Notes

Radical Nature of the [1,3]Sigmatropic Rearrangements of Electron-Rich Olefins[1]

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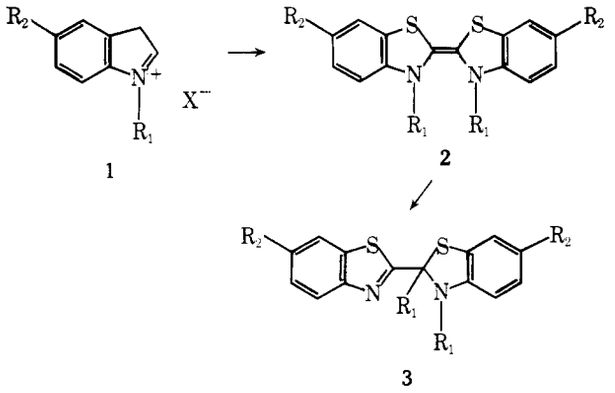
We have previously reported on the competing [1,3] and [3,3] rearrangements of the unstable dimer **2** formed by the action of triethylamine on appropriately substituted benzothiazolium salts **1**.[2] A significant rate enhancement in the rearrangement of the *p*-nitrobenzyl derivative **2a** relative to the benzyl derivative **2b** was cited as being consistent with a



Derivative	R_1	R_2	X (1 only)
a	$CH_2C_6H_4$ (*p*-NO_2)	H	Br
b i	$CH_2C_6H_5$	H	Br
b ii	$CH_2C_6H_5$	H	OTs
c	$CD_2C_6H_5$	H	OTs
d	$CH_2C_6H_5$	CH_3	Br

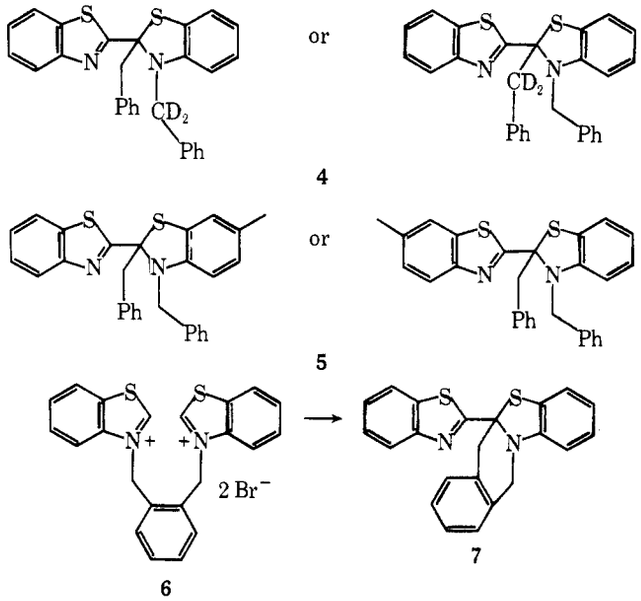
radical process. We now present evidence which demonstrates that a radical mechanism is responsible for the [1,3] rearrangement pathway.

If a concerted process were responsible for the [1,3] rearrangement,[3] then a mixture of **2b** and **2c** would rearrange to give only **3b** and **3c**, respectively. In fact, when this experiment was performed, a significant amount of the dideuterio stable dimer **4** was formed. The product ratios were determined by analysis of the molecular ions. The crossover product represented 28 ± 2% of the total. Although a statistically random intermolecular migration would provide for a 50% yield of dimer **4**, the lower yield is rationalized by a cage effect in a radical dissociation-recombination reaction. The observed product mixture is in accord with a dissociative mechanism having 57 ± 4% rearrangement within the cage.[4] A control experiment showed a mixture of **3b** and **3c** to be stable under the reaction conditions.

One possibility remained. The intermolecular crossover might be occurring prior to the [1,3]-benzyl shift; i.e., the formation of **2** might be reversible. Though there was much evidence against a dissociation to "nucleophilic carbenes",[6] the following experiment was devised to conclusively rule out this possibility. A mixture of **2b** and **2d**, allowed to rearrange under the standard conditions, gave a mixture of **3b** and **3d**. The monomethyl stable dimer **5** was undectable to the limits of the mass spectrometer.

The radical character of the [1,3]-benzyl shift was further confirmed by the gas chromatographic identification of bibenzyl in the crude product **3b**.

Knabe, Dyke, et al.[7] have studied a similar [1,3]-benzyl shift occurring when a 1-benzyl-1,2-dihydroisoquinoline is treated with aqueous acid. They have proposed a bimolecular double-exchange mechanism[8] to account for the intermolecular component which they too have found.[7c,10] The conversion of the bis(benzothiazolium salt) **6** to the stable dimer **7**, with no evidence for the formation of a tetramer, clearly rules out such a mechanism in the bibenzothiazoline series.



In conclusion, we have presented evidence that argues for a radical mechanism in this rearrangement. While it is somewhat unusual that a dissociative process should occur under such mild conditions, it is not without precedent. A number of [1,2] migrations are known to occur under mild conditions via a radical pathway.[11] Resonance stabilization of the bibenzothiazoline radical is surely responsible for the facility of this [1,3]-benzyl migration.

Experimental Section

General Procedures. Melting points were taken on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 700. Nuclear magnetic resonance spectra were recorded at either 60 MHz on a Varian Associates T-60 or at 90 MHz on a Perkin-Elmer R-22. Low-resolution mass spectra were determined at 70 eV on a Hitachi Perkin-Elmer RMU-6.

Analytical gas chromatography was performed on a Varian Aerograph Series 1200 with the appropriate column. Preparative TLC separations were carried out on Merck Silica Gel GF-254, No. 7730; column chromatography utilized Merck Silica Gel 60, No. 7734.

The microanalysis was performed by Midwest Microlab, Inc., Indianapolis, Indiana, and the high-resolution mass spectrum was obtained through the courtesy of Dr. Catherine E. Costello of this department.

3-Benzylbenzothiazolium Bromide [1b (i)]. Ten grams of benzothiazole (74.0 mmol) and 12.7 g of benzyl bromide (74.0 mmol) were heated in dry DMF (10 mL) for 6 h at 95 °C. On cooling, ether (150 mL) was added. The crude salt was collected by filtration and recrystallized from ethanol as pale-yellow needles, 14.7 g (65%): mp 184–186 °C (lit.[12] mp 184–186 °C); NMR (Me_2SO-d_6) δ 6.25 (s, 2 H), 7.3–8.0 (m, 7 H), 8.3–8.8 (m, 2 H), and 10.93 (s, 1 H).

Benzyl-α,α-d_2 Alcohol. A solution of 7.00 g of methyl benzoate

(51.4 mmol) in anhydrous ether (100 mL) was added dropwise (1.5 h) to a stirred suspension of 3.23 g of lithium aluminum deuteride (77.0 mmol) in anhydrous ether (200 mL). After stirring at reflux for 3 h, the reaction was carefully quenched with 5.60 mL of water (311 mmol). Filtration removed the solid residue which was washed with ether (four 50-ml portions). Removal of the solvent from the combined ether layers was followed by distillation. The isolated yield was 4.15 g (73%): bp 82–83 °C (3.2 mm) [lit.[13] 86–86.5 °C (9 mm)]; NMR ($CDCl_3$) δ 1.77 (s, 1 H) and 7.33 (s, 5 H); IR (film) 3350 cm^{-1} (br).

Benzyl Tosylate. Prepared by the method of Kochi and Hammond[14] from the sodium alkoxide and tosyl chloride. Recrystallization from hexane gave white needles, but yields were low due to a variable amount of decomposition which occurred during heating. The crude white product, isolable in nearly quantitative yield by removal of ether from the final solution at 0 °C, was sufficiently pure for further reaction: NMR ($CDCl_3$) δ 2.43 (s, 3 H), 5.03 (s, 2 H), 7.27 (s, 5 H), and 7.52 [(AB q)$_2$, J_{AB} = 8 Hz, $\Delta\nu_{AB}$ = 0.482 ppm, 4 H].

Benzyl-α,α-d_3 Tosylate.[15] Prepared as above from the sodium salt of benzyl-α,α-d_2 alcohol and tosyl chloride.

3-Benzylbenzothiazolium Tosylate [1b (ii)]. Benzothiazole (4.67 g, 34.5 mmol) and freshly prepared benzyl tosylate (8.67 g, 34.5 mmol) were heated in dry DMF (10 mL) for 2 h at 55 °C. On cooling, acetone (75 mL) was added. The white powdery precipitate was collected by filtration and washed with acetone (50 mL). The crude product was sufficiently pure for further use, although recrystallyzation from chloroform was possible: mp (crude) 134.5–135.5 °C; NMR ($CDCl_3$) δ 2.28 (s, 3 H), 6.20 (s, 2 H), 6.9–8.3 (m, 13 H), and 11.58 (s, 1 H).

3-Benzyl-α,α-d_2-benzothiazolium Tosylate (1c). Prepared as above from benzothiazole and benzyl-α,α-d_2 tosylate.

2-Mercapto-6-methylbenzothiazole. Prepared by the method of Sebrell and Boord[16] from *p*-toluidine, carbon disulfide, and sulfur. Recrystallized from benzene: mp 177–180 °C (lit.[16] 181 °C, lit.[17] 175.5–178.5 °C]; NMR ($CDCl_3$) δ 2.42 (s, 3 H) and 7.1–7.3 (m, 3 H).

6-Methylbenzothiazole. Prepared by the method of Blomquist and Diuguid[17] by reduction of 2-mercapto-6-methylbenzothiazole. Purification was accomplished by preparative TLC on silica gel with benzene/ether (1:1) as eluent: NMR ($CDCl_3$) δ 2.53 (s, 3 H), 7.27 (d of d, J_{AB} = 2 Hz, J_{BC} = 8 Hz, 1 H), 7.70 (d, J_{AB} = 2 Hz, 1 H), 8.05 (d, J_{BC} = 8 Hz, 1 H), and 8.92 (s, 1 H).

3-Benzyl-6-methylbenzothiazolium Bromide (1d). Prepared from 6-methylbenzothiazole and benzyl bromide by the procedure used for **1b**(i). The light pink crude product was recrystallized from ethanol as colorless prisms (48%): mp 210–214 °C; NMR (Me_2SO-d_6) δ 6.23 (s, 2 H), 7.2–8.5 (m, 8 H), and 10.88 (s, 1 H).

3,3′-(α,α'-*o*-Xylyl)bis(benzothiazolium bromide) (6). Five grams of benzothiazole (37.0 mmol) and 4.88 g of α,α'-dibromo-*o*-xylene (18.5 mmol) were heated in dry DMF (5 mL) for 2 h at 75 °C. The precipitate which formed was collected by filtration, washed with ether, and then dried in vacuo to give 6.94 g (70%). Recrystallization from ethanol gave a slightly yellow powder: charred ~180–200 °C, mp 216–219 °C; NMR (Me_2SO-d_6) δ 6.53 (s, 4 H), 7.0–8.8 (m, 12 H), and 10.63 (s, 2 H).

3,3′-Dibenzyl-$\Delta^{2,2'}$-bibenzothiazoline (2b). To 1.00 g of **1b**(i) (3.28 mmol) in DMF (15 mL) was added at 0 °C under nitrogen 2.00 mL of triethylamine (14.3 mmol). After 30 min of stirring, the mixture was poured into ice–water (100 mL) and quickly extracted with ether (four 50-mL portions). The combined extracts were washed with cold water (three 50-mL portions), dried ($MgSO_4$), and concentrated in vacuo to give 0.66 g (90%) of a light-yellow solid: NMR ($CDCl_3$) δ 4.68 (s, 4 H), 6.4–7.2 (m, 8 H), and 7.23 (s, 10 H).

This procedure for the preparation of **2b** could also be carried out starting instead with **1b**(ii).

3,3′-Di(benzyl-α,α-d_2)-$\Delta^{2,2'}$-bibenzothiazoline (2c). Prepared from **1c** as described above.

3,3′-Dibenzyl-$\Delta^{2,2'}$-bi(6-methylbenzothiazoline) (2d). Prepared from **1d** as described above.

2-(2-Benzothiazolyl)-2,3-dibenzylbenzothiazoline (3b). To 10.0 g of **1b**(i) (32.8 mmol) in DMF (150 mL) was added with stirring under nitrogen 20.0 mL of triethylamine (143 mmol). The mixture was heated to 90 °C for 2 h, cooled to ambient temperature, and poured into water (800 mL). Extraction with ether (four 400-mL portions) followed by washing the combined extracts with water (four 400-mL portions) gave, after drying ($MgSO_4$), and removal of the solvent in vacuo, 7.0–7.1 g of crude product. Recrystallization from ethanol–ethyl acetate gave 6.15 g (84%) of colorless prisms: mp 144–147 °C; NMR ($CDCl_3$) δ 4.05 (AB q, J_{AB} = 13 Hz, $\Delta\nu_{AB}$ = 0.595 ppm, 2 H), 4.70 (AB q, J_{AB} = 17 Hz, $\Delta\nu_{AB}$ = 0.548 ppm, 2 H), and 5.9–8.2 (m, 18 H); MS (70 eV) *m/e* 450 (M^+).

This procedure for the preparation of **3b** could also be carried out starting instead with **1b**(ii).

Anal. Calcd for $C_{28}H_{22}N_2S_2$: C, 74.63; H, 4.92. Found: C, 74.63; H, 5.06.

2-(2-Benzothiazolyl)-2,3-di(benzyl-α,α-d_2)benzothiazoline (3c). Prepared from **1c** as described above: mp 144.5–146.0 °C; MS (70 EV) *m/e* 454 (M^+).

2-[2-(6-Methylbenzothiazolyl)]-2,3-dibenzyl-6-methylbenzothiazoline (3d). Prepared from **1d** as described above. Recrystallized from ethanol–ethyl acetate as light-yellow prisms (78%): mp 151–152.5 °C; NMR ($CDCl_3$) δ 2.18 (s, 3 H), 2.45 (s, 3 H), 4.04 (AB q, J_{AB} = 13 Hz, $\Delta\nu_{AB}$ = 0.630 ppm, 2 H), 4.65 (AB q, J_{AB} = 17 Hz, $\Delta\nu_{AB}$ = 0.548 ppm, 2 H), and 5.8–8.1 (m, 16 H); MS (70 eV) *m/e* 478 (M^+).

10a-(2-Benzothiazolyl)-10,10a-dihydro-5*H*-11-thia-4b-azabenzo[*b*]fluorene (7). Prepared from **6** described above. The product was isolated in 16% yield by column chromatography on silica gel with hexane–benzene gradient elution and then recrystallized from ethanol–chloroform as white needles (12%): mp 171–174 °C; NMR ($CDCl_3$) δ 4.08 (AB q, J_{AB} = 14.5 Hz, $\Delta\nu_{AB}$ = 0.279 ppm, 2 H), 4.61 (AB q, J_{AB} = 16 Hz, $\Delta\nu_{AB}$ = 0.112 ppm, 2 H) and 6.6–8.0 (m, 12 H); MS (70 eV) *m/e* 372 (M^+).

Anal. Calcd for $C_{22}H_{16}N_2S_2$: mol wt, 372.07550. Found: mol wt 372.07902. There was no peak at *m/e* 744, indicating the absence of any tetramer.

Gas Chromatographic Identification of Bibenzyl as a Byproduct in the Formation of Stable Dimer 3b. The crude dimer, prepared as described above, was dried and then triturated with pentane. The pentane-soluble fraction contained bibenzyl. Its identity was established by coinjection with an authentic sample on two different columns (5% SE-30 on Chrom G and 5% Carbowax 20M on Chrom G). An upper limit of 0.1% can be placed on the yield of bibenzyl.[18]

Crossover Experiment Demonstrating Intermolecularity in the [1,3]-Benzyl Shift. Twenty-eight milligrams of each of freshly prepared **2b** (d_0) and **2c** (d_4), the unstable dimers, was dissolved in dry DMF (2.5 mL) under nitrogen and heated for 2 h at 90 °C. Workup was as usual. After eliminating the contribution of P + 2 and P − 2 ions, the mass spectrum showed approximately 28% formation of **4** (either of two d_2 isomers) with *m/e* 452 (M^+). This corresponds to 57 ± 4% rearrangement within a radical cage (and 43 ± 4% intermolecular rearrangement by escape from the radical cage).

Control Experiment Demonstrating the Stability of Dimers 3 under the Reaction Conditions. A mixture of 20 mg each of **3b** and **3c**, the stable dimers, was dissolved in DMF and subjected to the standard reaction conditions necessary to effect rearrangement. No dideuterio dimer **4** was detectable by mass spectral analysis (upper limit = 5%).

Control Experiment Demonstrating Irreversible Formation of Unstable Dimers. Forty-nine milligrams of **2b** (0.109 mmol) and 52 mg of **2d** (0.109 mmol) were allowed to rearrange under the standard conditions. Workup as usual.[19] The crossover product **5** (either of two monomethyl isomers) was undetectable by mass spectral analysis (upper limit = 3%).

Registry No.—**1b**(i), 4614-22-6; **1b**(ii), 63703-01-5; **1c**, 63703-11-7; **1d**, 63703-02-6; **2b**, 37128-00-0; **2c**, 63703-03-7; **3b**, 51479-81-3; **3c**, 63703-04-8; **3d**, 63703-05-9; **4** isomer 1, 63703-06-0; **4** isomer 2, 63703-07-1; **6**, 63703-08-2; **7**, 63703-09-3; benzothiazole, 95-16-9; benzyl bromide, 100-39-0; benzyl-α,α-d_2 alcohol, 21175-64-4; methyl benzoate, 93-58-3; benzyl tosylate, 1024-41-5; 2-mercapto-6-methylbenzothiazole, 2268-79-3; 6-methylbenzothiazole, 2942-15-6; α,α'-dibromo-*o*-xylene, 91-13-4.

References and Notes

(1) We would like to thank the National Science Foundation and the Petroleum Research Fund, administered by the American Chemical Society, for their generous financial support.
(2) J. E. Baldwin and J. A. Walker, *J. Am. Chem. Soc.*, **96**, 595 (1974).
(3) Two possible thermally allowed pathways exist for the *N*-benzyl rearrangement: (1) antarafacial with retention of configuration at the migrating benzylic center, and (2) suprafacial with inversion of configuration at the migrating benzylic center. The former possibility seemed remote based on geometrical considerations, but the latter remained.
(4) The Stevens rearrangement, a well-accepted radical process, shows a similar effect.[5] For other leading references, see: T. Koenig and H. Fischer, in "Free Radicals", Vol. I, J. K. Kochi, Ed., Wiley, New York, N.Y., 1973, Chapter 4.
(5) J. E. Baldwin, W. F. Erickson, R. E. Hackler, and R. M. Scott, *J. Chem. Soc., Chem. Commun.*, 576 (1970).
(6) See ref 2 (ref 7 therein).
(7) (a) Preliminary communication: J. Knabe, R. Dörr, S. F. Dyke, and R. G. Kinsman, *Tetrahedron Lett.*, 5373 (1972); (b) J. Knabe and R. Dörr, *Arch. Pharmaz.*, **306**, 784 (1973); (c) R. G. Kinsman, A. W. C. White, and S. F. Dyke, *Tetrahedron*, **31**, 449 (1975).
(8) Being an eight-electron suprafacial process, it violates the basic tenets of orbital symmetry.[9] Furthermore, inspection of models indicates that such

a mechanism involves simultaneous front side attacks at both sp^3 benzylic centers.
(9) R. B. Woodward and R. Hoffman, "The Conservation of Orbital Symmetry", Verlag Chemie, Weinham, 1970. See especially chapter 12.
(10) J. Knabe and K. Detering, *Chem. Ber.*, **99**, 2873 (1966).
(11) For example: U. Schöllkopf, U. Ludwig, M. Patsch, and W. Franken, *Justus Liebigs Ann. Chem.*, **703**, 77 (1967).
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(15) K. Mislow, S. Borcić, and V. Prelog, *Helv. Chim. Acta*, **40**, 2477 (1957).
(16) L. B. Sebrell and C. E. Boord, *J. Am. Chem. Soc.*, **45**, 2390 (1923).
(17) A. T. Blomquist and L. I. Diuguid, *J. Org. Chem.*, **12**, 718 (1947).
(18) For a discussion on rate constants for reactions between two dissimilar free radicals, see: K. U. Ingold in ref 4, Chapter 2.
(19) Purification of the crude solid was not attempted as this might possibly have led to enrichment of one of the products.

Fluorene Derivatives: Friedel–Crafts Reaction of 2-Fluorenyl Basic Ethers

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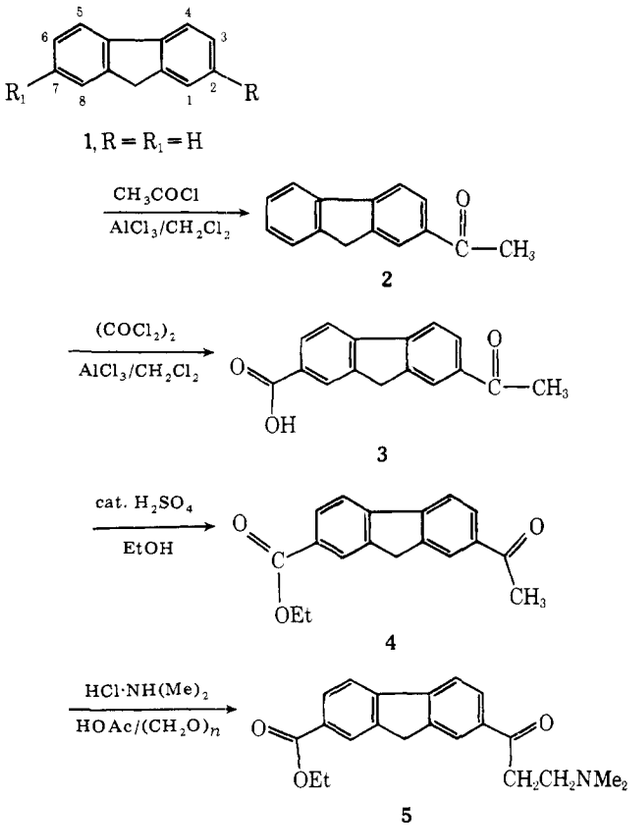
Fluorene 1 (R = R′ = H) has been reported to undergo bis-electrophilic substitution in the 2 and 7 positions.[1,2] While a great deal of synthetic effort has been concentrated on the preparation of symmetrically 2,7-disubstituted compounds, very little work has been done on derivatives of 1 in which R and R′ comprise different functional types.[3,4]

In connection with the synthesis of certain bis-basic derivatives of fluorene having antiviral activity, we were interested in devising synthetic routes to such disymmetric fluorenes. In particular we were interested in synthetic methods to compounds such as **4**, **8**, and **9**. These compounds would be valuable intermediates since simple chemical manipulations could lead to bis-basic fluorene and fluorenone derivatives having dissimilar substituents, e.g., **10**. The preparation and characterization of 2,7 disubstituted **1** compounds in which R and R′ comprise different functional types are described in this paper.

Treatment of 2-acetylfluorene (**2**) with oxalyl chloride led to the corresponding acid derivative **3**. Compound **3** was esterified to ester **4** and then converted to the base **5** (Scheme I). The ether analogues were prepared as shown in Scheme II. Baeyer-Villiger oxidation of **2** followed by hydrolysis of the intermediate acetate afforded **6**. Alkylation of **6** with the appropriate ω-halodialkylamine gave **7a** and **7b**. Although initial attempts to prepare compounds **8a–c** with BF_3·Et_2O used as the catalyst were unsuccessful, they were successfully prepared in good yield by acylation of **7** in methylene chloride with aluminum chloride used as the catalyst. Compounds of formula **8** were isolated as their hydrochloride salts by treatment of the reaction mixture with an aqueous hydrochloric

Scheme I



Scheme II