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Photochemical Synthesis of Benzo[*f*]quinolines[1]

Nicholas R. Beller,[2] Douglas C. Neckers,*[3] and Eleftherios P. Papadopoulos[4]

Departments of Chemistry, The University of New Mexico, Albuquerque, New Mexico 87131, and Bowling Green State University, Bowling Green, Ohio 43403

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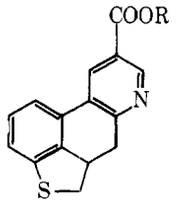
Benzo[*f*]quinolines with a sulfur-containing substituent at position 7 have been synthesized photochemically from the corresponding 2-stilbazoles. An improved synthesis of *o*-(methylthio)benzaldehyde is described.

In the course of a general study of the photochemistry of benzo[*b*]thiophene,[5] we became interested in the possibility of photochemical synthesis of a heterocyclic ring system, 1, capable of subsequent elaboration to 1-deaza-1-thialysergic acid (**2**).



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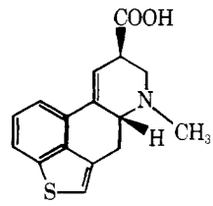

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Since benzo[*b*]thiophene is an isostere of indole, sulfur analogs of biologically active indole derivatives are obvious targets of research and their synthesis as well as pharmacology have been investigated extensively.[6] Among other derivatives, sulfur isosteres of various tryptamines, including serotonin, have been synthesized and found to have pharmacological properties similar to those of the nitrogen compounds.[7] In view of the extraordinary pharmacological activity of lysergic acid and many of its derivatives, it is not surprising that an attempt has been made to synthesize its sulfur isostere, 1-deaza-1-thialysergic acid (**2**). Campaigne and Knapp modeled their approach to **2**[8] after Kornfeld and Woodward's synthesis of lysergic acid,[9] but their effort could not be carried through to the desired compound.

In attacking the problem of the synthesis of a ring skeleton of **2**, we chose to construct first the benzo[*f*]quinoline system **8**, functionalized appropriately with a sulfur containing group at position 7, intending to close the sulfur ring after the simpler heterocycle was intact.

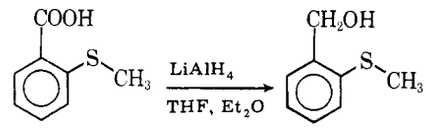
We present herein photochemical preparations of some benzo[*f*]quinolines as possible intermediates in the synthesis of a parent ring system of thiolysergic acid.

Results and Discussion

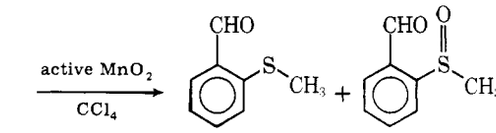
Our choice as a method of preparation of the three-ring system of **8** was the photocyclization of appropriate 2-stilbazoles. Because of its simplicity, this oxidative ring closure has been used on numerous occasions as a direct route to azaphenanthrenes,[10] in spite of generally modest yields. Thus, Kumler and Dybas prepared a variety of benzo[*f*]quinolines by photochemical ring closure of corresponding 2-stilbazoles.[11]

A suitable synthesis had to be developed for *o*-(methylthio)benzaldehyde (**5a**), the starting material for most of the stilbazoles we needed. The reported synthesis of **5a** by $LiAlH_4$ reduction of *N*-methyl-*o*-(methylthio)benzanilide in THF[12] failed in our hands, giving only trace quantities of the desired product. Lithium tri-*tert*-butoxyaluminohydride reduction of *o*-(methylthio)benzoyl chloride using Brown and Subba Rao's procedure[13] gave aldehyde **5a** in 37% yield, still not a particularly satisfactory yield for further synthetic use. An attempt to carry out a Reimer–Tiemann formylation of thiophenol combined with methylation of the mercapto group also was unsuccessful.

Good yields of the desired aldehyde were obtained, however, from a 2-step synthesis in which *o*-(methylthio)benzoic acid (**3**) was reduced to *o*-(methylthio)benzyl alcohol (**4**) which was



3 4



5a 5b

then oxidized to aldehyde **5a** using active manganese dioxide. The oxidation procedure[14] was adapted from Papadopoulos, Jarrar, and Issidorides[15] using the Morton[16] method to prepare active manganese dioxide.

Although certain sulfides are oxidized with active manganese dioxide,[17] we were able to arrive at conditions of solvent and temperature (Table I) in which very little oxidation to the corresponding sulfoxide **5b** occurred. Thus, treatment of 0.1 mol of **4** with a 5-fold (w/w) amount of active MnO_2 in CCl_4, at room temperature, led to reproducible, excellent yields of **5a** containing virtually no alcohol **4** and only traces of sulfoxide **5b**.

Because use of this procedure routinely resulted in overall conversion of about 80% starting from *o*-(methylthio)benzoic acid, we feel that it deserves consideration as a method of preparation of *o*-(methylthio)benzaldehyde. For purposes of identification, but also for use as starting material for the synthesis of appropriate benzo[*f*]quinolines, *o*-(methylsulfinyl)benzaldehyde (**5b**) was prepared in essentially quantitative yield by sodium metaperiodate oxidation of **5a**.[18]

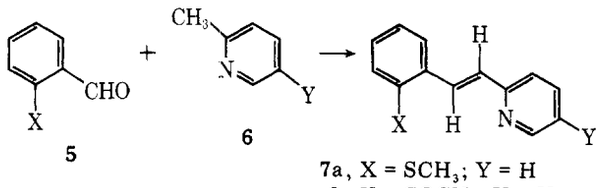
The precursor 2-stilbazoles needed in our work were pre-

Table I. Product Distribution for the Active Manganese Dioxide Oxidation of o-(Methylthio)benzyl Alcohol in Various Solvents[a]

Solvent	Mol %[b] Unreacted 4	5a	5b
Benzene	22	64	14
Cyclohexane	8	89	3
Anhydrous ether	12	70	18
Carbon tetrachloride	5	91	4
Chloroform	15	73	12
Methylene chloride	27	64	9
Ethyl acetate	30	65	5
Acetone	34	59	7
Water	46	45	9

[a] A mixture of 0.5 g of 4 in 25 ml of solvent and 2.5 g of active manganese dioxide was magnetically stirred at room temperature for 8 h. [b] Determined from the peak areas of the benzylic protons of 4 (δ 4.57), methylthio protons of **5a** (δ 2.39) and methylsulfinyl protons of **5b** (δ 2.70) in the NMR spectra of the crude products.

pared mostly by aldol-type condensations of suitably substituted benzaldehydes **5** with 2-picolines **6**.[11,19] Thus, refluxing of benzaldehyde or o-(methylthio)benzaldehyde and ethyl 6-methylnicotinate in acetic anhydride yielded stilbazoles **7d** and **7e**, respectively.



5 6

7a, X = SCH_3; Y = H
b, X = $SOCH_3$; Y = H
c, X = SO_2CH_3; Y = H
d, X = H; Y = COOEt
e, X = SCH_3; Y = COOEt
f, X = $SOCH_3$; Y = COOEt
g, X = SO_2CH_3; Y = COOEt

Stilbazole **7a** was obtained by heating o-(methylthio)-benzaldehyde and 2-picoline with a catalytic amount of zinc chloride in a sealed tube. The sulfur in the side chain of **7a** and **7e** was readily oxidized using the elegant Leonard–Johnson procedure[18] and, in this manner, methylsulfinylstilbazoles **7b**, **7f** and methylsulfonylstilbazoles **7c**, **7g** were prepared.

Stilbazoles **7a–g** were assigned the trans configuration about the double bond on the basis of spectral data. Thus, in their NMR spectra, the vinyl proton peaks (readily identifiable even though overlapping to a varying extent with other signals) exhibited a coupling constant of 16 Hz. Further, the infrared spectra contained absorption bands at 990–965 cm^{-1} typical of trans olefinic C–H bonds (out-of-plane bending). Finally, the ultraviolet spectra showed two absorption bonds beyond 250 nm, of which the one at longer wavelength was more intense, again indicating trans configuration about the double bond.[11,20]

The photocyclization of *trans*-2-stilbazoles is believed to occur stepwise, through the *cis*-2-stilbazoles and the dihydrobenzo[f]quinolines.[11] From the work of Kumler and Dybas it was known that *tert*-butyl alcohol or nonpolar solvents and irradiation through Corex filters gave the best yields of benzo[f]quinolines. Filter selection is critical in order that light absorption by the product be prevented and light absorption by the stilbazole be maximized. The ultraviolet spectra of stilbazoles **7a–g** are similar to that of unsubstituted 2-stilbazole, having *K* bands in the 310–330-nm region and aromatic absorption bands at shorter wavelengths. As shown in Figure 1, use of a Corex 9700 filter appears to allow excitation

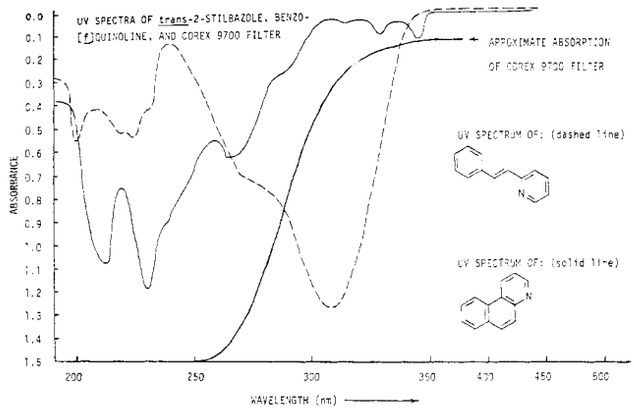
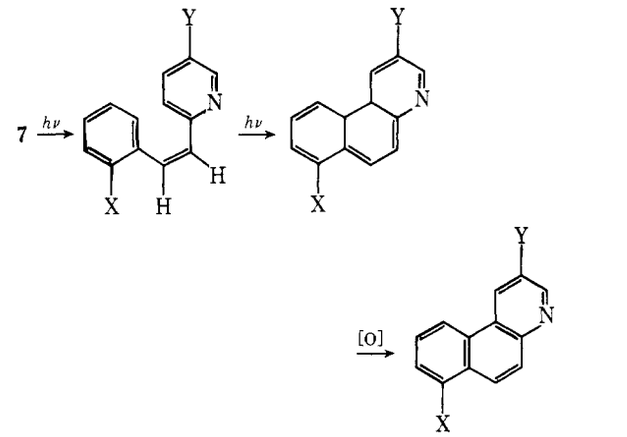


Figure 1.

of the stilbazoles at their wavelength of maximum absorption and at the same time protect the photoproducts from wavelengths of light that could cause further reaction.

Photolyses of stilbazoles **7a–g** were carried out in *tert*-butyl alcohol–benzene mixtures, in the presence of oxygen, using a Corex 9700 filter and were monitored by thin-layer chromatography. Any material which did not correspond to the precursor stilbazole was removed from the TLC plate and had its ultraviolet spectrum compared with that of unsubstituted benzo[f]quinoline.[21] Photolysates which gave UV spectra similar to that of the parent benzo[f]quinoline were then subjected to isolation procedures.

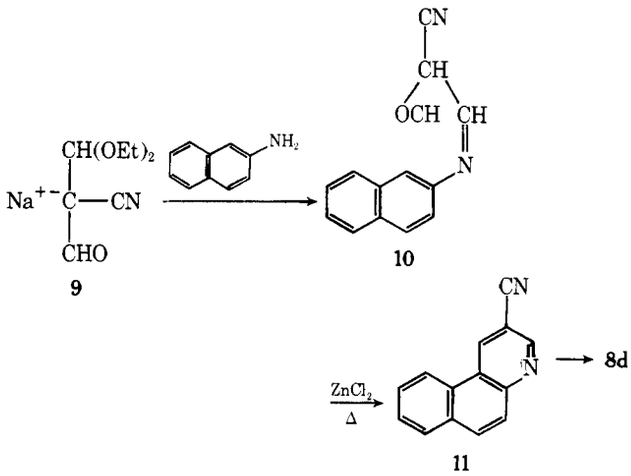
Photolysis of stilbazoles **7c**, **d**, and **g** yielded the corresponding benzo[f]quinolines **8c**, **d**, and **g**, in 21, 19, and 26%



8c, X = SO_2CH_3; Y = H
d, X = H; Y = COOEt
g, X = SO_2CH_3; Y = COOEt

yield, respectively. No useful product could be isolated from the photolysates of stilbazoles **7a**, **b**, **e**, and **f**. There was extensive decomposition (perhaps not unexpectedly, in view of the known lability of the carbon–sulfur bond under photolytic conditions[22]) and no evidence could be found for the presence of a cyclized product in any fraction of the photolysates, except in the case of stilbazole **7f**. Repeated column and thin-layer chromatographic treatments of that photolysate yielded traces of a colorless solid, which had a UV spectrum consistent with a cyclized product, but which could not be fully characterized because of insufficient available material.

The structure of photoproduct **8d** was confirmed by an independent, nonphotochemical preparation based on a series of reactions used by Uhle and Jacobs[23] for the synthesis of dihydrolysergic acid. Thus, the sodium salt of the diethyl acetal of cyanomalondialdehyde (**9**) was condensed with 2-naththylamine to imine **10**, which was cyclized by heating with



zinc chloride to 2-cyanobenzo[*f*]quinoline (**11**). Hydrolysis of **11** followed by esterification yielded **8d**, identical in all respects with the photochemically obtained material.

Work will be continued at a later date on the subsequent step of the synthetic sequence, base catalyzed ring closure involving the 7-methylsulfonyl group and position 6 of benzo[*f*]quinolines **8c** and **8g**, to complete construction of the benzo[*b*]thiophene portion of the thioergoline ring system **1**.

Experimental Section[24]

***o*-(Methylthio)benzoic acid** was prepared from *o*-mercaptobenzoic acid (Aldrich) by the method of Arndt.[25]

***o*-(Methylthio)benzyl alcohol (4).** Into a three-neck, 1-L round-bottom flask equipped with a reflux condenser, calcium chloride drying tube, and mechanical stirrer was placed 25.0 g (149 mmol) of *o*-(methylthio)benzoic acid (**3**). After the addition of 200 mL of anhydrous THF, the acid was made to dissolve by stirring and heating the contents of the flask. The resulting solution was cooled to room temperature, diluted with 400 mL of anhydrous ether, and further cooled in an ice bath for 15 min. Then 5.08 g (134 mmol) of lithium aluminum hydride was added, in small portions with stirring and cooling, during 10 min, and the reaction mixture was allowed to stir at room temperature for an additional 2.5 h. Excess lithium aluminum hydride was then decomposed, first by cautious addition of wet ether and then addition of 500 mL of 10% hydrochloric acid. Following separation of the ether layer, the aqueous layer was extracted with three 250-mL portions of ether and the combined ether solutions were washed with two 250-mL portions of 10% aqueous sodium hydroxide and finally with water. After drying over anhydrous sodium sulfate, the solvent was removed on a rotary evaporator and the residual oil distilled under reduced pressure to yield 18.6 (81%) of **4** as a clear liquid: bp 115–118 °C (1.1 Torr); lit.[26] bp 88 °C (10^{-3} Torr); IR (neat) 3650–3100 cm^{-1} (OH); ^1H NMR δ 2.28 (s, 3 H, CH_3–), 3.43 (s broad, 1 H, –OH), 4.52 (s, 2H, benzyl H's), 6.96 (s, 4H, Ar H's).

***o*-(Methylthio)benzaldehyde (5a).** Into a 2-L, three-neck flask equipped with a mechanical stirrer and calcium chloride drying tube were placed 100 g of freshly powdered active manganese dioxide, 1 L of carbon tetrachloride, and 20.0 g (130 mmol) of *o*-(methylthio)benzyl alcohol. The reaction mixture was allowed to stir for 24 h at room temperature and filtered, and the filter cake of manganese dioxide was washed with three 250-mL portions of acetone. The combined carbon tetrachloride and acetone filtrates were filtered again through a pad of Celite and the clear, light-yellow solution distilled of solvent on a rotary evaporator to give a residual oil. Distillation of this oil under reduced pressure yielded 19.0 g (96%) of **5a** as a light-yellow liquid: bp 96–101 °C (1.4 Torr); lit.[12] bp 149 °C (19 Torr); IR (neat) 1700–1675 cm^{-1} (C=O); ^1H NMR δ 2.35 (s, 3 H, CH_3–), 6.8–7.7 (m, 4 H, Ar H's), 9.97 (s, 1 H, CHO).

***o*-Methylsulfinylbenzaldehyde (5b).** To 138 mL of 0.5 M aqueous sodium metaperiodate (69 mmol of $NaIO_4$), stirred magnetically and maintained at 3 °C, was added 10.0 g (66 mmol) of *o*-(methylthio)benzaldehyde (**5a**) and the resulting mixture was stirred at 3 °C for 15 h. After filtration, the filter cake of sodium iodate was washed with two 50-mL portions of chloroform and the two-phase filtrate shaken in a separatory funnel. The chloroform layer was separated and the aqueous layer extracted with two 50-mL portions of chloroform. The combined chloroform solutions were dried over anhydrous sodium sulfate and the solvent was distilled under reduced pressure to yield a yellow oil which solidified when triturated with cold ether. The resulting crystalline material was collected, washed with a small amount of cold ether, and air dried to yield 10.7 g (96%) of an off-white crystalline product: mp 73–74 °C, lit.[12] mp 73–75 °C; IR (KBr) 1695–1670 cm^{-1} (C=O), 1025(S–O); ^1H NMR δ 2.73 (s, 3 H, CH_3–), 7.4–8.3 (m, 4 H, Ar H's), 9.85 (s, 1 H, CHO).

***trans*-2′-Methylthio-2-stilbazole (7a).** A mixture of 15.2 g (0.100 mol) of *o*-(methylthio)benzaldehyde, 9.31 g (0.100 mol) of 2-picoline and 0.200 g of zinc chloride was heated in a sealed tube, at 200 °C, for 16 h. The product was distilled under reduced pressure to yield 13.1 g (58%) of **7a** as a yellow, viscous oil: bp 158–164 °C (0.25 Torr); IR 970 cm^{-1} (*trans*-CH=CH); NMR δ 2.34 (s, 3, CH_3S–), 6.7–8.1 (m, 9, Ar H and =CH), 8.31 (d, 1, J = 4 Hz, 6-H); UV λ_{max} ($\epsilon \times 10^{-3}$) sh 352 nm (6.8), 310 (18.2), 266 (17.2), 208 (14.2).

Anal. Calcd for $C_{14}H_{13}NS$: C, 73.97; H, 5.76; N, 6.16. Found: C, 73.89; H, 5.61; N, 6.04.

***trans*-2′-Methylsulfinyl-2-stilbazole (7b).** The mixture of a solution of 1.14 g (5 mmol) of **7a** in 80 mL of MeOH and 11.0 mL of 0.500 M aqueous sodium metaperiodate (5.5 mmol of $NaIO_4$) was stirred at room temperature for 24 h. After filtration, the filter cake of sodium iodate was washed with 40 mL of MeOH and the combined filtrate and washings evaporated to about 20 mL. This concentrate was diluted with 250 mL of water and the resulting solution extracted with three 75-mL portions of $CHCl_3$. The extract was dried (Na_2SO_4) and distilled to a viscous, oily residue. This material could not be induced to crystallize, nor could it be distilled under reduced pressure without decomposition. Partial purification by chromatography on an alumina column yielded 0.79 g (65%) of **7b** in the form of a viscous, yellow oil, the NMR spectrum of which showed that it was uncontaminated by the corresponding sulfide or sulfone: IR 1070, 1035 (S–O), 970 cm^{-1} (*trans*-CH=CH); NMR δ 2.61 (s, 3, CH_3SO–), 6.7–8.0 (m, 9, Ar H and =CH), 8.35 (d, 1, J = 4 Hz, 6-H); UV λ_{max} ($\epsilon \times 10^{-3}$) 314 nm (21.0), 226 (11.6), 233 (11.2), 207 (13.8).

Anal. Calcd for $C_{14}H_{13}NOS$: C, 69.11; H, 5.39; N, 5.76. Found: C, 67.32; H, 5.14; N, 5.51.

***trans*-2′-Methylsulfonyl-2-stilbazole (7c).** The mixture of a solution of 4.55 g (17.5 mmol) of **7a** in 400 mL of MeOH and 100 mL of 0.5 M aqueous sodium metaperiodate (50 mmol of $NaIO_4$) was refluxed for 18 h. A second 100 mL of 0.5 M aqueous sodium metaperiodate was then added and followed by a further 18 h of reflux. The reaction mixture was cooled and filtered, and the filter cake washed with 40 mL of MeOH. The combined filtrate and washings were diluted with water to three times its original volume to yield 3.09 g (60%) of **7c** as a colorless solid: mp 100–102 °C; IR 1295, 1150, 1123 (SO_2), 980 cm^{-1} (*trans*-CH=CH); NMR δ 3.03 (s, 3, CH_3SO_2–), 6.8–8.5 (m, 10, Ar H and =CH); UV λ_{max} ($\epsilon \times 10^{-3}$) 312 nm (22.2); 271 (13.0), 231 (12.0), 208 (15.8).

Anal. Calcd for $C_{14}H_{13}NO_2S$: C, 64.84; H, 5.05; N, 5.40. Found: C, 64.99; H, 5.15; N, 5.37.

***trans*-5-Ethoxycarbonyl-2-stilbazole (7d).** A mixture of 10.6 g (0.100 mol) of benzaldehyde, 16.5 g (0.100 mol) of ethyl 6-methylnicotinate[27] and 20.4 g (0.200 mol) of acetic anhydride was refluxed for 12 h, then cooled and poured into ice. The resulting mixture was made basic to litmus with 10% aqueous NaOH and stirred until the organic material solidified. The solid was collected by filtration and recrystallized from EtOH–H_2O to yield 10.9 g (45%) of **7d** as tan crystals: mp 97–99 °C; IR 985 (*trans*-CH=CH), 1710 cm^{-1} (C=O); NMR δ 1.32 (t, 3 H, J = 7 Hz, CH_3CH_2–), 4.23 (q, 2 H, J = 7 Hz, CH_3CH_2–), 6.7–8.1 (m, 9 H, Ar H and vinylic H's), 8.90 (d, 1 H, J = 2 Hz, 6-H); UV λ_{max} ($\epsilon \times 10^{-3}$) 333 nm (33.0), 232 (10.2), 207 (15.0).

Anal. Calcd for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 75.74; H, 5.92; N, 5.58.

***trans*-5-Ethoxycarbonyl-2′-methylthio-2-stilbazole (7e).** From 15.2 g (0.100 mol) of *o*-(methylthio)benzaldehyde, 16.5 g (0.100 mol) of ethyl 6-methylnicotinate and 15.3 g (0.150 mol) of acetic anhydride, as described for **7d**, there was obtained (after recrystallization from MeOH) 18.8 g (63%) of **7e** in the form of a yellow solid: mp 89.5–91 °C; IR 1720 (C=O), 960 cm^{-1} (*trans*-CH=CH); NMR δ 1.37 (t, 3, J = 7 Hz, CH_3CH_2–), 2.42 (s, 3, CH_3S–), 4.29 (9, 2, J = 7 Hz, CH_3CH_2–), 6.7–8.2 (m, 8, Ar H and =CH), 8.97 (d, 1, J = 2 Hz, 6-H); UV λ_{max} ($\epsilon \times 10^{-3}$) sh 352 nm (12.6), 324 (19.5), 272 (13.2), 226 (16.2), 209 (15.9).

Anal. Calcd for $C_{17}H_{17}NO_2S$: C, 68.20; H, 5.72; N, 4.68. Found: C, 68.18; H, 5.83; N, 4.62.

***trans*-5-Ethoxycarbonyl-2′-methylsulfinyl-2-stilbazole (7f).** The mixture of a solution of 1.50 g (5 mmol) of **7e** in 125 mL of MeOH and 11.0 mL of 0.5 M aqueous sodium metaperiodate (5.5 mmol of $NaIO_4$) was stirred at room temperature for 24 h. Following filtration,

the filter cake of sodium iodate was washed with 40 mL of MeOH and the combined filtrate and washings diluted with 600 mL of ice-cold water to yield 1.21 g (77%) of **7f** as a cream-colored solid: mp 128–130 °C; IR 1710 (C=O), 1075, 1035 (S–O), 970 cm^{-1} (*trans*-CH=CH); NMR δ 1.38 (t, 3, J = 7 Hz, CH_3CH_2–), 2.65 (s, 3, CH_3SO–), 4.30 (q, 2, J = 7 Hz, CH_3CH_2–), 6.8–8.2 (m, 8, Ar H and =CH), 8.97 (d, 1, J = 2 Hz, 6-H; UV λ_{max} ($\epsilon \times 10^{-3}$) sh 351 nm (16.5), 330 (28.8), 273 (10.5), 230 (12.9), 208 (16.2).

Anal. Calcd for $C_{17}H_{17}NO_3S$: C, 64.74; H, 5.43; N, 4.44. Found: C, 64.54; H, 5.51; N, 4.44.

***trans*-5-Ethoxycarbonyl-2'-methylsulfonyl-2-stilbazole (7g).** The mixture of a solution of 1.50 g (5 mmol) of **7e** in 200 mL of MeOH and 30 mL of 0.5 M aqueous sodium metaperiodate (15 mmol of $NaIO_4$) was refluxed for 24 h. After addition of a second 30 mL of 0.5 M aqueous sodium metaperiodate and refluxing for a further 24 h, the reaction mixture was cooled and filtered. The filter cake was washed with 40 mL of MeOH and the combined filtrate and washings diluted with 500 mL of ice-cold water to yield 1.54 g (93%) of **7g** as a cream-colored solid: mp 157–159 °C; IR 1720 (C=O), 1315, 1155, 1120 (SO_2), 960 cm^{-1} (*trans*-CH=CH); NMR δ 1.38 (t, 3, J = 7 Hz, CH_3CH_2–), 3.04 (s, 3, CH_3SO_2–), 4.32 (q, 2, J = 7 Hz, CH_3CH_2–), 6.8–8.6 (m, 8, Ar H and =CH), 8.97 (d, 1, J = 2 Hz, 6-H); UV λ_{max} ($\epsilon \times 10^{-3}$) sh 351 nm (12.6), 325 (29.4), 280 (11.1), 236 (11.1), 209 (16.2).

Anal. Calcd for $C_{17}H_{17}NO_4S$: C, 61.62; H, 5.17; N, 4.23. Found: C, 61.55; H, 5.25; N, 4.01.

7-Methylsulfonylbenzo[*f*]quinoline (8c). A solution of 1.30 g (5 mmol) of **7c** in 1 L of *tert*-butyl alcohol–benzene (1:1) was placed in a 1-L photochemical reaction vessel and irradiated with a 450-W Hanovia, medium-pressure, mercury-arc (type 679 A36) lamp contained in a quartz, water-cooled jacket and surrounded by a tubular Corex 9700 filter. Oxygen was bubbled through the solution for 0.5 h prior to and during the 8-h photolysis period, at the end of which the reaction mixture was distilled of solvent to give 3.36 g of a gummy residue. This was dissolved in 50 mL of $CHCl_3$ and the resulting solution mixed with 7.0 g of neutral alumina (Baker No. 0540) to a slurry which was evaporated to dryness under reduced pressure. The solid material was then ground to a powder and placed at the top of a chromatography column[28] of 25.0 g of neutral alumina in a 1 in. glass tube. Elution with benzene–chloroform (1:1) allowed isolation of 0.47 g of a viscous, yellow oil corresponding to a yellow band on the column. This was made to crystallize by trituration with anhydrous ether and yielded 0.27 g (21%) of **8c** as a light-yellow solid: mp 153–156 °C; IR 1307, 1148 cm^{-1} (SO_2); NMR δ 3.17 (s, 3, CH_3SO–), 7.1–8.4 (m, 4, Ar H), 8.64 (d, 4, J = 9 Hz, Ar H); UV λ_{max} ($\epsilon \times 10^{-3}$) 343 nm (0.09), 327 (0.09), 300 (12.0), sh 286 (14.4), 275 (22.2), 242 (34.2), 211 (20.1).

Anal. Calcd for $C_{14}H_{11}NO_2S$: C, 65.35; H, 4.31; N, 5.44. Found: C, 65.17; H, 4.43; N, 5.43.

2-Ethoxycarbonylbenzo[*f*]quinoline (8d). A. Photochemical Synthesis. A solution of 1.27 g (5 mmol) of **7d** in 1 L of *tert*-butyl alcohol–benzene (9:1) was photolyzed as described for **8c**, for 8 h. The resulting solution was evaporated under reduced pressure to 1.55 g of a viscous, brown residue which was dissolved in the minimum amount of chloroform and chromatographed on a column of 40.0 g of neutral alumina in a 1 in. glass tube. The column was eluted with chloroform and the progress of the band corresponding to the photoproduct was monitored by its fluorescence under UV light. The eluate containing the fluorescent band was evaporated to 1.03 g of a viscous, tan residue which was dissolved in the minimum amount of acetone. A portion of this solution, containing 275 mg of the residue, was applied on an 8 × 8 in., 2 mm silica gel preparative thin layer chromatographic plate. Development of the plate with chloroform yielded a fluorescent band near the origin. The absorbent material containing this band was scraped off the plate and extracted with acetone to yield, after removal of the solvent, 70 mg of a viscous oil which was made to crystallize by trituration with cyclohexane. There was obtained 64 mg (19%) of **8d** as a tan solid, mp 103–105 °C (a 1:1 mixture of this material with that obtained by the following nonphotochemical synthesis (mp 101–104 °C) had a melting point range of 102.5–104 °C); IR 1725 cm^{-1} (C=O); NMR δ 1.45 (t, 3, J = 7 Hz, CH_3CH_2–), 4.42 (q, 2, J = 7 Hz, CH_3CH_2–), 7.3–7.75 (m, 3, 7-H, 8-H, and 9-H), 7.81 (s, 2, 5-H and 6-H), 8.37–8.50 (m, 1, 10-H), 9.26 (s, 2, 1-H and 3-H); UV λ_{max} ($\epsilon \times 10^{-3}$) 350 nm (3.6), 337 (4.8), 313 (8.4), 271 (16.4), 263 (16.8), 237 (35.2), sh 220 (24.8).

Anal. Calcd for $C_{16}H_{13}NO_2$: C, 76.48; H, 5.21; N, 5.57. Found: C, 76.54; H, 5.27; N, 5.60.

B. Nonphotochemical Synthesis. A 125-mL Erlenmeyer flask containing 10.0 g of zinc chloride was immersed in an oil bath the temperature of which was being raised at a rate of about 5 °C/min. When the bath temperature reached 180 °C, 10.0 g (45 mmol) of **10** was added into the flask over a period of 2 min with continual stirring of the solid mixture. At a bath temperature of 210 °C the mixture melted and shortly thereafter the flask was removed from the heating bath and allowed to cool. The solidified product was mixed with water, broken into pieces, collected by filtration, and ground into a powder. After it had been washed repeatedly with water, the powdered material was refluxed overnight with 250 mL of 18% hydrochloric acid. The resulting solution was evaporated under reduced pressure to a solid residue which was then refluxed overnight with 1 L of absolute ethanol containing 20 mL of concentrated sulfuric acid. Following distillation of most of the ethanol, the concentrate was mixed with a solution of 100 g of K_2CO_3 in 400 mL of H_2O and the resulting mixture was extracted with several portions of chloroform. After the combined extracts had been dried (Na_2SO_4), the chloroform solution was evaporated to a solid residue, which was mixed with a small amount of anhydrous ether and filtered to yield 2.24 g (20%) of **8d** as a light tan solid: mp 101–104 °C. The IR and NMR spectra of this product were identical with those of the product of the immediately preceding photochemical synthesis.

***N*-(2-Cyano-2-formylethylidene)-2-naphthylamine (10).** Sodium (2.30 g, 0.100 mol) was added to a solution of 14.3 g (0.100 mol) of 1-cyano-2,2-diethoxyethane[23] and 8.00 g (0.108 mol) of ethyl formate in 250 mL of anhydrous ether and the resulting mixture was stirred until all of the sodium had reacted. Following addition of 100 mL of water and separation of the layers, the aqueous solution was run into a warm solution of 14.3 g (0.100 mol) of 2-naphthylamine in a mixture of 100 mL of ethanol and 360 mL of 3% hydrochloric acid. The precipitated yellow solid was collected by filtration and recrystallized from ethanol to yield 10.6 g (48%) of **10** as a salmon-colored solid: mp 214–216 °C; IR 2225 (C≡N), 1645 cm^{-1} (C=O); NMR (Me_2SO-d_6) δ 7.0–8.0 (m, 7, Ar H's), 8.60 (d, 1, J = 15 Hz, –N=CH–), 9.16 (s, 1, –CHO), 11.06 (d, 1, J = 15 Hz, >CH–CN).[29]

Anal. Calcd for $C_{14}H_{10}N_2O$: C, 75.66; H, 4.54; N, 12.60. Found: C, 75.52; H, 4.67; N, 12.60.

2-Ethoxycarbonyl-7-methylsulfonylbenzo[*f*]quinoline (8g). A solution of 1.66 g (5 mmol) of **7g** in 1 L of *tert*-butyl alcohol–benzene (1:1) was photolyzed, as before, for 7 h. The resulting solution was evaporated under reduced pressure to 3.28 g of a gummy residue which was chromatographed, as described for **8c**, on a column of 25.0 g of neutral alumina in a 1-in. glass tube. Elution with benzene–chloroform (1:1) yielded 0.87 g of a light yellow solid corresponding to a yellow band in the column. This crude product, triturated and washed with anhydrous ether, gave 0.53 g of an off-white solid, mp 219–222 °C. NMR analysis of this material indicated that, in addition to **8g**, it contained 18% of the starting stilbazole **7g**. Attempts to purify the photoproduct by recrystallization resulted in an increase of the stilbazole starting material, as evidenced by NMR analysis. A somewhat purer sample was obtained by purification of the photoproduct using preparative TLC on silica gel: IR 1720 cm^{-1} (C=O); NMR δ 1.47 (t, 3, J = 7 Hz, CH_3CH_2–), 3.22 (s, 3, $-SO_2CH_3$), 4.47 (q, 2, J = 7 Hz, CH_3CH_2–), 7.5–8.5 (m, 3, 5-H, 6-H, and 9-H), 8.82 (s, 1, 8-H or 10-H), 8.95 (d, 1, J = 3 Hz, 8-H or 10-H), 9.40 (s, 2, 1-H and 3-H); UV λ_{max} ($\epsilon \times 10^{-3}$) 347 nm (1.2), 333 (2.1), 310 (12.3), 300 (12.3), 281 (15.3), 243 (32.4), 216 (21.0).

Anal. Calcd For $C_{17}H_{15}NO_4S$: C, 61.99; H, 4.59; N, 4.25. Found: C, 60.71; H, 4.74; N, 4.07.

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Registry No.—**3,** 3724-10-5; **4,** 33384-77-9; **5a,** 7022-45-9; **5b,** 62351-49-9; **5** (X = H), 100-52-7; **6** (Y = H), 109-06-8; **6** (Y = COOEt), 21684-59-3; **7a,** 63133-63-1; **7b,** 63104-22-3; **7c,** 63104-23-4; **7d,** 63104-24-5; **7e,** 63104-25-6; **7f,** 63104-26-7; **7g,** 63104-27-8; **7** (X = Y = H), 538-49-8; **8c,** 63104-28-9; **8d,** 63104-29-0; **8g,** 63104-30-3; **8** (X = Y = H), 85-02-9; **10,** 63104-31-4; 1-cyano-2,2-diethoxyethane, 2032-34-0; 2-naphthylamine, 91-59-8; ethyl formate, 109-940-4.

References and Notes

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(2) Department of Chemistry, Oklahoma State University, Stillwater, Okla., 74074.
(3) Fellow of the Alfred P. Sloan Foundation, 1971–1976; Department of Chemistry, Bowling Green State University.
(4) Department of Chemistry, The University of New Mexico.
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Carbon-13 Nuclear Magnetic Resonance Studies of Sulfur Heterocycles. Evidence for Intramolecular 1,3 Electronic Interaction in 3,3-Disubstituted 2*H*-Tetrahydrothiapyran-1-*N*-*p*-tosylsulfimides[1]

John R. DeMember,* Richard B. Greenwald, and David H. Evans

Research Laboratories, Polaroid Corporation, Cambridge, Massachusetts 02139

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Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra of several mono- and disubstituted 2*H*-tetrahydrothiapyrans and dithianes have been recorded and assigned. The compounds studied provide a series which is amenable to correlation by the additivity of substituent effects in ^{13}C NMR spectroscopy. The $\Delta\delta$'s between calculated and observed ^{13}C NMR shifts provided a sensitive probe for substituent–substituent interactions in compounds **6–8, 13,** and **14.** The ^{13}C NMR data obtained suggest an intramolecular 1,3 electronic interaction in 3,3-dimethyl- and 3,3-dialkoxy-1-*N*-*p*-tosylthianes and dithianes (**6–8**) and **13** and **14.** Specifically, the data suggest a weak coulombic attractive interaction between the molecular orbitals of the sulfur with the formal positive charge S^1 and the electrons of the C^2–C^3 bond.

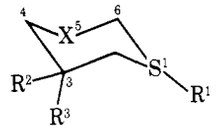
Proton nuclear magnetic resonance (^1H NMR) studies of 2*H*-tetrahydrothiapyran (thiane) and dithiane derivatives have centered primarily on conformational analyses.[2] Recent reports of ^{13}C NMR studies of substituted six-membered-ring hydrocarbons and heterocycles have shown the power of ^{13}C NMR in conformational analysis.[2i,j,3] In many cases, ^{13}C NMR data related to intramolecular 1,3 steric and/or electronic interactions which lead to conformational preferences for six-membered rings have been obtained.[2m] However, definitive elucidation and differentiation of steric and/or electronic interactions based on ^{13}C NMR data have not been possible generally.[4]

Since the chemistry of sulfur compounds is important in many biological and photographic processes, the elucidation of intramolecular interactions and their relation to the physical and chemical properties of thiane derivatives are of interest. Presently, we report a ^{13}C NMR study which provides *direct* ^{13}C NMR spectroscopic evidence for a transannular 1,3 *electronic* interaction in 3,3-disubstituted thiane derivatives.

Results and Discussion

The compounds studied are thiane (**X = CH_2**) derivatives **1–8** and dithiane derivatives (**X = S**) **9–14.**[2,13]

Data for the thiane ring carbon atoms of compounds **1–14** are shown in Table I. Assignments for **1–14** are based on line



X = CH_2		X = S
1	≡ R^1 = electron pair; R^2, R^3 = H	≡ **9**
2	≡ R^1 = *N*-*p*-tosyl; R^2, R^3 = H	≡ **10**
3	≡ R^1 = electron pair; R^2, R^3 = C^7H_3, C^8H_3	≡ **11**
4	≡ R^1 = electron pair; R^2, R^3 = OC^7H_3, OC^8H_3	
5	≡ R^1 = electron pair; R^2, R^3 = $-O-C^7H_2C^8H_2-O-$ (cyclic ketal)	≡ **12**
6	≡ R^1 = *N*-*p*-tosyl; R^2, R^3 = C^7H_3, C^8H_3	≡ **13**
7	≡ R^1 = *N*-*p*-tosyl; R^2, R^3 = OC^7H_3, OC^8H_3	
8	≡ R^1 = *N*-*p*-tosyl; R^2, R^3 = $-O-C^7H_2C^8H_2-O-$ (cyclic ketal)	≡ **14**

intensity, ^{13}C–H coupling constants and the chemical shifts of model compounds. The ^{13}C NMR spectrum of **2** was recorded at −90 °C in CH_2Cl_2.[2c] The high-field signals in the spectrum (−90 °C) of compound **2** have been assigned to those of the axial 1-*N*-*p*-tosyl isomer.[2c] From the relative area of the ^{13}C NMR signals of C^2 in **2** at 41.7 ppm (axial) and 47.9 (equatorial), the axial/equatorial isomer ratio has been determined to be 1.44. This correlates well with the ratio of 1.50 determined from ^1H NMR by Lambert et al.[2c]

Calculated shifts for the ring carbon atoms of compounds