tageous in that it requires neither cryogenic temperatures nor heavy metals.

Experimental Section[8-10]

Oxidation of 1 to 2 (Large Scale). A flame-dried, two-necked, 500-mL round-bottomed flask equipped with an N_2 inlet, dropping funnel, and mechanical stirrer was charged with alcohol 1 (64.5 g, 375 mmol) in CH_2Cl_2 (0.2 M in starting alcohol). The flask was immersed in an ice–water bath. Dimethyl sulfoxide (58.5 g, 750 mmol, 2 equiv) and phosphorus pentoxide (95.85 g, 675 mmol, 1.8 equiv) were added sequentially. The reaction mixture was allowed to stir and warm to room temperature until disappearance of starting material by TLC (30 min). The flask was immersed again in the ice–water bath; then triethylamine (132.6 g, 1322 mmol, 3.5 eq) was added dropwise over 10 min. Stirring was continued for 30 min. The reaction was quenched with 10% aqueous HCl and extracted with CH_2Cl_2. The organic extracts were washed with saturated aqueous NaCl, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The residue was distilled bulb-to-bulb (bp_{10} 140–150 °C) to give 54 g (85%) of **2** as a colorless oil, TLC R_f (20% EtOAc/hexane) 0.54. ^1H NMR δ: 1.62 (d, 6.6 Hz, 3 H); 2.3 (q, 7.4 Hz, 2 H); 2.6 (t, 7.3 Hz, 2 H); 3.5 (s, 2 H); 3.7 (s, 3 H); 5.3–5.5 (m, 2 H). ^{13}C NMR δ: 12.6, q; 20.9, t; 42.6, t; 48.9, t; 52.2, q; 125.4, d; 128.0, d; 167.5, s; 202.2, s. IR cm^{-1}: 3020, 1745, 1715, 1655, 1540, 1450, 1325, 1270, 1050. MS m/z (relative intensity): 170 (43); 154 (33); 123 (25); 101 (100).

Oxidation of 3 to 4 (Small Scale). A flame-dried, one-necked, 25-mL round-bottomed flask equipped with an N_2 inlet was charged with alcohol **3** (1.0 g, 4.1 mmol) in CH_2Cl_2 (0.2 M in starting alcohol). The flask was immersed in an ice–water bath. Dimethyl sulfoxide (643 mg, 8.25 mmol, 2 equiv) and phosphorus pentoxide (1.17 g, 8.25 mmol, 2.0 equiv) were added sequentially. The reaction mixture was allowed to stir and warm to room temperature until disappearance of starting material by TLC (30 min). The flask was immersed again in the ice–water bath; then triethylamine (2.02 mL, 14.4 mmol, 3.5 equiv) was added dropwise over 1 min. Stirring was continued for 30 min. The reaction was quenched with 10% aqueous HCl and extracted with CH_2Cl_2. The organic extracts were washed with saturated aqueous NaCl, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The residue was chromatographed[11] on 50 g of TLC mesh silica gel to give 4 (826 mg, 83% yield) as a white solid, TLC R_f (20% EtOAc/hexane) 0.67. ^1H NMR δ: 0.9 (t, 5.3 Hz, 3 H); 1.0–1.6 (m, 26 H); 2.4 (t, 7.1 Hz, 2 H); 9.7 (s, 1 H). ^{13}C NMR δ: 14.0, q; 22.0, t; 22.6, t; 29.1, t; 29.3, t; 29.4, t; 29.5, t (×2); 29.6, t (×5); 31.9, t; 43.9, t; 202.7, d. IR cm^{-1}: 2976, 2853, 2715, 1730, 1466, 1350.

Preparation of 3-Pentadecanone (8). This same small-scale procedure was used to oxidize 130 mg of alcohol **7**, yielding, after chromatography, ketone **8** (105 mg, 81% yield), TLC R_f (20% EtOAc/hexane) 0.68. ^1H NMR δ: 0.9 (t, 5.8 Hz, 3 H); 1.05 (t, 7.3 Hz, 3 H); 1.3 (m, 18 H); 1.6 (m, 2 H); 2.4 (m, 4 H). ^{13}C NMR δ: 7.9, q; 14.1, q; 22.7, t; 24.0, t; 29.4, t (×2); 29.5, t (×2); 29.9, t (×3); 31.9, t; 35.9, t; 42.5, t; 212, s. IR cm^{-1}: 2955, 2855, 1719, 1450, 1102. MS m/z (relative intensity): 198 (43); 141 (10); 85 (31).

Preparation of 1-Phenylheptan-1-one (12). This same small-scale procedure was used to oxidize 939 mg of alcohol **11**, yielding, after chromatography, ketone **12** (768 mg, 83% yield), TLC R_f (20% EtOAc/hexane) 0.61. ^1H NMR δ: 0.9 (t, 6.4 Hz, 3 H); 1.3–1.4 (m, 8 H); 2.9 (t, 7.1 Hz, 2 H); 7.5 (m, 3 H); 7.9 (d, 8.2 Hz, 2 H). ^{13}C NMR δ: 14.0, q; 22.5, t; 24.4, t; 29.0, t; 31.7, t; 38.6, t; 128.0, d (×2); 128.5, d (×2); 132.8, d; 137.2, s; 200.5, s. IR cm^{-1}: 3062, 2970, 2850, 1694, 1581, 1223, 974.

Acknowledgment. We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this work.

(8) For the preparation of **13** and **14**, see: Taber, D. F.; Raman, K.; Gaul, M. D. *J. Org. Chem.* **1987**, *52*, 28.

(9) For general experimental procedures, see ref 8, above.

(10) The authenticity of products **6** and **10** was established by direct comparison (^1H NMR, TLC) with the commercially available ketones.

(11) Taber, D. F. *J. Org. Chem.* **1982**, *47*, 1351.

Registry No. 1, 110874-82-3; 2, 110874-83-4; 3, 36653-82-4; 4, 629-80-1; 5, 1724-39-6; 6, 830-13-7; 7, 53346-71-7; 8, 18787-66-1; 9, 1490-04-6; 10, 10458-14-7; 11, 614-54-0; 12, 1671-75-6; 13, 86852-75-7; 14, 111001-29-7; DMSO, 67-68-5; Et_3N, 121-44-8; P_2O_5, 1314-56-3.

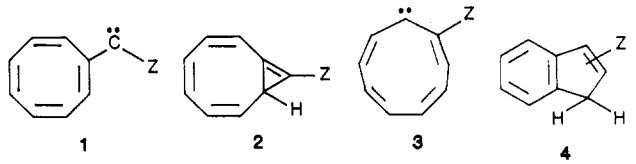
Simple Entries to 1*H*-Cyclooctapyrazoles. A New 8,5-Heterocyclic System

D. C. Sanders, A. Marczak, J. L. Melendez, and H. Shechter*

Department of Chemistry, The Ohio State University, Columbus, Ohio 43210

Received July 14, 1986

An interest of this laboratory is the electrophilic behavior of 1,3,5,7-cyclooctatetraen-1-ylmethylenes (**1**) and the rearrangements of **1** to bicyclo[6.1.0]nona-2,4,6,8-tetraenes (**2**), cyclononatetraenylidenes (**3**), and then indenes (**4**). As part of this study we now describe the preparations



1 2 3 4

(eq 1) and the pyrolytic decompositions (eq 2) of sodium salts (**7a–c**) of *p*-tosylhydrazones (**6a–c**) of 1,3,5,7-cyclooctatetraene-1-carboxaldehyde (**5a**), 1,3,5,7-cyclooctatetraen-1-yl methyl ketone (**5b**) and 1,3,5,7-cyclooctatetraen-1-yl phenyl ketone (**5c**).[1] Sodium *p*-tosylhydrazonates **7a–c** are obtained readily (eq 1) by reactions of *p*-tosylhydrazine with **5a–c**, respectively, and then displacement of hydrogen from **6a–c** with sodium hydride.

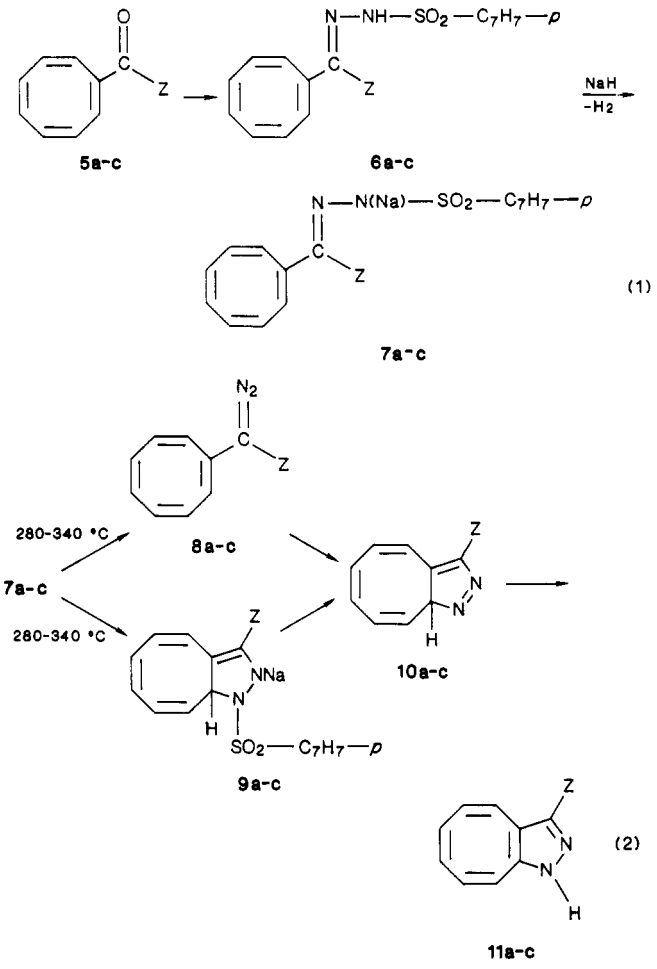
Vacuum thermolyses of **7a–c** (eq 2) are presently reported because elimination of sodium *p*-toluenesulfinate, retention of nitrogen, heterocyclization, and prototropic isomerization occur efficiently (76–99%) at 280–340 °C (0.1–0.3 Torr) to give 1*H*-cyclooctapyrazoles **11a–c**, members of a new system of 8,5-heterocycles. At the temperatures necessary for effective decomposition of **7a–c** (eq 2), it cannot be concluded whether **8a–c** or/and **9a–c** are the reaction intermediates leading to **10a–c**.[2] Cyclooctapyrazoles **11a–c** are acidic crystalline solids whose gross structures are derived from their elemental analyses, their IR, ^1H NMR, UV, and mass spectra, and their origins. The products are assigned dominantly as tautomers **11a–c** in equilibrium with **12a–c**.[3] The choices as **11a–c** are

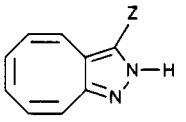
(1) (a) Decomposition of salts of sulfonylhydrazones of aldehydes and ketones in aprotic environments to give diazo compounds and/or their products is a widely used method for effecting carbenic reaction processes. (b) Bamford, W. R.; Stevens, T. C. *J. Chem. Soc.* **1952**, 4735–4740. (c) Powell, J. W.; Whiting, M. C. *Tetrahedron* **1959**, *7*, 305–310. (d) Friedman, L.; Shechter, H. *J. Am. Chem. Soc.* **1959**, *81*, 5512–5513. (e) Kaufman, G. M.; Smith, J. A.; Van der Stouw, G. G.; Shechter, H. *J. Am. Chem. Soc.* **1965**, *87*, 935–936.

(2) (a) Intramolecular processes leading to pyrazoles have been reported which are similar to those proposed in equation 2.[2b-e] (b) Closs, G. L.; Böll, W. A. *Angew. Chem., Int. Ed. Engl.* **1963**, *2*, 399. (c) Closs, G. L.; Böll, W. A. *J. Am. Chem. Soc.* **1963**, *85*, 3904–3905. (d) Bartlett, R. K.; Stevens, T. S. *J. Chem. Soc. C* **1967**, 1964–1968. (e) Bailey, R. J.; Shechter, H. *J. Am. Chem. Soc.* **1974**, *96*, 8116–8117.

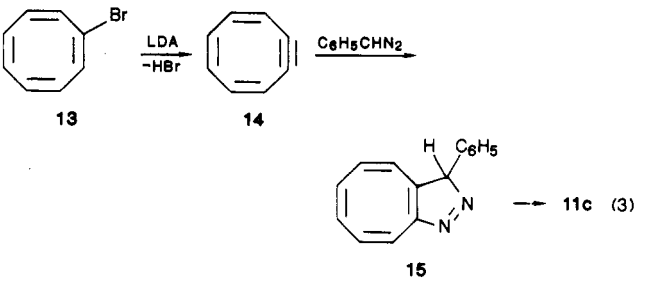
(3) (a) Annular tautomerism in pyrazoles is discussed by: Katritsky, A. R.; Lagowski, J. M. In *Advances in Heterocyclic Chemistry*; Katritsky, A. R., Boulton, A. J., Eds.; Academic: New York, 1963; Vol. 2, pp 27–81. Katritsky, A. R.; Lagowski, J. M. In *Comprehensive Heterocyclic Chemistry*; Katritsky, A. R., Rees, C. W., Eds.; Pergamon: Oxford, 1984; Vol. 5(4A), pp 1–38. (b) The proposition is advanced that, since the NH moiety is closer to the cycloocta system and more conjugating in a 1*H*- than in a 2*H*-cyclooctapyrazole, there will be greater 10-π electron cyclooctatetraenoid delocalization in **11a–c** than in a comparable **12a–c**.[5]

0022-3263/87/1952-5622$01.50/0





based on the presumptions of (1) greater delocalization within their cycloocta units as compared to **12a–c**, (2) the NH moiety is a more effective resonance donor in **11a–c** than in **12a–c**,[3] and (3) the ortho-quinoidal character is less in **11a–c** than in **12a–c**.[4,5] Of further note is that 3-phenyl-1*H*-cyclooctapyrazole (**11c**, eq 3) is produced (>60% yield) by (1) 1,3-dipolar cycloaddition of phenyldiazomethane to 1,3,5-cyclooctatrien-7-yne (**14**) as generated in situ at −40–0 °C from 1-bromo-1,3,5,7-cyclooctatetraene (**13**) and lithium diisopropylamide (LDA)[6] and (2) isomerization of the 3-phenyl-3*H*-cyclooctapyrazole (**15**) formed.



Studies of the acidities, the basicities, and the alkylation, acylation, substitution, photolysis, and cycloaddition reactions of **11a–c** and addition of varied diazo compounds to **14** are in progress.

Experimental Section

Materials. 1,3,5,7-Cyclooctatetraene-1-carboxaldehyde (**5a**) was prepared by reaction of diisobutylaluminum hydride (Dibal-H) with 1,3,5,7-cyclooctatetraene-1-carbonitrile[7a,b] as derived from Beckmann fragmentation of bicyclo[4.2.1]nona-2,4,7-trien-9-one oxime with *p*-tosyl chloride and pyridine at 0 °C. 1,3,5,7-Cyclooctatetraen-1-yl methyl ketone (**5b**) was obtained by oxidation of 1,3,5,7-cyclooctatetraene-1-ethanol with chromic oxide in aqueous sulfuric acid.[8] Synthesis of 1,3,5,7-cyclooctatetraen-1-yl phenyl ketone (**5c**)[9] was accomplished by (1) reaction of 1-bromo-1,3,5,7-cyclooctatetrarene with *n*-butyllithium in ethyl ether at −70 °C, (2) addition of the 1,3,5,7-cyclooctatetraen-1-yllithium generated to benzonitrile at −70 °C in ethyl ether, and (3) warming and then hydrolysis of the reaction adduct with aqueous hydrochloric acid.

1,3,5,7-Cyclooctatetraene-1-carboxaldehyde (5a). Dibal-H (17.6 g, 25% in hexane, 0.033 mol) was injected into a rapidly stirred solution of 1,3,5,7-cyclooctatetraene-1-carbonitrile (2.0 g, 0.016 mol) in ethyl ether (40 mL) at −78 °C under nitrogen. The mixture darkened as injection was made. The reaction solution was stirred for 3 h, methanolyzed (2 mL), acidified with 10% sulfuric acid (2 mL), and then poured into water. After the products had been extracted with ethyl ether, the organic extracts were combined, washed with brine, dried ($MgSO_4$), filtered, evaporated, and chromatographed on silica gel to give **5a**[7c] (1.6 g, 80%) as a slightly yellow liquid, which was stored at −78 °C until use: IR (liquid film) 1685 (C=O stretch), 2720, 2840 (C-*H*=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.40 (s, 1 H, CO*H*), 6.5–5.5 (m, 7 H, *H*C=C*H*); mass spectrum, *m/e* 132.

A sample of **5a** (0.1 g) in ethanol (1 mL), on addition to (2,4-dinitrophenyl)hydrazine (0.15 g) in water (0.75 mL), concentrated sulfuric acid (0.5 mL), and 95% ethanol (2.5 mL), yielded, after crystallization from methylene chloride/hexane, 1,3,5,7-cyclooctatetraene-1-carboxaldehyde (2,4-dinitrophenyl)hydrazone (0.13 g, 52%): orange crystals; mp 218–219 °C. Anal. Calcd for $C_{15}H_{12}N_4O_4$: C, 57.70; H, 3.87. Found: C, 57.42; H, 3.63.

1,3,5,7-Cyclooctatetraene-1-carboxaldehyde *p*-Tosylhydrazone (6a). A solution of **5a** (1.22 g, 0.0092 mol) and *p*-

(4) (a) Ortho-quinoidal derivatives such as 2*H*-indole (isoindole, 1*H*-benzo[*c*]pyrrole), benzo[*c*]furan (isobenzofuran), and benzo[*c*]thiophene (isobenzothiophene) are much less stable than their [*b*] isomers: indole, benzo[*b*]furan, and benzo[*b*]thiophene, respectively. For a discussion of the differences in the behavior and the theory of these heterocyclic systems, see: (b) White, J. D.; Mann, M. E. In *Advances in Heterocyclic Chemistry*; Katritsky, A. R., Boulton, A. J., Eds.; Academic: New York, 1969; Vol. 10, pp 113–147. (c) Bonnett, R.; North, S. A. In *Advances in Heterocyclic Chemistry*; Katritsky, A. R., Boulton, A. J., Eds.; Academic: New York, 1981; Vol. 29, pp 341–399. (d) Friedrichsen, W. In *Advances in Heterocyclic Chemistry*; Katritsky, A. R., Boulton, A. J. Eds.; Academic: New York, 1980; Vol. 26, 135–241. (e) Iddon, B. In *Advances in Heterocyclic Chemistry*; Katritsky, A. R., Boulton, A. J., Eds.; Academic: New York, 1972; Vol. 14, pp 331–381.

(5) X-ray crystallography, further spectral analyses, and varied calculations for **11a–c** and their N-substituted derivatives and isomers **12a–c** are to be initiated.

(6) (a) 1,3,5-Cyclooctatrien-7-yne (**14**) has been previously generated from **13** and potassium *tert*-butoxide in tetrahydrofuran and trapped by dipolar addition of furan, tetraphenylcyclopentadienone, 1,3-diphenylisobenzofuran, and 1-(*N*,*N*-diethylamino)buta-1,3-diene.[6b,c] Additions of other conjugated dienes and various alcohols and amines to **14** also occur readily.[6d–g] (b) Krebs, A. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 953–954. (c) Krebs, A.; Byrd, D. *Justus Liebigs Ann. Chem.* **1967**, *707*, 66–74. (d) Lankey, A. S.; Ogliaruso, M. A. *J. Org. Chem.* **1971**, *36*, 3339–3342. (e) Elix, J. A.; Sargent, M. V. *J. Am. Chem. Soc.* **1969**, *91*, 4734–4739. (f) Elix, J. A.; Sargent, M. V.; Sondheimer, F. *J. Am. Chem. Soc.* **1970**, *92*, 962–968. (g) Harmon, C. A.; Streitwieser, A. *J. Org. Chem.* **1973**, *38*, 549.

(7) (a) Antkowiak, T. A.; Sanders, D. C.; Trimitsis, G. B.; Press, J. B.; Shechter, H. *J. Am. Chem. Soc.* **1972**, *94*, 5366–5373. (b) 1,3,5,7-Cyclooctatetraene-1-carbonitrile has also been prepared from **13**, potassium cyanide, and $K_4Ni_2(CN)_6$.[6g] (c) See also: Paquette, L. A.; Henzel, K. A. *J. Am. Chem. Soc.* **1975**, *97*, 4649–4658.

(8) Cope, A. C.; Pike, R. M. *J. Am. Chem. Soc.* **1953**, *75*, 3220–3223.

(9) (a) Cope, A. C.; Marshall, D. J. *J. Am. Chem. Soc.* **1953**, *75*, 3208–3211. (b) Houghton, R. P.; Waight, E. S. *J. Chem. Soc. C* **1969**, 978–981.

tosylhydrazine (1.73 g, 0.0093 mol) in methanol (8 mL) at room temperature for 2 h was concentrated, chromatographed on silica gel with 1:1 chloroform/hexane as the developer, and then recrystallized from methylene chloride/hexane to yield **6a** (2.21 g, 80%) as light yellow crystals: mp 114–116 °C; ^{1}H NMR (DMSO-d_6) δ 8.42 (s, 1 H, H at C-9), 7.13–7.94 (m, 5 H, aromatic *H* and N*H*), 6.10–5.64 (m, 7 H, cycloocta-*HC*=C*H*), and 2.40 (s, 3 H, CH_3). Anal. Calcd for $C_{16}H_{16}N_2SO_2$: C, 63.97; H, 5.37; N, 9.32. Found: C, 64.30; H, 5.46; N, 9.45.

1*H*-Cyclooctapyrazole (11a). Sodium hydride (0.127 g of 57% NaH in mineral oil, 0.0032 mol) was added slowly to **6a** (0.87 g, 0.0029 mol) in methylene chloride (20 mL) at 0 °C. After evolution of hydrogen ceased, the solvent was stripped at reduced pressure leaving sodium salt **7a** as a white powder coated on the flask wall. The flask was attached via an adapter (partially packed with glass wool to prevent spatter entrainment) to a vacuum system. Upon decomposing **7a** at 280 °C (0.3 Torr), a yellow liquid collected in the adapter and on the glass wool. The condensate solidified on cooling and was dissolved in methylene chloride. Concentration and recrystallization of the product from methylene chloride/hexane yielded yellow needles of **11a** (0.32 g, 76%): mp 103–105 °C; IR (KBr) 3270 cm^{-1} (N–H stretch); ^{1}H NMR ($CDCl_3$) δ 8.4 (s, 1 H, N*H*, the resonance is washed out by D_2O), 7.20 (s, 1 H, H at C-9) and 6.20–5.76 (m, 6 H, cycloocta-HC=C*H*); UV λ_{max} (95% C_2H_5OH) 209 (ϵ 6,040), 226 (9,760), 264 (14,180), 271 (13,960), and 283 (7,750); mass spectrum, *m/e* 144; exact mass calcd 144.0688, found 144.0687. Anal. Calcd for $C_9H_8N_2$: C, 74.97; H, 5.91. Found: C, 74.97; H, 5.80.

1,3,5,7-Cyclooctatetraen-1-yl Methyl Ketone *p*-Tosylhydrazone (6b). A solution of **5b** (2.08 g, 14.2 mmol) in absolute methanol (5 mL) was added to a warm mixture of *p*-tosylhydrazine (2.52 g, 14.2 mmol) in methanol (13 mL) containing concentrated hydrochloric acid (1 drop). After ~0.5 h, a yellow precipitate (2.36 g, 53%) of **6b** formed: mp 166–166.5 °C dec; ^{1}H NMR (DMSO-d_6) δ 7.28–7.92 (m, 4 H, aromatic *H*), 5.8 with shoulders at 6.08 and 6.2 (m, 7 H, HC=C*H*), 1.93 (s, 3 H, CH_3); mass spectrum, *m/e* 314.1. Anal. Calcd for $C_{17}H_{18}N_2SO_2$: C, 64.94; H, 5.77; N, 8.91. Found: C, 65.10; H, 5.76; N, 8.99.

3-Methyl-1*H*-cyclooctapyrazole (11b). A solution of **6b** (1.6 g, 5.1 mmol) in methylene chloride (20 mL) was added to a slurry of sodium hydride (57% NaH in mineral oil; 0.22 g, 5.1 mmol; washed well with pentane to remove the mineral oil) in methylene chloride (20 mL). Stirring the mixture at room temperature for 2.5 h and rotary evaporation gave **7b**, a yellow solid (dec ~100 °C). The reactor flask was attached to an adapter, a series of traps, and a vacuum system. Decomposition of **7b** was effected at 285 °C (0.2 Torr). The condensate in the adapter was dissolved in methylene chloride, filtered, concentrated, and recrystallized from hexane/methylene chloride to give **11c** (0.80 g, 99%), a yellow solid: mp 121 °C (from methylene chloride/hexane); IR (KBr) 3170 cm^{-1} (N–H stretch); ^{1}H NMR ($CDCl_3$) δ 12.04 (s, 1 H, N*H*, the absorption disappears in D_2O), 6.2–5.6 (m, 6 H, cycloocta-*HC*=C*H*), and 2.16 (s, 3 H, CH_3); mass spectrum, *m/e* 158.2. Anal. Calcd for $C_{10}H_{10}N_2$: C, 75.92; H, 6.37. Found: C, 75.48; H, 6.37.

1,3,5,7-Cyclooctatetraen-1-yl Phenyl Ketone *p*-Tosylhydrazone (6c). Reaction of **5c** (1.85 g, 8.93 mmol) and *p*-tosylhydrazine (1.66 g, 8.93 mmole) in methanol (7 mL) containing hydrochloric acid (1 drop) yielded yellow crystals of **6c** (2.63 g, 78%): mp 175 °C (from EtOH, dec); ^{1}H NMR (DMSO-d_6) δ 7.8–6.9 (m, 10 H, aromatic H and NH), 5.82 (m, 7 H, cycloocta-*HC*=C*H*), and 2.45 (s, 3 H, CH_3). Anal. Calcd for $C_{22}H_{20}SO_2N_2$: C, 70.19; H, 5.36; N, 7.44; S, 8.52. Found: C, 70.01; H, 5.40; N, 7.44; S, 8.58.

3-Phenyl-1*H*-cyclooctapyrazole (11c) from 6c. To 6c (1.40 g, 3.72 mmol) in methylene chloride (20 mL) was added sodium hydride (0.16 g of 57% NaH in mineral oil, 3.72 mmol; washed with pentane). After gas evolution ceased, the solvent was rotary evaporated to give **7c**, a yellow solid, mp >265 °C dec. (Acidification of **7c** with hydrochloric acid yielded **6c** quantitatively.) Decomposition of **7c** [340 °C (0.1 Torr)] in the adapter–trap–vacuum system and crystallization of the volatilate from cyclohexane yielded **11c** (0.80 g, 95%): a yellow solid; mp 96–99 °C; IR (KBr) 3230 cm^{-1} (N–H stretch); ^{1}H NMR ($CDCl_3$) δ 10.8 (br s, 1 H, N*H*, there is no N*H* absorption in D_2O), 5.9–5.6 (m, 6 H, cycloocta-*HC*=C*H*), and 7.4–7.2 (m, 5 H, aromatic *H*); mass spectrum, *m/e* 220.1. Anal. Calcd for $C_{15}H_{12}N_2$: C, 81.78; H, 5.50; N, 12.71. Found: C, 81.61; H, 5.58; N, 12.55.

3-Phenyl-1*H*-cyclooctapyrazole (11c) from 14 and Phenyldiazomethane. *n*-Butyllithium (3.4 mL, 1.6 M in hexane, 5.4 mmol) was syringed into a solution of diisopropylamine (0.55 g, 0.54 mmol) and tetrahydrofuran (10 mL) at room temperature. The mixture was cooled to −78 °C and then added to a solution of 1-bromo-1,3,5,7-cyclooctatetraene (**13**; 1.00 g, 5.4 mmol) and phenyldiazomethane (1.0 g, 8.6 mmol) in tetrahydrofuran (25 mL) at −40 °C. The mixture was kept at −40 °C for 1 h, then allowed to warm slowly to room temperature, concentrated at reduced pressure, and diluted with ethyl ether. After the ether solution had been washed with water, dried (Na_2SO_4), and concentrated, the residue was crystallized from hexane to give **11c** (0.71 g, 60%, mp 97–99 °C) identical with that obtained by thermal decomposition of **7c**.

Acknowledgment. We thank the National Science Foundation and the National Institutes of Health for support of this research.

Registry No. **5a**, 30844-12-3; **5a** (DNPH), 110661-69-3; **5b**, 6004-57-5; **5c**, 6004-58-6; **6a**, 110661-70-6; **6b**, 110661-72-8; **6c**, 110661-75-1; **7a**, 110661-71-7; **7b**, 110661-73-9; **7c**, 110661-76-2; **11a**, 16767-46-7; **11b**, 110661-74-0; **11c**, 110661-77-3; **13**, 7567-22-8; 1,3,5,7-cyclooctatetraene-1-carbonitrile, 37164-17-3; phenyldiazomethane, 766-91-6.

Total Synthesis of 4-Demethoxy-13-dihydro-8-nordaunomycin

Chih-yun Johnny Tu* and Daniel Lednicer[1]

Biological Science Division, Adria Laboratories, Division of Erbamont Inc., Columbus, Ohio 43216

Received May 1, 1987

Anthracycline antitumor antibiotics have received considerable attention in recent years.[2] During the course of our work in this area, we desired a synthetic method for the construction of 8-nor analogues. While this work was in progress, alternative syntheses for the 8-nor aglycon were reported.[3,4] Our approach provides a direct and efficient entry into functionalized cyclopent[*b*]anthracenedione ring systems via geminal dialkylation of ethyl acetoacetate with bis(bromomethyl)anthraquinone. Subsequent functional group manipulation and osmium tetraoxide hydroxylation resulted in the desired protected *cis*-diol aglycon. Glycosidation followed by deprotection afforded the target compound.

Dimethylquinizarin **1**[5] served as starting material and was converted to dibromide **3** according to modified literature procedures[5,6] (Scheme I). Geminal dialkylation of ethyl acetoacetate with dibromide **3** (LDA, THF, room temperature) afforded the key intermediate cyclopent[*b*]anthracenedione **4** (40–45%) accompanied by bis-alkylated diketo diester **15** (10–15%). Saponification fol-

(1) Analytical Bio-Chemistry Laboratories, P. O. Box 1097, Columbia, MO 65205.

(2) (a) Arcamone, F. *Doxorubicin: Anticancer Antibiotics*; Academic Press: New York, 1981. (b) Elkhadem, E., Ed. *Anthracycline Antibiotics*; Academic Press: New York, 1982. (c) Arcamone, F. *Med. Res. Rev.* **1984**, *4*, 153.

(3) Flynn, G. A.; Vaal, M. J.; Stewart, K. T.; Wenstrup, D. L.; Beight, D. W.; Bohme, E. H. *J. Org. Chem.* **1984**, *49*, 2252.

(4) Mitscher, L. A.; Khanna, I. K. *Tetrahedron Lett.* **1985**, *26*, 691.

(5) Kerdesky, F. A. J.; Ardecky, R. J.; Lakshmikantham, M. V.; Cava, M. P. *J. Am. Chem. Soc.* **1981**, *103*, 1992 and references therein.

(6) Clark, G. W., personal communication.

0022-3263/87/1952-5624$01.50/0