9.0 Hz, H-6 indolyl). Anal. Calcd for $C_{15}H_{14}N_2O_4$: C, 62.93; H, 4.93; N, 9.79. Found: C, 62.99; H, 4.92; N, 9.80.

2-(6-Nitrobenzothiazol-7-yl)-1-fur-2-ylethanol: mp 97–99 °C; ^{1}H NMR ($CDCl_3$) δ 3.13 (br s, 1 H, OH), 3.77 (d, 2 H, J_{CH-CH} = 7.0 Hz, CH_2), 5.30 (t, 1 H, CH), 6.27–6.47 (m, 2 H, H-3 and H-4 furyl), 7.43–7.57 (m, 1 H, H-5 furyl), 8.00–8.33 (m, 2 H, H-4 and H-5 benzothiazolyl), 9.33 (s, 1 H, H-2 benzothiazolyl). Anal. Calcd for $C_{13}H_{10}N_2O_4S$: C, 53.80; H, 3.47; N, 9.65; S, 11.03. Found: C, 53.81; H, 3.47; N, 9.63; S, 11.00.

2-(2-Nitro-5-carbomethoxyphenyl)-1-phenylethanol: mp 113–114 °C; ^{1}H NMR ($CDCl_3$) δ 2.93 (br s, 1 H, OH), 3.27 (d, 2 H, J_{CH-CH} = 6.0 Hz, CH_2), 3.90 (s, 3 H, OMe), 4.93 (t, 1 H, CH), 7.17–7.53 (m, 5 H, Ph), 7.87–8.13 (m, 3 H, Ar). Anal. Calcd for $C_{16}H_{15}NO_5$: C, 63.78; H, 5.02; N, 4.65. Found: C, 63.85; H, 5.00; N, 4.66.

1-(3-Methoxy-4-nitronaphthyl)pent-3-en-2-ol: oil; ^{1}H NMR ($CDCl_3$) δ 1.70 (d, 3 H, J_{CH-CH} = 4.0 Hz, CH_3), 1.93 (br s, 1 H, OH), 3.27 (d, 2 H, J_{CH-CH} = 6.0 Hz, CH_2), 4.00 (s, 3 H, OMe), 4.40 (t, 1 H, CH), 5.53–5.77 (m, 2 H, CH=CH), 7.23–8.23 (m, 5 H, Ar). Anal. Calcd for $C_{16}H_{17}NO_4$: C, 66.88; H, 5.96; N, 4.88. Found: C, 66.81; H, 5.95; N, 4.87.

Reaction of 4-Nitro-3-[(trimethylsilyl)methyl]benzonitrile with Benzaldehyde. The reaction was carried out as described above at −10 °C, and after flash chromatographic purification on silica gel (diethyl ether/light petroleum (bp 40–60 °C), 7:3, as eluant), 1-phenyl-2-(2-nitro-5-cyanophenyl)ethanol was recovered in 68% yield: oil, ^{1}H NMR ($CDCl_3$) δ 2.37 (br s, 1 H, OH), 3.13–3.41 (m, 2 H, CH_2), 4.77–5.17 (m, 1 H, CH), 7.20–8.13 (m, 8 H, Ar). Anal. Calcd for $C_{15}H_{12}N_2O_3$: C, 67.15; H, 4.51; N, 10.44. Found: C, 67.20; H, 4.50; N, 10.46.

When the reaction mixture was stirred overnight (16 h) at room temperature, 5-cyano-2,3-dihydro-2-phenylbenzo[*b*]furan was obtained in 70% yield after the usual workup: mp 86–88 °C; ^{1}H NMR ($CDCl_3$) δ 2.80–3.93 (m, 2 H, CH_2), 5.60–6.03 (m, 1 H, CH), 6.73–7.70 (m, 8 H, Ar); IR (KBr) 2223 (CN) and 1249 (C–O) cm^{-1}. Anal. Calcd for $C_{15}H_{11}NO$: C, 81.43; H, 5.01; N, 6.33. Found: C, 81.51; H, 4.99; N, 6.35.

Reaction of 4-Nitro-3-[(trimethylsilyl)methyl]anisole (5) with *n*-Heptanal. When the reaction was carried out with equimolar amounts of TBAF after the usual workup, the starting aldehyde (95% yield) and 3-methyl-4-nitroanisole (85% yield) were recovered. Both compounds were identified by comparison with authentic samples.

The same results were obtained by using a 5% molar amount of TBAF. However, this reaction was followed by GLC-MS analysis using a Hewlett-Packard HP-59970 work station formed by an HP-5890 gas chromatograph equipped with a methyl silicone capillary column and by an HP-5970 mass detector. Reaction samples submitted to this analysis at various reaction times showed the disappearance of the reactants and the formation of 3-methyl-4-nitroanisole and of 1-[(trimethylsilyl)oxy]hept-1-ene as a mixture of the cis and trans isomers, two peaks being detected with similar fragmentation patterns.

3-[(Trimethylsilyl)methyl]-4-nitroanisole (5): *m/e* 224 ($M^+ - CH_3$), 150, 135, 122, 106, 95, 75, 73.

Heptanal (6): *m/e* 114 (M^+), 113, 96, 86, 81, 70, 57, 55, 44.

3-Methyl-4-nitroanisole (7): *m/e* 167 (M^+), 150, 122, 95, 91, 78, 77, 65.

1-[(Trimethylsilyl)oxy]hept-1-ene (9): *m/e* 186 (M^+), 171, 157, 143, 129, 99, 95, 76, 73.

The TLC analysis of the reaction showed the presence of the aldehyde from hydrolisis on silica of the silyl enol ether of the nitro compounds **5** and **7** and of traces of the addition product **10**.

Reaction of 5 with 4-Nitroacetophenone and Acetophenone. The reaction between **5** and acetophenone was carried out as described above by using a 5% molar of TBAF. After about 30 min, the quenching of the reaction mixture followed by the usual workup led to the methyl derivative **7** (80% yield) and to the starting acetophenone (recovered about 95%). The products were identified by comparison with authentic samples.

The reaction of **5** with 4-nitroacetophenone (**11**) was carried out with the same procedure described for aldehydes. After chromatography, with light petroleum (bp 40–60 °C)/diethyl ether (1:1) as eluant, the following products were isolated.

7: 54.4% yield; identified by comparison with a true sample.

11: 50% recovered unaltered; identified by comparison with a true sample.

1-(5-Methoxy-2-nitrophenyl)-2-(4-nitrophenyl)propan-2-ol: 37.4% yield; mp 132–134 °C; ^{1}H NMR ($CDCl_3$) δ 1.66 (s, 3 H, CH_3), 2.80 (s, 1 H, OH), 3.18–3.38 and 3.64–3.84 (AB system, 1 H + 1 H, CH_2), 3.70 (s, 3 H, OMe), 6.34 (d, 1 H, $J_{6,4}$ = 2.0 Hz, Ar), 6.80 (dd, 1 H, $J_{3,4}$ = 10 Hz, Ar), 7.50–7.70 and 8.12–8.28 (A_2B_2 system, 2 H + 2 H, Ar), 8.00 (d, 1 H, Ar). Anal. Calcd for $C_{16}H_{16}N_2O_6$: C, 57.83; H, 4.85; N, 8.43. Found: C, 57.75; H, 4.84; N, 8.41.

1,3-Bis(4-nitrophenyl)-3-hydroxybutan-1-one: 7.3% yield; identified by comparison with a true sample.

Registry No. **5**, 109434-09-5; (*E*)-**9**, 52186-50-2; (*Z*)-**9**, 50300-19-1; 2-(2-nitro-5-methoxyphenyl)-1-phenylethanol, 109433-96-7; 2-(2-nitro-5-methoxyphenyl)-1-fur-2-ylethanol, 109433-97-8; 2-(2-nitro-5-methoxyphenyl)ethanol, 21857-42-1; 2-(2-nitro-5-methoxyphenyl)-1-(4-nitrophenyl)ethanol, 109433-98-9; 1-(2-nitro-5-methoxyphenyl)-3,3,3-trichloropropan-2-ol, 109433-99-0; 2-(2-nitro-5-methoxyphenyl)-1-(2-bromophenyl)-ethanol, 109434-00-6; 2-(2-nitro-5-methoxyphenyl)-1-(4-cyanophenyl)ethanol, 109434-01-7; 1-(2-nitro-5-methoxyphenyl)pent-3-en-2-ol, 109434-02-8; 2-(2-nitro-5-cyanophenyl)-1-phenylethanol, 109434-03-9; 2-(1-methyl-5-nitroindol-4-yl)-1-phenylethanol, 109434-04-0; 2-(1-methyl-5-nitroindol-4-yl)-1-fur-2-ylethanol, 109434-05-1; 2-(6-nitrobenzothiazol-7-yl)-1-fur-2-ylethanol, 109434-06-2; 2-(2-nitro-5-carbomethoxyphenyl)-1-phenylethanol, 109434-07-3; 1-(3-methoxy-4-nitronaphthyl)pent-3-en-2-ol, 109434-08-4; 2-(3-methoxy-4-nitronaphthyl)-1-phenylethanol, 103369-02-4; 2-(2-nitro-5-chlorophenyl)-1-phenylethanol, 103369-01-3; 4-nitro-3-[(trimethylsilyl)methyl]benzonitrile, 103368-89-4; 1-methyl-4-[(trimethylsilyl)methyl]-5-nitroindole, 103368-99-6; 6-nitro-7-[(trimethylsilyl)methyl]benzothiazole, 103368-98-5; methyl 4-nitro-3-[(trimethylsilyl)methyl]benzoate, 103368-91-8; 1-nitro-2-methoxy-4-[(trimethylsilyl)methyl]-naphthalene, 103368-96-3; 4-chloro-2-[(trimethylsilyl)methyl]-nitrobenzene, 103368-87-2; benzaldehyde, 100-52-7; 2-furancarboxaldehyde, 98-01-1; formaldehyde, 50-00-0; 4-nitrobenzaldehyde, 555-16-8; trichloroacetaldehyde, 75-87-6; 2-bromobenzaldehyde, 6630-33-7; 4-cyanobenzaldehyde, 105-07-7; crotonaldehyde, 4170-30-3; tetrabutylammonium fluoride, 429-41-4; 5-cyano-2,3-dihydro-2-phenylbenzo[*b*]furan, 109434-10-8; heptanal, 111-71-7; 2-methyl-4-methoxynitrobenzene, 5367-32-8; 4-nitroacetophenone, 100-19-6; acetophenone, 98-86-2; 1-(5-methoxy-2-nitrophenyl)-2-(4-nitrophenyl)propan-2-ol, 109434-11-9; 1,3-bis-(4-nitrophenyl)-3-hydroxybuten-1-one, 109434-12-0.

Functionalized Pyrazoles from Indazol-4-ols

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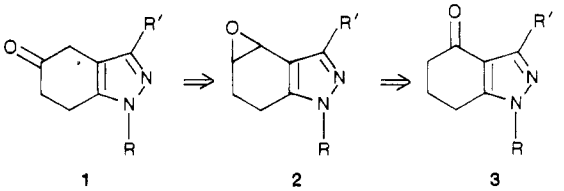
We recently required indazolones **1** as starting materials for the preparation of fused indazolones for biological evaluation. Retrosynthetically, it seemed attractive to envision 1,2-carbonyl transposition methodology[1] starting from indazolones **3**, which are available from 1,3-cyclohexanedione.[2] Since epoxides can be rearranged to ke-

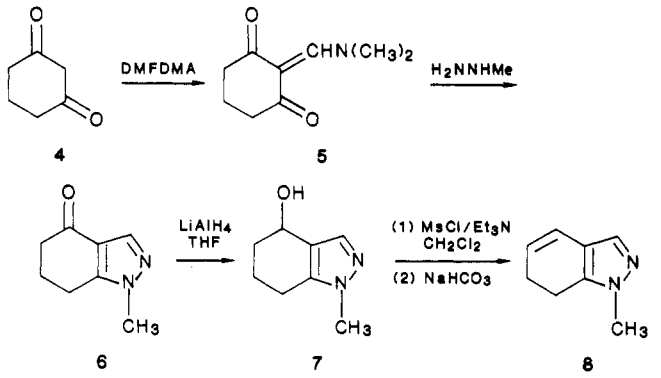


1 **2** **3**

(1) Kane, V. V.; Singh, V.; Martin, A.; Doyle, D. L. *Tetrahedron* **1983**, *39*, 345.

0022-3263/87/1952-4384$01.50/0

Scheme I



tones with a variety of acid and Lewis acid catalysts,[1,3] we felt that epoxides **2** would be good immediate precursors to **1**. Acid-catalyzed rearrangement of **2** should give only **1** and not **3**, since the pyrazole ring would stabilize the carbonium ion precursor of **1**. We planned to prepare epoxides **2** from the corresponding olefins, which would be prepared from indazolones **3** by reduction and dehydration.

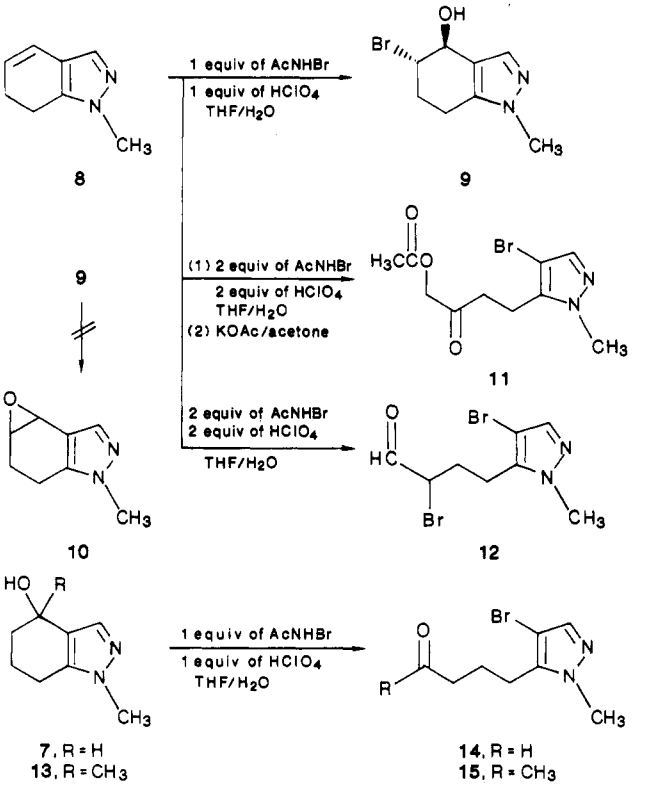
In practice, we were unable to prepare epoxides **2** from the corresponding olefins. Under oxidative conditions, one of these olefins and related compounds underwent unique and potentially useful fragmentations to produce functionalized pyrazoles. These transformations are the subject of this report.

Results and Discussions

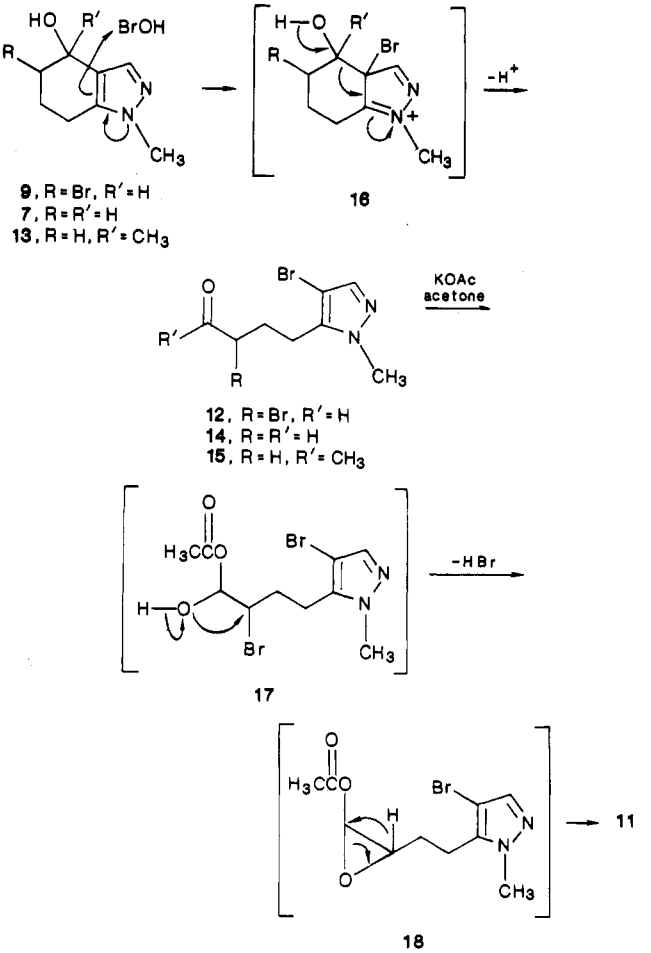
Enedione **5** was prepared from 1,3-cyclohexanedione (**4**) and dimethylformamide dimethyl acetal (DMFDMA) and subsequently treated with methylhydrazine to give 1,5,6,7-tetrahydro-1-methylindazol-4-one (**6**),[2] as shown in Scheme I. Reduction of **6** with lithium aluminum hydride gave carbinol **7**, which was dehydrated by base-induced elimination of its methanesulfonate derivative to give 1-methyl-7,8-dihydroindazole (**8**).

When olefin **8** was treated with 1 equiv of hypobromous acid, which was generated in situ from *N*-bromoacetamide and perchloric acid, bromohydrin **9** was obtained in 53% yield, as shown in Scheme II. We were unable to prepare epoxide **10** from **9** by base-induced cyclization.[4] Oliveto et al.[5] have epoxidized cortisone acetate with hypobromous acid (3 equiv) followed by treatment with potassium acetate. Thus, we next treated olefin **8** with 2 equiv of hypobromous acid followed by potassium acetate. Under these conditions, bromohydrin **9** was further transformed by the second equivalent of hypobromous acid and the potassium acetate, and we obtained 1-(acetyloxy)-4-(4-bromo-1-methyl-1*H*-pyrazol-5-yl)-2-butanone (**11**) in 43% yield. All spectral data for **11**, including ^{13}C NMR, were in complete agreement with structure. Pyrazole **11** is the result of consecutive rearrangement processes which fragment the indazole carbon skeleton and reorganize the alkyl side chain. The latter process was averted when we treated **8** with 2 equiv of hypobromous acid without subsequent addition of potassium acetate. Under these conditions, we isolated α,4-dibromo-1-methyl-1*H*-pyrazole-5-

Scheme II



Scheme III



(2) Schenone, P.; Mosti, L.; Menozzi, G. *J. Heterocycl. Chem.* **1982**, *19*, 1355.
(3) House, H. O. *Modern Synthetic Reactions*, 2nd ed.; W. A. Benjamin: Menlo Park, CA, 1972; p 319.
(4) We were unable to convert bromohydrin **9** to epoxide **10** with ethanolic silver oxide, potassium *tert*-butoxide, or sodium hydride in dimethylformamide.
(5) Oliveto, E. P.; Gerold, C.; Hershberg, E. B. *J. Am. Chem. Soc.* **1957**, *79*, 3596.

butanal (**12**) in 77% yield. We feel that these rearrangements are surprisingly efficient in view of their complexities.

To further examine the scope of this novel rearrangement we treated carbinols **7** and **13** (prepared from ketone **6** and methylmagnesium bromide) each with 1 equiv of hypobromous acid, as shown at the bottom of Scheme II. These indazoles also underwent efficient fragmentation to bromopyrazoles **14** and **15**, respectively, in yields of 92% and 75%.

A mechanism which accounts for the formation of pyrazoles **11**, **12**, **14**, and **15** is shown in Scheme III. We feel that cleavage of the indazole skeleton is initiated by bromination at the electron-rich 3a-position. It is well-documented that electrophilic attack on pyrazoles occurs preferentially at the 4-position,[6] which corresponds to the 3a-position of our fused pyrazoles. Cleavage of the 3a,4-carbon–carbon bond as shown in intermediate **16** would produce pyrazoles **12**, **14**, and **15**. In the presence of potassium acetate, α-bromo aldehyde **12** is further transformed to pyrazole **11**, a process which could arise from attack of acetate at the carbonyl center. Subsequent epoxide formation from the resulting bromohydrin (intermediate **17**) would give intermediate **18**, which could rearrange with hydride transfer to acetoxy ketone **11**.[7]

We have not found literature examples of acetate-induced rearrangement of α-bromo aldehydes to acetoxymethyl ketones. However, a similar transformation of an α-bromo aldehyde, 23-bromocholanal, to 23-ketocholanol (quantitative yield), has been reported by Yanuka et al.,[8] using 2% bicarbonate in *tert*-butyl alcohol–water (9:1). These authors propose the intermediacy of 23-hydroxycholanal in this conversion, which is a reasonable suggestion for the reaction conditions which they used. We are presently investigating the generality of acetate-induced rearrangements of α-bromo aldehydes.

Although our attempts with ketone transposition on indazolone **6** were unsuccessful, we did discover a general method for producing certain functionalized pyrazoles from indazol-4-ols.[10] A subsequent report will describe alternative methods which we used to prepare fused indazolones which circumvented the need for indazolones of general structure **1**.

Experimental Section

All melting points are uncorrected. The IR spectra were recorded with a Perkin-Elmer Model 710B spectrophotometer, ^{1}H NMR spectra were recorded with Varian EM-360A and Varian XL-300 (multinuclear probe) spectrometers and mass spectra with a Finnigan Model 4500 (electron impact and chemical ionization) mass spectrometer. Combustion analyses for C, H, and N were performed by Merrell Dow Analytical Laboratories, Cincinnati, OH.

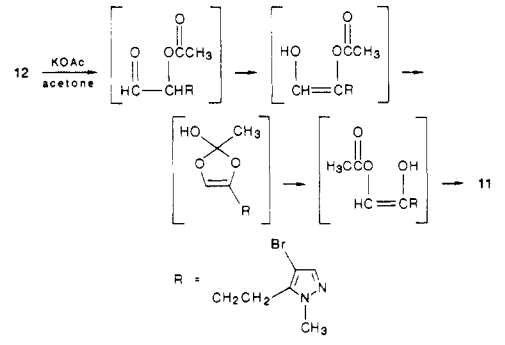
4,5,6,7-Tetrahydro-1-methyl-1*H*-indazol-4-ol (7). To an ice-cold suspension of 20.9 g (0.550 mol) of $LiAlH_4$ in anhydrous THF (400 mL) was added, dropwise, a solution of 75.0 g (0.493 mol) of ketone **6**[2] in anhydrous THF (400 mL). The reaction mixture was mechanically stirred for 3 h at room temperature and then hydrolyzed at 0 °C by successive addition of water (21 mL) in THF (50 mL), 15% NaOH (21 mL), and water (21 mL). The precipitates were removed by filtration and the filtrate was concentrated to leave 71.5 g (95%) of **7**, mp 103.5–105 °C (toluene): ^{1}H NMR ($CDCl_3$) δ 7.40 (s, 1 H, C3-H), 4.95–4.65 (m, 1 H, C*H*OH), 3.70 (s, 3 H, CH_3), 3.55–3.30 (m, 1 H, OH), 2.70–2.35 (m, 2 H, CH_2), 2.05–1.65 (m, 4 H, CH_2CH_2); mass spectrum (100 eV, CI) 153 ($M^+ + 1$), 181 ($M^+ + 29$), 193 ($M^+ + 41$). Anal. Calcd for $C_8H_{12}N_2O$: C, 63.13; H, 7.95; N, 18.41. Found: C, 63.39; H, 7.93; N, 18.39.

6,7-Dihydro-1-methyl-1*H*-indazole (8). To an ice-cold solution of 71.5 g (0.470 mol) of carbinol **7** and 72.5 mL (0.520 mol) of triethylamine in CH_2Cl_2 (800 mL) was added, dropwise, a solution of 39.5 mL (0.510 mol) of methanesulfonyl chloride in CH_2Cl_2 (200 mL). The reaction mixture was stirred at room temperature for 2.5 h and saturated $NaHCO_3$ (500 mL) was added. The organic layer was dried ($MgSO_4$) and concentrated to leave 46.4 g (74%) of **8** as a yellow oil, which crystallized on standing. A portion was purified by flash chromatography (1:1 EtOAc/hexane) for combustion analysis to give white needles, mp 56–59 °C: ^{1}H NMR ($CDCl_3$) δ 7.30 (s, 1 H, C3-H), 6.40 (dt, J = 9, 2 Hz, 1 H, C4-H), 5.55 (dt, J = 9, 5 Hz, 1 H, C5-H), 3.75 (s, 3 H, CH_3), 3.00–2.00 (m, 4 H, CH_2CH_2); mass spectrum (70 eV, EI), m/z 134 (molecular ion). Anal. Calcd for $C_8H_{10}N_2$: C, 71.61; H, 7.51; N, 20.88. Found: C, 71.53; H, 7.43; N, 20.59.

5-Bromo-4,5,6,7-tetrahydro-1-methyl-1*H*-indazol-4-ol (9). To an ice-cold solution of 2.68 g (20.0 mmol) of **8** in THF (160 mL) and water (40 mL) was slowly added $HClO_4$ (20 mL of a 1.0 M solution; 20.0 mmol) followed by 2.76 g (20.0 mmol) of *N*-bromoacetamide, in portions. The mixture was stirred at room temperature for 18 h and concentrated, and the residue was

(6) Elguero, J. In *Comprehensive Heterocyclic Chemistry*; Potts, K. T., Ed; Pergamon: New York, 1984; Vol. 5, Part 4A, pp 236–242.

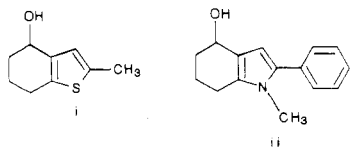
(7) The following mechanism for the conversion of bromo aldehyde **12** to acetoxy ketone **11**, which is initiated by displacement of bromide by acetate, was suggested by a reviewer.



(8) Yanuka, Y.; Katz, R.; Sarel, S. *Tetrahedron Lett.* **1970**, 5229. These authors have earlier reported an efficient preparation of α-bromo aldehydes[9a] and their stepwise degradation via α-hydroxy semiacetals.[9b] The latter materials were prepared by treatment of the α-bromo aldehydes with ethanolic potassium hydroxide and may have arisen from ethoxy epoxide intermediates analogous to acetoxy epoxide intermediate **18**.

(9) (a) Yanuka, Y.; Katz, R.; Sarel, S. *J. Chem. Soc., Chem. Commun.* **1968**, 849, (b) 851.

(10) The scope of the ring-cleavage reaction may be limited to indazol-4-ols. We did not observe analogous transformations with 4,5,6,7-tetrahydro-2-methylbenzo[*b*]thiophen-4-ol (i) or 4,5,6,7-tetrahydro-1-methyl-2-phenyl-1*H*-indol-4-ol (ii). Thus, when i was treated with 2 equiv of hypobromous acid, only i was recovered. Treatment of ii with 2 equivalents of hypobromous acid gave a mixture of products, whose ^{1}H NMR spectrum did not display an aldehyde signal.



(11) Prior to exchange, the hydroxyl proton appeared at δ 4.93 as a doublet, J = 3.6 Hz. Interestingly, coupling of 2.2 Hz is seen between C3-H and C4-H. Since the C4-H, C5-H couple was 4.8 Hz, the Karplus equation[12] predicts a C4-H, C5-H dihedral angle of ca. 125° or 40°, and we are unable to unequivocally designate the C4–C5 stereochemistry of **9** on the basis of ^{1}H NMR. We are uncertain whether halohydrin formation arises from a bromonium ion or a pyrazole-stabilized carbocation. However, the former should give the trans isomer, by backside attack,[13] and the latter should also give the trans isomer in this rigid system, for steric reasons.

(12) Silverstein, R. M.; Bassler, G. C.; Morrill, T. C. *Spectrometric Identification of Organic Compounds*, 4th ed.; Wiley: New York, 1981; pp 208–210.

(13) March, J. *Advanced Organic Chemistry*, 3rd Ed.; Wiley: New York, 1985; pp 658–662.

diluted with water (100 mL) containing sodium sulfite. The mixture was extracted with CH_2Cl_2 and the extracts were dried ($MgSO_4$) and concentrated to give 2.70 g (58%) of **9** as a white solid, mp 144–145.5 °C (toluene): ^1H NMR ($CDCl_3$–D_2O) δ 7.49 (d, J = 2.2 Hz, 1 H, C3-H), 4.28 (dd, $J_{4,5}$ = 4.8 Hz, $J_{4,3}$ = 2.2 Hz, 1 H, C4-H), 3.76 (s, 3 H, CH_3), 2.83–2.62 (m, 2 H, C7-H_2), 2.49 (ddd, $J_{5,4}$ = 4.8 Hz, $J_{5,6}$ = 7.5 Hz, $J_{5,6}$ = 2.8 Hz, 1 H, C5-H, 2.37–2.22 (m, 2 H, C6-H_2);[10] mass spectrum (70 eV, EI), m/z 232 and 230 (molecular ions). Anal. Calcd for $C_8H_{11}BrN_2O$: C, 41.58; H, 4.80; N, 12.12. Found: C, 41.95; H, 4.83; N, 12.28.

1-(Acetyloxy)-4-(4-bromo-1-methyl-1*H*-pyrazol-5-yl)-2-butanone (11). To an ice-cold solution of 2.68 g (20.0 mmol) of **8** in THF (160 mL) and water (40 mL) was slowly added $HClO_4$ (40 mL of a 1.0 M solution; 40.0 mmol) followed by 5.52 g (40.0 mmol) of *N*-bromoacetamide, in portions. The reaction mixture was stirred at room temperature for 18 h and concentrated to half-volume. The concentrate was partitioned between CH_2Cl_2 and water (100 mL) containing sodium sulfite, and the organic phase was dried ($MgSO_4$) and concentrated to provide a yellow oil. This oil was diluted with acetone (250 mL) and 20 g of potassium acetate was added. The reaction mixture was heated at reflux for 18 h, cooled, and filtered. The precipitate was washed with acetone, and the combined filtrates were concentrated. The residue was reconstituted in CH_2Cl_2, and the solution was dried ($MgSO_4$) and concentrated to a viscous, amber oil, which was purified by flash chromatography on silica gel (9:1 acetone/CH_2Cl_2) to give 2.50 g (43%) of **13** as a yellow oil, bp 120–130 °C (2 mm): IR (neat) 1760 (ester C=O), 1740 (ketone C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.30 (s, 1 H, C3-H), 4.55 (s, 2 H, CH_2O), 3.85 (s, 3 H, NCH_3), 3.00–2.70 (m, 4 H, CH_2CH_2), 2.15 (s, 3 H, CH_3CO); ^{13}C NMR ($CDCl_3$) δ 203 (C2), 170 (ester C=O), 138 (pyrazole C3 and C5), 93.0 (pyrazole C4), 68.0 (C1), 38.0 (NCH_3), 37.0 (C3), 21.0 (C4), 18.0 (acetyl CH_3); mass spectrum (70 eV, EI), m/z 288 and 290 (molecular ions). Anal. Calcd for $C_{10}H_{13}BrN_2O_3$: C, 41.54; H, 4.53; N, 9.69. Found: C, 41.52; H, 4.54; N, 9.31.

α,4-Dibromo-1-methyl-1*H*-pyrazole-5-butanal (12). To an ice-cold solution of 2.68 g (20.0 mmol) of **8** in THF (160 mL) and water (40 mL) was slowly added $HClO_4$ (40 mL of a 1.0 M solution; 40.0 mmol) followed by 5.52 g (40.0 mmol) of *N*-bromoacetamide, in portions. The reaction mixture was stirred at room temperature for 18 h and concentrated. The residue was partitioned between CH_2Cl_2 and water (100 mL) containing sodium sulfite, and the organic phase was dried ($MgSO_4$) and concentrated. The resulting yellow oil was purified by flash chromatography on silica gel (9:1 CH_2Cl_2/acetone) to provide 4.80 g (78%) of **12** as a yellow oil: ^1H NMR ($CDCl_3$) δ 9.45 (d, J = 2 Hz, 1 H, CHO), 7.40 (s, 1 H, C-3H), 4.45–4.15 (m, 1 H, CHBr), 3.85 (s, 3 H, NCH_3), 3.05–2.05 (m, 4 H, CH_2CH_2); mass spectrum (70 eV, EI), m/z 308, 310, and 312 (molecular ions). Anal. Calcd for $C_8H_{10}Br_2N_2O$: C, 30.99; H, 3.25; N, 9.04. Found: C, 30.99; H, 3.32; N, 9.15.

4,5,6,7-Tetrahydro-1,4-dimethyl-1*H*-indazol-4-ol (13). A solution of 15.0 g (0.100 mol) of ketone **6** in THF (100 mL) was added, dropwise, to a solution of methylmagnesium bromide (40.0 mL of a 2.80 M solution in ethyl ether; 0.112 mol) in THF (100 mL) at such a rate that the reaction temperature remained at 20–30 °C. The mixture was stirred at room temperature for 90 min and slowly poured onto ice containing NH_4Cl and NaCl. The resulting slurry was extracted with CH_2Cl_2, and the combined extracts were dried ($MgSO_4$) and concentrated. The residue was dissolved in warm toluene and the crystalline solid which formed on cooling was collected to give 11.2 g (67%) of **13**, mp 108–110 °C: ^1H NMR ($CDCl_3$) δ 7.40 (s, 1 H, C3-H), 3.65 (s, 3 H, NCH_3), 2.70–2.30 (m, 2 H, CH_2), 2.40 (s, 1 H, OH), 2.20–1.65 (m, 4 H, CH_2CH_2), 1.55 (s, 3 H, CCH_3); mass spectrum (70 eV, EI), m/z 166 (molecular ion). Anal. Calcd for $C_9H_{14}N_2O$: C, 65.03; H, 8.49; N, 16.86. Found: C, 65.00; H, 8.38; N, 16.67.

4-Bromo-1-methyl-1*H*-pyrazole-5-butanal (14). Preparation of **14** was analogous to that of **12**. Thus, 1.00 g (6.57 mmol) of carbinol **7**, $HClO_4$ (7.00 mL of a 1.0 M solution; 7.00 mmol), and 1.00 g (7.25 mmol) of *N*-bromoacetamide provided 1.40 g (92%) of **14** as a yellow oil, which was purified by flash chromatography on silica gel (9:1 CH_2Cl_2/acetone): IR (neat) 1720 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.70 (t, J = 1 Hz, 1 H, CHO), 7.35 (s, 1 H, C3-H), 3.80 (s, 3 H, NCH_3), 2.90–2.20 (m, 4 H, $CH_2CH_2CH_2$), 2.15–1.70 (m, 2 H, CH_2); mass spectrum (70 eV, EI), m/z 230 and 232 (molecular ions). Anal. Calcd for $C_8H_{11}BrN_2O$: C, 41.58; H, 4.80; N, 12.12. Found: C, 41.66; H, 4.81; N, 12.03.

5-(4-Bromo-1-methyl-1*H*-pyrazol-5-yl)-2-pentanone (15). Preparation of **15** was analogous to that of **12**. Thus, 3.32 g (20.0 mmol) of carbinol **13**, $HClO_4$ (20.0 mL of a 1.0 M solution; 20.0 mmol), and 2.76 g (20.0 mmol) of *N*-bromoacetamide provided crude **15** as a yellow oil. Purification by flash chromatography on silica gel (9:1 CH_2Cl_2/acetone) gave 3.70 g (76%) of **15** as a colorless oil: IR (neat) 1715 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.40 (s, 1 H, C3-H), 3.85 (s, 3 H, NCH_3), 2.85–2.40 (m, 4 H, $CH_2CH_2CH_2$), 2.20 (s, 3 H, CH_3CO), 2.10–1.70 (m, 2 H, CH_2); mass spectrum (100 eV, CI), 245 and 247 (M^+ + 1), 273 and 275 (M^+ + 29), 285 and 287 (M^+ + 41). Anal. Calcd for $C_9H_{13}BrN_2O$: C, 44.10; H, 5.34 N, 11.43. Found: C, 44.46; H, 5.54; N, 11.20.

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Enhancement of Alkali Metal Cation Binding in Water by Ring Sulfonation of Dibenzo-16-crown-5 Carboxylic Acids

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The presence of aromatic ring substituents on benzo- and dibenzocrown ethers may substantially influence the selectivity and binding strength for alkali metal cations.[1-3] In general, it has been observed that electron-donating substituents enhance cation binding as a result of increased basicity of oxygen atoms bonded to the aromatic ring. We now report the ring sulfonation of dibenzo-16-crown-5 carboxylic acids **1–3** to form crown carboxylic disulfonic acids **4–6** and an assessment of interactions of these novel proton-ionizable crown ethers with Na^+ and K^+ in water.

The first recorded crown ether sulfonation was by Pederson[4] who prepared dibenzo-18-crown-6 disulfonic acid as a dihydrate. Later, Cram and co-workers[5] reported tetrasulfonation of optically active bisnaphtho-22-crown-6. In neither instance were the alkali metal cation binding properties of the sulfonated crown ether examined.

Syntheses of crown carboxylic disulfonic acids **4–6** were accomplished in high yields (82–93%) by treatment of crown carboxylic acids **1–3** with a solution of H_2SO_4, Ac_2O, AcOH, and $CHCl_3$ (Scheme I). The presence of AcOH prevented sulfone formation.[6] The crown carboxylic disulfonic acids were isolated as solids that contained waters of hydration in the case of **4** and **5**. Increased lipophilicity within the crown carboxylic disulfonic acid reduced the number of water molecules present in the solid.

Sulfonated crown compounds **4–6** possess high water solubility and the *n*-butyl compound **6** was found to be soluble in acetone as well. These crown carboxylic disulfonic acids decomposed when stored for periods longer than a few weeks but could be converted into stable disulfonate salts when neutralized with calcium, sodium, or potassium carbonates. Stoichiometries of the disulfonate salts, as determined by atomic absorption, were two metal cations to one crown species for K^+ and Na^+ and one metal

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