reported to give only β-anomers. The desired compound **3** was also the major product of glycosylation of the 6-bromopurine **1**, although the minor component was apparently the 9-α isomer rather than the expected 7-β isomer. In addition, the facile and direct isolation of the 9-β-deoxyribofuranosyl isomers precludes lengthy chromatographic separation of glycosylation products. In the final step, the protected 2,6-dihalo nucleosides are converted nearly quantitatively to the target 2-halo-2′-deoxyadenosines. This chemical method appears to be adaptable to large-scale syntheses, as demonstrated by the 50-fold greater scale of the glycosylation of 2,6-dibromopurine as compared with the enzymatic glycosylation of 2-bromoadenine.[5]

Experimental Section

Melting points were determined on a Mel-Temp apparatus and are uncorrected. Elemental analyses were performed by the Microanalysis Laboratory, University of Massachusetts, Amherst; experimental analyses were within ±0.4% of calculated values. ^{1}H NMR spectra were obtained at 250 MHz with a Bruker WM250 instrument; chemical shifts are reported in parts per million (δ) relative to internal tetramethylsilane. UV spectra were obtained with a Gilford Response spectrophotometer.

2,6-Dibromo-9-(2-deoxy-3,5-di-*p*-toluoyl-β-D-ribofuranosyl)purine (3) and Its 9-α Isomer. A mixture of **1** (12 g, 0.043 mol) and sodium hydride (50% suspension in mineral oil, 2.27 g, 0.047 mol) in acetonitrile (225 mL) was stirred at room temperature for 1 h. 1-Chloro-2-deoxy-3,5-di-*p*-toluoyl-α-D-*erythro*-pentofuranose[9] was added in small portions during 1 h, and stirring was continued for 15 min. The mixture was filtered through Celite, and the adsorbent was washed with chloroform (250 mL). The combined filtrates were evaporated to a slurry and layered onto a short column of silica gel (ca. 300 g, 70–230 mesh). The products were eluted with chloroform (1 L), and after the solvent was evaporated, the residue was mixed with toluene. The resulting suspension was filtered and the solid washed with toluene to give 13.5 g (50%) of the 9-β isomer **3** as colorless crystals: mp 156–158 °C (from MeOH); UV (EtOH) λ_{max} 276.4 nm (ε 13 000); ^{1}H NMR ($CDCl_3$) δ 8.28 (s, 1 H, C8-H), 6.54 (pseudo t, 1 H, Cl′-H; J_{av} = 7.0 Hz), ca. 4.70 (m, 3 H, 4′, 5′, 5″-H). Anal. ($C_{26}H_{22}N_4O_5Br_2$) C, H, N, Br.

The filtrate containing residual **3** and the second product was purified by HPLC (silica gel, 50 cm × 22.5 mm). Elution with 4% acetone in toluene (550 mL) gave an additional 1.8 g (6.7%) of **3**. Continued elution (400 mL) gave 3 g (11%) of a product tentatively identified as the 9-α anomer: mp 98–100 °C (from EtOH); UV (EtOH) λ_{max} 276.6 nm (ε 12 400); ^{1}H NMR ($CDCl_3$) δ 8.45 (s, 1 H, C8–H), 6.61 (pseudo q, 1 H, Cl′-H; J = 6.0, 1.3 Hz), 4.93 (m, 1 H, 4′-H), 4.64 (m, 2 H, 5′, 5″–H). Anal. ($C_{26}H_{22}N_4O_5Br_2$) C, H, N, Br.

2-Bromo-2′-deoxyadenosine (5). A solution of **3** (2.56 g, 4 mmol) in methanol (80 mL) was saturated with anhydrous ammonia at 0 °C and heated in a steel bomb at 60 °C for 32 h. The solvent was evaporated and the residue was purified on a column of silica gel (50 g, 70–230 mesh) by elution with 20% methanol in chloroform to give 1.24 g (94%) of chromatographically pure **5**: mp, begins to turn brown at 193 °C and gradually darkens without melting (in agreement with the behavior of an authentic sample provided by J. A. Secrist, III); UV (EtOH) λ_{max} 265.5 nm (ε 14 900); ^{1}H NMR (Me_2SO-d_6) δ 8.32 (s, 1 H, C8-H), 6.27 (pseudo t, 1 H, Cl′-H, J_{av} = 7.5 Hz), all other ^{1}H NMR resonances as expected.

Acknowledgment. Proton NMR spectra at 250 MHz were obtained with a Bruker WM250 instrument at the Worcester Consortium NMR Facility, Clark University, supported in part by NSF Grant DMR 8108697. The work was supported by NIH Grant GM21747 and by a grant from the Milheim Foundation for Cancer Research.

Registry No. 1, 1196-41-4; 2, 5451-40-1; β-3, 110096-57-6; α-3, 110096-58-7; 4, 38925-80-3; 5, 89178-21-2; 1-chloro-2-deoxy-3,5-di-*p*-toluoyl-α-D-*erythro*-pentofuranose, 4330-21-6.

Functionalization of Aromatic and Heterocyclic Systems. Regioselective Introduction of 2-Oxoalkyl Chain or Cyano Functions via Organoiron Complexes

Ronald G. Sutherland,* Ratan L. Chowdhury, Adam Piórko, and Choi Chuck Lee*

Department of Chemistry, University of Saskatchewan, Saskatoon, Saskatchewan S7N 0W0, Canada

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Selective functionalization of aromatic and heterocyclic systems is an important problem in synthetic organic chemistry. Numerous methods have recently been described for selective alkylation of nitroarenes;[1-5] however, while each of the methods is illustrated by interesting synthetic applications, none of them is general.

Our earlier studies reported the ready formation of cyclohexadienyl adducts in reactions of arenes or heterocycles bearing an electron-withdrawing function and complexed with an iron (Cp) moiety, with ketone enolate, or cyano anions[6] (Scheme I).

Such adducts have synthetic potential, since removal of the iron (Cp) moiety in demetalation–rearomatization reactions would lead to functionalized arenes or heterocycles. We confirmed this conclusion with the isolation of a new compound, 2,5-dichlorophenylpropanone, from the demetalation of the precursor cyclohexadienyl complex[6a,b] using a procedure employing buffered CAN as an oxidant.[7]

Careful investigation of that reaction involving GC and GC–MS examination of liberated arenes or heterocycles proved that demetalation could be followed by rearomatization by the abstraction of either endo hydride or exo cyano/oxoalkyl function. Thus, in the case of complex **1**, besides **1a** (50%) a significant amount (20%) of *p*-dichlorobenzene was found, and other demetalations gave the following results: **5** gave 72% of **5a** and 20% of benzophenone; **8** gave 64% of **8a** and 22% of anthraquinone; **10** gave 30% of **10a** as well as 34% of xanthone.

In the present study we obtained functionalized arenes and heterocycles **1a–11a** (Scheme II) using a superior procedure for the oxidative demetalation. Buffered CAN has been replaced by DDQ (2,3-dichloro-5,6-dicyano-1,4-benzoquinone), which has been widely used in studies of arene systems[2-5] and occasionally with metal complexes.[8]

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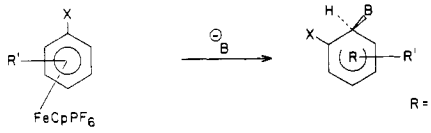
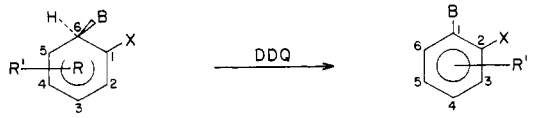
Scheme I



B = $CHR^{1'}COCHR^{2''}_2$; CN; $X = NO_2$; COPh; CO_2Me; R^1 = H; Me; Cl; o-X-C_6H_4-R^1 = OC-C_6H_4-CO; OC-C_6H_4-O; OC-C_6H_4-S; OC-C_6H_4-; OC-C_6H_4-SO_2

B = $CHR^{1'}COCHR^{2''}_2$; X = CN; Cl; SO_2-Ph-*p*-Me; R^1 = H; Me; Cl; o-X-C_6H_4-R^1 = O_2S-C_6H_4-CMe_2; O_2S-C_6H_4-;

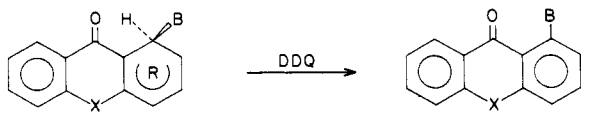
Scheme II



B = CH_2COCH_3:
1. X,R' = 1,4-Cl_2 — 1a. X,R' = 2,5-Cl_2; 72%
2. X,R' = 1,2-Cl_2 — 2a. X,R' = 2,3-Cl_2; 76%
3. X,R' = 1-CN; H — 3a. X,R' = 2,-CN,H; 65%
4. X,R' = 1-NO_2; 4-Me — 4a. X,R' = 2-NO_2; 5-Me; 80%

B = CD_2COCD_3:
5. X,R' = 1-COPh; H — 5a. X,R' = 2-COPh; H; 78%

B = CN
6. X,R' = 1-NO_2; H — 6a. X,R' = 2-NO_2; H; 75%
7. X,R' = 1-COPh; H — 7a. X,R' = 2-COPh; H; 82%



8. X = CO; B = CH_2COCH_3; 8a. 78%
9. X = S; B = CH_2COCH_3; 9a. 74%
10. X = O; B = CN; 10a. 60%
11. X = SO_2; B = CN; 11a. 85%

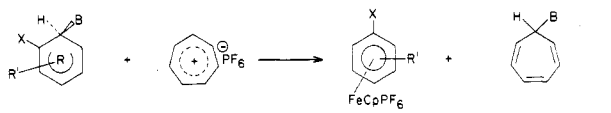
We found that DDQ is an effective oxidant of the cyclohexadienyl (Cp) iron system; we obtained higher yields of the desired products, and formation of the products from exo abstraction has been suppressed or eliminated. Such products were found only in decomplexation of **6** (3% of nitrobenzene) and **10** (10% of xanthone). All of these reactions were completed under very mild conditions within 30 min.

DDQ can be replaced by TBQ (3,4,5,6-tetrachloro-1,2-benzoquinone),[9] which gives comparable results. In this study, complexes **1** and **6** were also demetalated by TBQ, and the yields of the products **1a** and **6a** were found to be almost identical (±3%) with those obtained with DDQ.

As a result of our study we succeeded in introducing the acetonyl substituent selectively to *p*- (**1a**) or *o*-dichlorobenzene (**2a**), benzonitrile (**3a**), *p*-nitrotoluene (**4a**), anthraquinone (**8a**), and 9*H*-thioxanthen-9-one (**9a**) and [$^2H_5$]acetonyl to benzophenone (**5a**); while the cyano group was introduced into nitrobenzene (**6a**), benzophenone (**7a**), 9*H*-xanthen-9-one (**10a**), and 9*H*-thioxanthen-9-one 10,10-dioxide (**11a**).

We also attempted to abstract the endo hydride from complexes **1–11** without demetalation to synthesize functionalized arene (Cp) iron complexes using procedures described in the literature[8,10] for related systems. In each case, the exo function was lost with recovery of the starting cation (60–90%). In the reaction with tropylium hexafluorophosphate, beside the recovered cation, the transfer of the exo substituent to the cycloheptatriene ring was observed (Scheme III).

Scheme III



4. X,R' = 1-NO_2; 4-Me; B = CH_2COCH_3; — X,R' = 1-NO_2; 4-Me; 85% — 12a. B = CH_2COCH_3; 80%

7. X,R' = 1-COPh; H; B = CN; — X,R' = 1-COPh; H; 79% — 12b. B = CN; 82%

In conclusion, we note that this effective method of oxidative demetalation of cyclohexadienyl (Cp) iron complexes has considerable potential in synthetic organic chemistry. Selective ortho addition of 2-oxoalkyl or cyano anion to a substituted arene or heterocycle complex followed by demetalation with DDQ gives the selectively functionalized arene or heterocycle with an overall yield of 30–60% from the starting cation. To our knowledge, compounds **2a**, **4a**, **5a**, **8a**, **9a**, and **11a** have not been reported previously. Also, the observed transfer of a cyano or 2-oxoalkyl function from the cyclohexadienyl (Cp) iron complex to cycloheptatriene is worthy of further study.

Experimental Section

^1H NMR (300.133-MHz) and ^{13}C NMR (75.469-MHz) spectra were recorded on a Bruker AM 300 instrument in chloroform-*d* solutions (unless stated otherwise) with chemical shifts given in δ scale from TMS as an internal standard for ^1H NMR, while for ^{13}C NMR chemical shifts were calculated from the solvent signals. IR spectra were recorded on neat samples (oils) or in KBr disks. MS spectra (EI ionization) are reported in *m/e* units. Melting points are uncorrected. Starting cyclohexadienyl (Cp) iron complexes **1–11** were synthesized according to the literature: **1–5**;[6b] **6, 7, 10, 11**;[6c] **8, 9**.[6e] Tropylium hexafluorophosphate and the other reagents are commercially available. Demetalation experiments using Pearson's procedure were carried out as described previously;[6b] the products of decomplexation were analyzed by GC and then GC–MS techniques with corresponding nonfunctionalized arenes used as references. Attempts to abstract endo hydride were performed by following literature procedures.[8,10]

Demetalation with DDQ—General Procedure. To a stirred solution of complex (1 mmol) in 10 mL of acetonitrile was added rapidly 0.227 g (1 mmol) of solid DDQ, and the mixture was then stirred at room temperature for 30 min. After 1–5 min, the orange solution became dark green. The solution was then filtered through sintered glass and evaporated to dryness. The dry product was dissolved in methylene chloride, passed through a short alumina column (ca. 20 cm), dried ($MgSO_4$), and evaporated to give the product, which was analyzed by GC and GC–MS. The analytical results are given below, while yields are given in Scheme II.

1a: synthetized previously;[6b] ^{13}C NMR δ 203.66 (CO), 134.51 (q), 132.67 (q), 132.65 (q), 131.47, 130.48, 128.62, 47.90 (CH_2), 29.66 (CH_3).

2a: yellowish oil; MW calcd 203.0676; IR 1720 cm^{-1} (CO); MS 206 [$(M + 4)^+$, 3.0%], 204 [$(M + 2)^+$, 18.4%], 202 (M^+, 27.3%); ^1H NMR δ 7.40 (d, 7.7 Hz, 1 H, arom), 7.18 (t, 7.7 Hz, 1 H, arom), 7.12 (d, 7.7 Hz, d, 1.4 Hz, 1 H, arom), 3.89 (S, 2 H, CH_2), 2.23 (s, 3 H, CH_3); ^{13}C NMR δ 203.90 (CO), 135.20 (q), 133.28 (q), 133.02 (q), 129.73, (q), 129.36, 127.33, 48.93 (CH_2), 29.59 (CH_3); MW calcd 203.0676.

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(11) The equimolar (0.2 mmol) amounts of complex **4** or **7** and tropylium hexafluorophosphate in 10 mL of acetonitrile was stirred at room temperature for $^1/_2$ h. The solid obtained from evaporation of the solvent was extracted with chloroform (recovery of **12a** or **12b**) and next with methylene chloride (recovery of cations).

3a: reported;[12] oil; IR 2230 cm^{-1} (CN); MS 159 (M^+, 13.6%), 117 [$(M - CH_2{=}C{=}O)^+$, 100%]; ^1H NMR δ 7.66 (d, 7.6 Hz, 1 H, arom), 7.51 (d, 7.7 Hz, 1 H, arom), 3.99 (s, 2 H, CH_2), 2.30 (s, 3 H, CH_3); ^{13}C NMR δ 203.31 (CO), 138.07 (q), 132.78, 132.62, 130.78, 127.56, 117.66 (CN), 113.25 (q), 48.49 (CH_2), 29.92 (CH_3).

4a: white solid: mp 63-64 °C; MW calcd 193.2018 for $C_{10}H_{11}NO_3$; IR 1720 (CO), 1520 and 1345 cm^{-1} (NO_2); MS 193 (M^+, 0.1%), 151 [$(M - CH_2{=}C{=}O)^+$, 10.73%]; ^1H NMR δ 8.04 (d, 8.1 Hz, 1 H, arom), 7.26 (d, 8.1 Hz, 1 H, arom), 7.06 (s, 1 H, arom), 4.08 (s, 2 H, CH_2), 2.42 (s, 3 H, CH_3Ph), 2.32 (s, 3 H, CH_3CO); ^{13}C NMR δ 203.64 (CO), 146.19 (q), 144.83 (q), 134.08, 130.42 (q), 128.85, 125.27, 48.56 (CH_2), 29.84 (CH_3CO), 21.19 (CH_3Ph). Anal. Calcd: C, 62.17; H, 5.71; N, 7.25. Found: C, 62.01; H, 5.89; N, 7.13.

5a: white solid; mp 51-53 °C; MW calcd 243.3159 for $C_{16}H_9D_5O_2$; IR 1720 (CO aliph), 1670 cm^{-1} (CO arom); MS 243 (M^+, 0.1%), 197 [$(M - CD_3CO)^+$, 85.3%]; ^1H NMR δ 7.79 (m, 2 H, arom), 7.58 (t, 7.3 Hz, 1 H, arom), 7.45 (m, 4 H, arom); 7.30 (m, 2 H, arom); ^{13}C NMR δ 205.42 (CO aliph), 198.10 (CO arom), 137.92 (q), 137.88 (q), 134.52 (q), 132.80, 131.67, 130.97, 130.25 (3 C), 128.25 (2 C), 126.29, 47.74 (CD_2, m, 19.2 Hz), 29.77 (CD_3, m, 19.2 Hz). Anal. Calcd C, 79.00; H, 7.84. Found: C, 78.89; H, 7.89.

6a: reported;[13] mp 116 °C (lit.[13] mp 118 °C); ^1H NMR;[14] ^{13}C NMR δ 146.80 (q), 135.57, 134.26, 133.68, 125.52, 114.85 (CN), 108.07 (q).

7a: reported;[15] mp 84 °C (lit.[15] mp 84.5-85.5 °C); ^1H NMR δ 7.83 (m, 3 H, arom), 7.66 (m, 4 H, arom), 7.51 (t, 7.5 Hz, 2 H, arom); ^{13}C NMR δ 193.71 (CO), 141.60 (q), 136.02 (q), 134.17, 133.84, 132.36, 132.03, 131.26, 130.30 (2 C), 129.96, 128.66 (2 C), 116.96 (CN), 111.99 (q).

8a: yellowish microcystals; mp 140 °C dec; MW calcd 264.2800 for $C_{17}H_{12}O_3$; IR 1710 (CO aliph), 1660 cm^{-1} (CO arom); MS 264 (M^+, 18.65%), 222 [$(M - CH_2{=}CO)^+$, 100%]; ^1H NMR (acetone-d_6) δ 8.23 (m, 3 H, arom), 7.45 (m, 3 H, arom), 7.67 (d, 8.4 Hz, 1 H, arom), 4.39 (s, 2 H, CH_2), 2.35 (s, 3 H, CH_3); ^{13}C NMR (DMSO-d_6) δ 205.90 (CO aliph), 185.34 and 183.83 (CO arom), 139.59, 138.84 (q), 135.52 (q), 134.96 (q), 134.92, 134.55, 134.10, 133.39 (q), 131.83 (q), 127.20, 126.92, 50.21 (CH_2), 29.53 (CH_3). Anal. Calcd C, 77.26; H, 4.58. Found: C, 7.12; H, 4.53.

9a: yellow crystals; mp 160-161 °C; MW calcd 268.3336 for $C_{15}H_{12}O_2S$; IR 1720 (CO aliph), 1660 cm^{-1} (CO arom); MS 268 (M^+, 10%), 240 [$(M - CO)^+$, 100%]; ^1H NMR δ 8.43 (d, 8.0 Hz, d, 1.0 Hz, 1 H, arom), 7.55 (m, 5 H, arom), 7.16 (d, 5.7 Hz, d, 3.0 Hz, 1 H, arom), 4.27 (s, 2 H, CH_2), 2.43 (s, 3 H, CH_3); ^{13}C NMR δ 205.31 (CO aliph), 181.72 (CO arom), 139.57 (q), 139.12 (q), 136.07 (q), 131.94, 131.37 (2 C), 129.72, 129.57 (q), 127.52 (q), 126.21, 125.83, 125.23, 51.61 (CH_2), 30.07 (CH_3). Anal. Calcd C, 71.62; H, 4.51. Found: C, 71.58, H, 4.25.

10a: reported;[16] mp 194 °C (lit.[16] mp 196-198 °C); MW calcd 221.2148; MS 221 (M^+, 100%), 193 [$(M - CO)^+$; 68.48%]; ^1H NMR δ 8.33 (d, 7.7 Hz, 1 H, arom), 7.76 (m, 4 H arom), 7.50 (d, 7.7 Hz, 1 H arom), 7.43 (t, 7.7 Hz, 1 H arom); ^{13}C NMR δ 174.59 (CO), 156.20 (q), 155.40 (q), 135.59, 134.00, 131.64, 126.88, 124.86, 123.85 (q), 123.05, 121.47 (q), 117.81, 117.45 (CN), 110.85 (q).

11a: white powder; mp >200 °C; MW calcd 269.2782 for $C_{14}H_7NO_3S$; IR 2240 (CN), 1680 cm^{-1} (CO); MS 269 (M^+, 3.6%), 241 [$(M - CO)^+$, 100%]; ^1H NMR (DMSO-d_6) δ 8.52 (d, 8.0 Hz, 1 H, arom), 8.38 (d, 7.8 Hz, 1 H, arom), 8.34 (d, 7.7 Hz, 1 H, arom), 8.24 (d, 7.8 Hz, 1 H, arom), 8.20 (t, 7.9 Hz, 1 H, arom), 8.08 (t, 7.6 Hz, 1 H, arom), 8.00 (t, 7.6 Hz, 1 H, arom); ^{13}C NMR (DMSO-d_6) δ 177.07 (CO), 141.71 (q), 140.14, 139.19 (q), 135.57, 135.24, 134.25, 132.37 (q), 130.43 (q), 129.40, 127.46, 123.22, 116.99 (CN), 112.11 (q). Anal. Calcd C, 62.45; H, 2.62; N, 5.20. Found: C, 62.20; H, 2.43; N, 5.00.

12a: reported;[17] light yellow oil; MS 148 (M^+, 1.3%), 106 [$(M - CH_2{=}C{=}O)^+$, 100%]; ^1H NMR δ 6.65 (t, 3.0 Hz, 2 H), 6.19 (d, 9.4 Hz; t, 2.4 Hz; 2 H), 5.15 (d, 9.4 Hz; d, 5.8 Hz; 2 H), 2.79 (d, 7.5 Hz, 2 H, CH_2), 2.29 (d, 5.8 Hz, 1 H), 2.14 (s, 3 H, CH_3); ^{13}C NMR δ 207.28 (CO), 130.88 (2 C), 125.10 (2 C), 124.88 (2 C), 46.67 (CH_2), 34.43 (CH), 29.90 (CH_3).

12b: reported;[18] colorless oil; MS 117 (M^+, 8.2%), 91 [$(M - CN)^+$, 100%]; ^1H NMR[19] δ 6.74 (t, 3.3 Hz, 2 H), 6.34 (d, 8.9 Hz; t, 2.7 Hz; d, 0.7 Hz; 2 H), 5.40 (d, 8.9 Hz d, 6.1 Hz; 2 H), 3.00 (t, 6.1 Hz, 1 H).

Acknowledgment. Financial support given by the Natural Sciences and Engineering Research Council of Canada is gratefully acknowledged.

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Reaction of 2-(Alkylsulfinyl)-, 2-(Arylsulfinyl)-, and 2-(Aralkylsulfinyl)benzimidazoles with Thiols: A Convenient Synthesis of Unsymmetrical Disulfides

David R. Graber, Raymond A. Morge, and John C. Sih*

Diabetes and Gastrointestinal Diseases Research, The Upjohn Company, Kalamazoo, Michigan 49001

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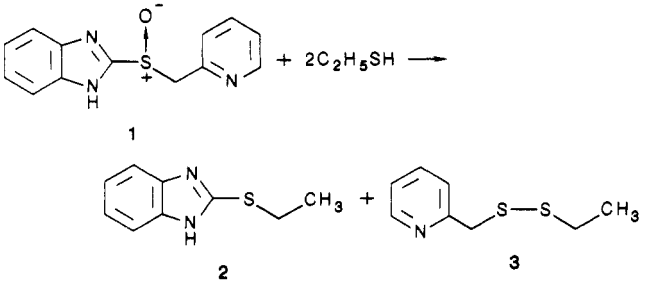
In the course of some studies dealing with proton-pump inhibitors, we had occasion to investigate the displacement of the (pyridinylmethyl)sulfinyl side chain of **1** with various mercaptans. Treatment of **1** in 95% ethanol with ethanethiol gave not only thioether **2**, as one may have predicted, but unexpectedly yielded disulfide **3** in 63% yield.



1

2 3

We were attracted to this reaction by the convenience and the mild reaction conditions under which disulfide **3** was formed, i.e., 2.5 equiv of ethanethiol, room temperature, and 15 h reaction time. To define the scope of this reaction, we carried out a systematic study employing 2-(alkylsulfinyl)-, 2-(phenylsulfinyl)- and 2-(aralkylsulfinyl)benzimidazoles. These 2-sulfinyl-substituted benzimidazoles[1] [Bim-$S^+(\rightarrow O^-)$-R] were allowed to react

(1) The sulfoxide starting materials were prepared by oxidation of the corresponding thioethers with *m*-chloroperbenzoic acid (1 equiv, 0-5 °C) in chloroform. See the Experimental Section for details. The 2-(alkylthio)- and 2-(aralkylthio)benzimidazoles were prepared by alkylation of 2-mercaptobenzimidazole with the appropriate alkyl or aralkyl halide in 95% ethanol in the presence of aqueous sodium hydroxide. 2-(Phenylthio)benzimidazole was prepared by reaction of 2-chlorobenzimidazole in ethanol with excess thiophenol at 90-100 °C. See: Harrison, D., Ralph, R. T. *J. Chem. Soc.* **1965**, 3132.

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