 H, dd,  $J = 10.3, 6.2$  Hz,  $\text{CH}_2\text{OSi}$ ), 3.73 (3 H, s,  $\text{CO}_2\text{CH}_3$ ), 3.94 (1 H, m, H-4), 4.81 (1 H, bd,  $J = 8.0$  Hz, NH), 5.83 (2 H, m, H-2 and H-3), 7.31 (2 H, d,  $J = 8.0$  Hz, tosyl H), 7.77 (2 H, d,  $J = 8.0$  Hz, tosyl H);  $^{13}\text{C}$  ( $\text{CDCl}_3$ )  $\delta$  -5.40 ( $\text{CH}_2\text{Si}$ ), 18.38 ( $\text{Me}_2\text{CSi}$ ), 21.59 ( $\text{CH}_2\text{Ar}$ ), 25.99 ( $(\text{CH}_3)_3\text{CSi}$ ), 27.79 (C-5), 39.76 (C-6), 47.22 (C-4), 52.20 (ester  $\text{CH}_3$ ), 53.00 (ether  $\text{CH}_3$ ), 62.11 ( $\text{CH}_2\text{O}$ ), 78.52 (C-1), 127.02 (C-2'), 128.60 (C-2/C-3), 129.78 (C-3'), 131.96 (C-2/C-3), 138.14 (C-4'), 143.36 (C-1'), 173.22 ( $\text{CO}_2\text{Me}$ ); IR ( $\text{CHCl}_3$ ) 3362 (NH), 1744 (C=O), 1696 (C=C), 1413, 1337, 1221, 1160, 1091  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{22}\text{H}_{28}\text{N}_2\text{O}_6\text{SSi}$ : C, 57.11; H, 7.71; N, 2.90. Found: C, 56.98; H, 7.75; N, 2.94.

Methyl 1 $\beta$ -(Benzyloxy)-6 $\beta$ -[(*tert*-butyldimethylsilyloxy)methyl]-4 $\alpha$ -(4'-methylbenzenesulfonamido)cyclohex-2-ene-1-carboxylate (10bh). To a solution of LiOMe (2.26 mL of

*n*-BuLi 1.6 M in hexanes in 15 mL of anhydrous MeOH) at 0 °C was added a solution of compound 9bh (128 mg, 0.242 mmol) in  $\text{CH}_2\text{Cl}_2$  (2 mL) via cannula. The reaction mixture was warmed to room temperature and stirred for 16 h, quenched with saturated aqueous  $\text{NH}_4\text{Cl}$  (5 mL), extracted with  $\text{CH}_2\text{Cl}_2$  (3  $\times$  50 mL), dried ( $\text{MgSO}_4$ ), filtered, and concentrated, and the resultant residue was purified by column chromatography (50%  $\text{EtOAc}$  in hexanes) to give 10bh as a clear oil (117.3 mg, 67%).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  -0.02 (3 H, s,  $\text{CH}_3\text{Si}$ ), -0.016 (3 H, s,  $\text{CH}_3\text{Si}$ ), 0.84 (9 H, s,  $(\text{CH}_3)_3\text{CSi}$ ), 1.60 (1 H, m, H-6 $\beta$ ), 1.84 (1 H, ddd,  $J_{\text{H-5,6}} = 13.6$  Hz,  $J_{\text{H-5,7}} = 12.1$  Hz,  $J_{\text{H-5,8}} = 5.29$  Hz, H-5 $\alpha$ ), 2.30-2.37 (1 H, m, H-6 $\alpha$ ), 2.44 (3 H, s,  $\text{CH}_3\text{-C4'}$ ), 3.36 (1 H, dd,  $J_{\text{H-5,6}} = 10.17$  Hz,  $J_{\text{H-5,7}} = 7.32$  Hz,  $-\text{CH}_2\text{H}_6\text{OSi}$ ), 3.72 (3 H, s,  $\text{CH}_3\text{O}$ ), 3.77 (1 H, dd,  $J_{\text{H-5,6}} = 10.17$  Hz,  $J_{\text{H-5,7}} = 6.76$  Hz,  $-\text{CH}_2\text{H}_5\text{OSi}$ ), 3.94 (1 H, m, H-4), 4.39 (1 H, d,  $J = 10.78$  Hz,  $\text{PhCH}_2$ ), 4.89 (1 H, d,  $J = 8.62$  Hz, NH), 4.70 (1 H, d,  $J = 10.78$  Hz,  $\text{PhCH}_2$ ), 5.83 (1 H, ddd,  $J_{\text{H-2,3}} = 9.81$  Hz,  $J_{\text{H-2,4}} = 4.44$  Hz,  $J_{\text{H-2,5}} = 3.53$  Hz, H-3), 5.98 (1 H, dd,  $J_{\text{H-3,4}} = 9.91$  Hz,  $J_{\text{H-3,5}} = 1.46$  Hz, H-2), 7.27-7.31 (7 H, m), 7.77 (2 H, d,  $J_{\text{H-4,5}} = 8.31$  Hz, H-2' and H-6');  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  -5.44 ( $\text{CH}_2\text{Si}$ ), -5.31 ( $\text{CH}_2\text{Si}$ ), 19.06 ( $(\text{CH}_3)_2\text{CSi}$ ), 21.66 ( $\text{CH}_2\text{-C4'}$ ), 28.10 ( $(\text{CH}_3)_3\text{CSi}$ ), 27.45 (C-5), 40.05, 47.40 (C-4, C-6), 52.29 ( $\text{CH}_3\text{O}$ ), 62.58 ( $\text{CH}_2\text{OSi}$ ), 67.23 ( $\text{CH}_2\text{OPh}$ ), 78.13 (C-1), 127.18, 127.45, 127.49, 128.27, 129.27 (C-3), 129.93, 131.85 (C-2), 138.07, 139.24, 143.58, 172.99 (C=O); IR ( $\text{CHCl}_3$ ) 1743, 1695, 1397, 1225, 1155  $\text{cm}^{-1}$ ; MS  $m/e$  (EI) 603 (2), 602 ( $\text{M}^+ - t\text{-Bu}$ , 4), 395 (2), 394 (4), 171 (14), 166 (3), 115 (15), 113 (25), 107 (2), 91 (100), 69 (17), 57 (20);  $m/e$  (CI/ammonia) 677 ( $\text{MNH}_4^+$ , 4), 560 ( $\text{MH}^+$ , 8); HRMS calcd for  $\text{C}_{28}\text{H}_{32}\text{N}_2\text{O}_6\text{SSi}$  ( $\text{M}^+ - t\text{-Bu}$ ) 502.1720, found 502.1722.

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**Registry No.** 1a, 141667-29-0; 1b, 141667-30-3; 1c, 141667-31-4; 1d, 141667-32-5; 2a (EWG =  $\text{CH}_2\text{OH}$ ), 141667-33-6; 2ag, 141667-34-7; epi-2ag, 141725-48-6; 2ab, 141667-35-8; 2ai, 141667-36-9; 2af, 141667-37-0; 2b (EWG =  $\text{CH}_2\text{OH}$ ), 141667-38-1; 2bg, 141667-39-2; epi-2bg, 141725-49-7; 2bh, 141667-40-5; 2c (EWG =  $\text{CH}_2\text{OH}$ ), 141667-41-8; 2cg, 141667-42-7; 2ch, 141667-43-8; 2ci, 141667-44-9; 2ej, 141667-45-0; 2dg, 141667-46-1; epi-2dg, 141725-50-0; 2dh, 141667-47-2; 3, 141667-48-3; 3 (EWG =  $\text{CH}_2\text{OH}$ ), 141667-49-4; 4, 141667-50-7; 5, 141667-51-8; 6, 141667-52-3; 7, 141667-53-0; 7 (Z = H), 141667-54-1; 8, 141667-55-2; 9ah, 141667-56-3; 9bh, 141667-57-4; 10ah, 141684-41-5; 10bh, 141684-42-6; 3-(benzyloxy)-2-pyridone, 94475-64-6; 3-[(*tert*-butyldimethylsilyloxy)-2-pyridone, 141667-58-5; 3-(4-methylbenzenesulfonyl)-2-pyridone, 107383-65-3; 3-methoxy-1-(methanesulfonyl)-2-pyridone, 141667-59-6; 3-[(*tert*-butyldimethylsilyloxy)-1-(methanesulfonyl)-2-pyridone, 141667-60-9; 1-(methanesulfonyl)-3-(4'-methylbenzenesulfonyl)-2-pyridone, 141667-61-0; 2-[(4'-methylbenzenesulfonyloxy)pyridine, 57785-36-1; 3-methoxy-2-[(4'-methylbenzenesulfonyloxy)pyridine, 141667-62-1; 3-methoxy-2-[(methanesulfonyloxy)pyridine, 141667-63-2; 3-[(*tert*-butyldimethylsilyloxy)-2-[(methanesulfonyloxy)pyridine, 141667-64-3; dimethyl 1 $\beta$ -methoxy-4 $\alpha$ -[(4'-methylbenzenesulfonyl)amino]cyclohex-5-ene-1,2-dicarboxylate, 141667-65-4; 3-methoxy-2-pyridone, 20928-68-6; 2,3-dihydropyridine, 16687-04-2; nitroethylene, 3668-64-0; acrolein, 107-02-8; methyl acrylate, 96-33-3; methyl vinyl ketone, 78-94-4; methacrolein, 78-85-3.

**Supplementary Material Available:** Characterization of new compounds by NMR (41 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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**SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO  
DIVISION DE NUEVAS CREACIONES**

REF: **EXPEDIENTE No. 05.050.160  
SOLICITUD DE PATENTE A NOMBRE DE THE PROCTER &  
GAMBLE COMPANY.**

Yo, **JIMENA ESCOBAR URIBE**, identificada como aparece al pie de mi firma, domiciliada en la Carrera 11 No. 86-53 Piso 6, atentamente digo a usted que sustituyo el poder con que obro a la doctora **DILIA RODRIGUEZ D'ALEMAN**, domiciliada en Bogotá, D.C., portadora de la tarjeta profesional No. 20.824, con las mismas facultades con que me fueron conferidas para este caso.



**JIMENA ESCOBAR URIBE**

C.C. 39.779.452 de Usaquén

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Acepto sustitución

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# PRESENTACION PERSONAL

El anterior escrito fue presentado ante el  
NOTARIO ONCE (E) DEL CIRCULO DE BOGOTA, D.C.  
personalmente por **JOSE ALVARO COPAR**

quien exhibió la c.c. **EDUARDO JACQUE**  
y Tarjeta Profesional No. **68228** C.S.J.

Firma

Fecha

3 JUN 2008

Nelson J. Sánchez García  
NOTARIO (E)

