give evidence that transition state A is more probable than B.

Registry No.—I, 5769-15-3; II, 4083-64-1; III, 31593-65-4; IV, 31593-66-5.

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Asymmetric Synthesis of Diastereomeric Hydroxy Sulfides, Sulfoxides, and Sulfones by Condensation and Oxidation Reactions

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The oxidation of diastereomeric 2-thiophenoxy-1,2-diphenyl-1-ethanols to the corresponding sulfoxide-alcohols is shown to be dependent upon the configuration of the carbon bearing the hydroxyl group. Condensations of the lithium salts of phenyl benzyl sulfide, sulfoxide, and sulfone with benzaldehyde give predominately threo products. Crossover products and other evidence for epimerization were found in the sulfoxide condensation. Reduction of 2-phenylsulfinyl-1,2-diphenylethanone gives just one erythro sulfoxide. Evidence for configuration of sulfur and the pseudocontact shifts of the isomeric sulfoxides are briefly discussed.

Sulfoxide chemistry is characterized by a considerable number of relatively highly stereospecific reactions.[1-5] The present work is an inquiry into the stereospecificity of reactions which form the isomeric 2-phenylsulfinyl-1,2-diphenyl-1-ethanols (**4**–**7**), compared to reactions which form the corresponding sulfides **2** and **3** and the sulfones **8** and **9**. The compounds in question are shown in Scheme I in their preferred conformation at carbon.[6]

Condensation of phenyl benzyl sulfide (**10**) with benzaldehyde (**13**) gave a *ca.* 55% overall yield of the 2-thiophenoxy-1,2-diphenyl-1-ethanols of which 40% was the erythro isomer **3** and 60% was the threo isomer **2**.[7-9] This ratio of isomers was insensitive to reaction time. Isomer **2** could also be prepared by reaction of thiophenoxide with cis-stilbene oxide, which proved its threo configuration. Similarly, **3** was formed by reaction of thiophenoxide with *trans*-stilbene oxide.

Condensation of phenyl benzyl sulfoxide (**11**) with **13** gave a mixture of the four sulfoxide–alcohols in *ca.* 40% overall yield. When the reaction was worked up immediately, the following relative yields were observed: 41% **4**, 19% **5**, 8% **6**, and 32% **7**. Reactions using several other aldehydes were similar, showing low yields of the isomers analogous to **5** and **6**. When the reaction was allowed to stir for *ca.* 10 hr before work-up, the isolated products were observed to be significantly richer in the threo isomer **5**: 34% **4**, 29% **5**, 6% **6**, and 31% **7**. A crossover experiment was attempted in which *p*-chlorobenzaldehyde was added to the final reaction mixture of **11** and **13**. Two crossover products (the *p*-chlorophenyl analogs of **4** and **7**) were isolated, which suggests that the mechanism of the epimerization may be a decondensation–recondensation sequence, similar to that found for the Darzens condensation.[10]

The initial product ratio was somewhat richer in the two sulfoxide–alcohols, **4** and **7**, which exhibit substantial intramolecular hydrogen bonding through a six-membered ring. The transition state for the formation of **4** and **7** also very likely involves a six-membered ring, in which a lithium cation is chelated by two oxygen groups (Figure 1). Similar transition states involving highly coordinating cations have been postulated for the Ivanov reaction[7b] and certain carboxylation reactions.[11,12]

Reaction of phenyl benzyl sulfone (**12**) and **13** was the least successful of the condensations, as frequent failure of the reaction occurred. In most successful runs, a *ca.* 59% overall yield was observed, of which 77% was the threo product, **8**, and 23% was the erythro product, **9**.[13] Thus, each condensation gave more of the threo isomer(s), which probably reflects the stability of this isomer,[7c] and the semiequilibrating nature of the reaction.

Oxidation of the cyclic sulfide, penicillin to its sulfoxide has been reported to give predominately one

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(1) This field has been reviewed by C. R. Johnson and J. C. Sharp, *Quart. Rev. Sulfur Chem.*, **4**, 4 (1969).

(2) T. Durst, *J. Amer. Chem. Soc.*, **91**, 1034 (1969).

(3) (a) D. J. Abbott, S. Colonna, C. Stirling, *Chem. Commun.*, 471, 472 (1971); (b) J. Coxon, M. Hartshorn, G. Little, and S. Maister, *ibid.*, 271 (1971).

(4) E. V. Bell and G. M. Bennett, *J. Chem. Soc.*, 86 (1928).

(5) C. R. Johnson and D. McCants, Jr., *J. Amer. Chem. Soc.*, **87**, 1109 (1965).

(6) A previous paper has covered the conformational studies: C. Kingsbury and R. Auerbach, *J. Org. Chem.*, **36**, 1737 (1971).

(7) The stereochemistry of various condensation reactions has been investigated in older work: (a) H. E. Zimmerman and L. Ahramjian, *J. Amer. Chem. Soc.*, **81**, 2086 (1959); (b) H. E. Zimmerman and M. D. Traxler, *ibid.*, **79**, 1920 (1957); (c) H. E. Zimmerman, L. Singer, and B. Thyagaryan, *ibid.*, **81**, 108 (1959); (d) M. Stiles, R. Winkler, Y. Chang, and L. Traynor, *ibid.*, **86**, 3337 (1964); (e) A. T. Nielsen, *J. Org. Chem.*, **30**, 3650 (1965); (f) A. Wettstein, K. Hensler, H. Ueberwasser, and P. Wieland, *Helv. Chim. Acta*, **40**, 323 (1957); (g) P. Rabe, *Justus Liebigs Ann. Chem.*, **313**, 129 (1900), and related papers; (h) O. Widman, *Chem. Ber.*, **51**, 533 (1918); (i) E. P. Kohler and C. Allen, *J. Amer. Chem. Soc.*, **46**, 1522 (1924), and many related papers; (j) R. A. Abramovitch and J. Muchowski, *Can. J. Chem.*, **38**, 554 (1960); (k) I. Iwai and J. Ide, *Chem. Pharm. Bull.*, **13**, 663 (1965); (l) W. S. Fones, *J. Org. Chem.*, **17**, 1534 (1952).

(8) The earliest example of this type of reaction is (a) E. Fromm and E. Erfurt, *Chem. Ber.*, **42**, 3823 (1909); **41**, 3397 (1909).

(9) For other work on condensations involving sulfinyl anions, see (a) E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, **86**, 1639 (1964); (b) *ibid.*, **87**, 1345 (1965); (c) G. A. Russell and G. J. Mikol, *ibid.*, **88**, 5498 (1966); (d) G. A. Russell, E. T. Sabourin, and G. J. Mikol, *J. Org. Chem.*, **31**, 2854 (1966); G. A. Russell and H.-D. Becker, *J. Amer. Chem. Soc.*, **85**, 3406 (1963); (e) T. J. Wallace, H. Pobiner, J. Hoffman, and A. Schriesheim, *Proc. Chem. Soc.*, 137 (1963); L. Field, *J. Amer. Chem. Soc.*, **74**, 3919 (1952); (f) W. E. Truce and K. R. Buser, *ibid.*, **76**, 3577 (1954).

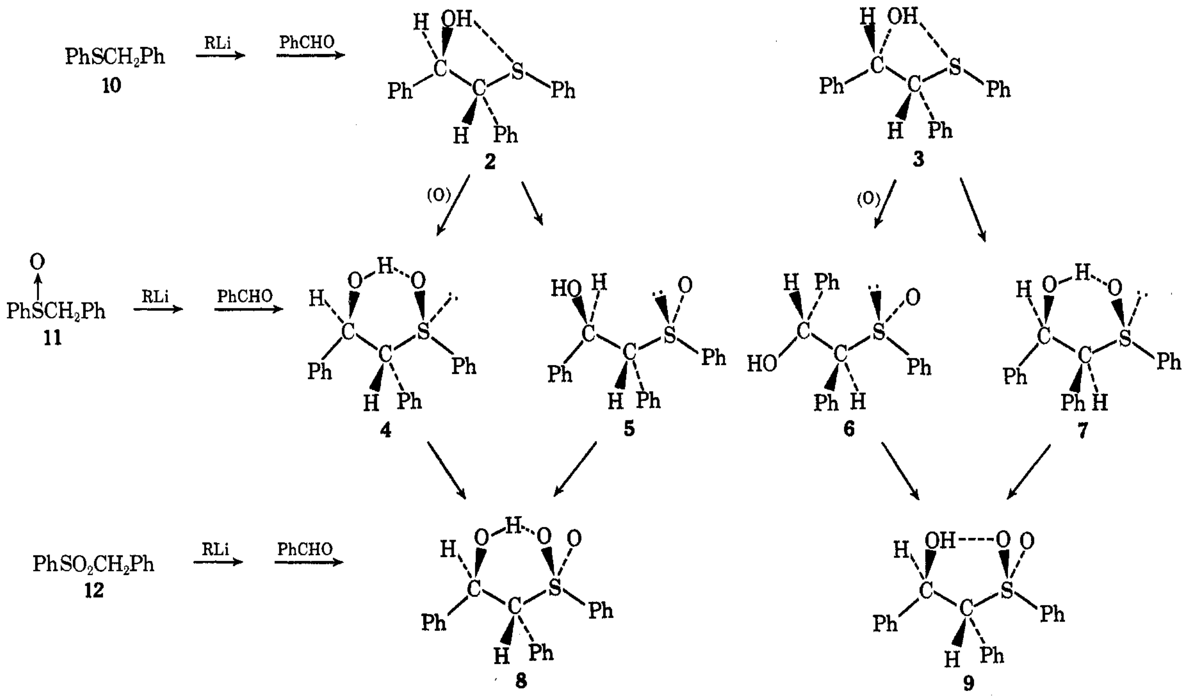
(10) H. E. Zimmerman and L. Ahramjian, *ibid.*, **82**, 5459 (1960). See also A. J. Speziale and D. Bissing, *ibid.*, **85**, 1888, 3878 (1963); M. Schlosser and K. Christmann, *Angew. Chem., Int. Ed. Engl.*, **4**, 689 (1965); E. J. Corey and H. Yamamoto, *J. Amer. Chem. Soc.*, **92**, 226 (1970).

(11) M. Stiles, *ibid.*, **81**, 2598 (1959); M. Stiles and H. Finkbeiner, *ibid.*, **81**, 505 (1959).

(12) See also (a) R. Steinberger and F. H. Westheimer, *ibid.*, **73**, 429 (1951); (b) M. Bender, *Advan. Chem. Ser.*, No. 37, 19 (1963); (c) T. C. Bruice and S. Benkovic, "Bio-organic Mechanisms," Vol. I, W. A. Benjamin, New York, N. Y., 1966, pp 110–118.

(13) A crossover experiment was again successful for the condensation of **12** and **13**.

SCHEME I



diastereomer.[14] The results were interpreted in terms of a hydrogen bond between the amide group and the oxidant, which leads the oxidant to attack one side of the molecule. It was of interest to see if the hydroxyl group of **2** and **3** would exert a similar directive effect in these conformationally mobile molecules.[15] Two different oxidants were used, sodium metaperiodate (**14**) and *m*-chloroperoxybenzoic acid (**15**). These oxidants gave widely varying isomer ratios in the oxidation of a non-hydrogen-bonding system, the 4-substituted thianes.[16] In general, oxidation of **2** and **3** gave predominately the most highly hydrogen bonded sulfoxide. Thus, oxidation of **2** with **14** produced 76% **4** and 24% **5**. Similar oxidation of **2** with **15** formed *ca.* 95% **4** and 5% **5**. Oxidation of the erythro sulfide with **14** formed 89% **7** and 11% **6**. With the peracid **15**, 85% **7** and 15% **6** were observed. These results are completely consistent with a *de facto* directive effect by hydroxyl.

The above synthesis, at best, produced only small yields of the erythro sulfoxide–alcohol **6**. The most convenient synthesis of **6** was the reduction of 2-phenylsulfinyl-1,2-diphenylethanone (**16**). This ketone was formed by condensation of **11** and methyl benzoate.[9c] Two isomeric ketones, **16** and **17**, resulted from the reaction in approximately equal ratios, as observed by nmr, but only **16** could be isolated in a pure state. The isomer **17** was inexplicably labile, although equilibration in *dry* deuteriochloroform catalyzed by piperidine showed 50 ± 5% **16** and 50% **17**. $LiAlH_4$ reduction of **16** in cold tetrahydrofuran gave >95% **6** (>30% overall yield). Other hydrides gave similar results.

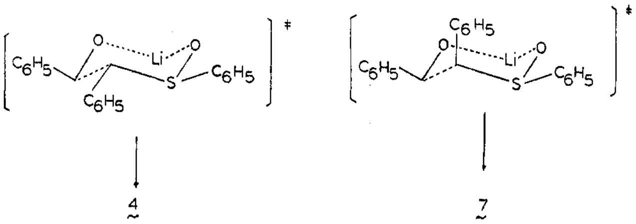
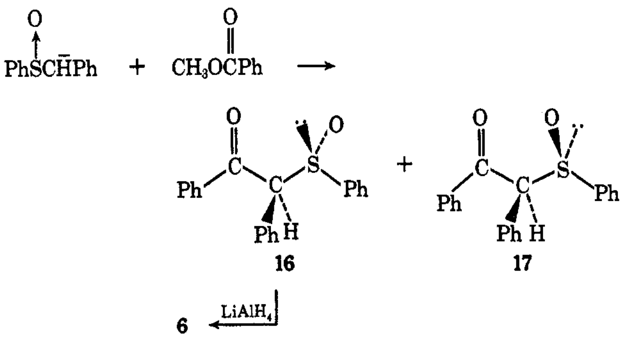


Figure 1.—Condensation transition states leading to isomers 4 and 7.

The steric course of the reduction is consistent with Cram's rule if the phenyl group is considered larger than the phenylsulfinyl group. The *de facto* larger size of phenyl than phenylsulfinyl is not obvious from molecular models, but it is consistent with cyclohexane conformational free energies.[17]



Configuration at Sulfur. Pseudocontact Shifts.—The configurations at sulfur have been given in Scheme I, and in a previous paper without proof, although these configurations were consistent with hydrogen-bonding studies[6] and with oxidation product ratios. Additional evidence for configuration was sought from rela-

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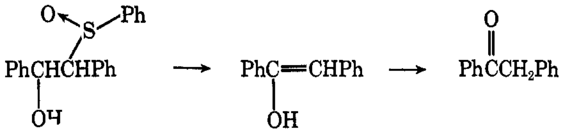
[14] (a) R. A. Archer and P. V. DeMarco, *J. Amer. Chem. Soc.*, **91**, 1530 (1969); (b) R. Cooper, P. V. DeMarco, J. Cheng, and N. Jones, *ibid.*, **91**, 1408 (1969); (c) see, however, D. H. R. Barton, F. Comer, and P. Sammes, *ibid.*, **91**, 1529 (1969).

[15] Similar directive effects by hydroxyl have been noted in other reactions: (a) H. E. Henbest and R. Wilson, *J. Chem. Soc.*, 1958 (1957); (b) M. Mousseron-Canet, B. Labeeuw, and V.-C. Lanet, *Bull. Soc. Chim. Fr.*, 2125, 4165, 4171 (1968); (c) J. Chan and B. Rickborn, *J. Amer. Chem. Soc.*, **90**, 6406 (1968); (d) S. Yamada and K. Koga, *Tetrahedron Lett.*, 1711 (1967).

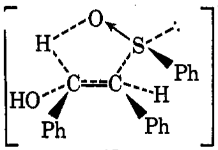
[16] C. R. Johnson and D. McCants, Jr., *ibid.*, **87**, 1109 (1965).

[17] (a) E. Eliel, N. Allinger, S. Angyal, and G. Morrison, "Conformational Analysis," Interscience, New York, N. Y., 1965, p 438; (b) D. J. Cram and F. A. Abd Elhafez, *J. Amer. Chem. Soc.*, **74**, 5828 (1952); (c) see also T. Leitereq and D. J. Cram, *ibid.*, **90**, 4011 (1968).

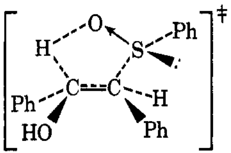
tive rates of pyrolysis of **4**–**7**.[18] The order of reactivity is **6** > **7** > **4** > **5**, by rough factors of 40:7:2:1. The erythro sulfoxides, **6** and **7**, which initially form the trans enol **18**, were the more reactive. By use of Stuart–Briegleb models, **5** was assigned the structure that gave the most sterically hindered transition state, *i.e.*, **19**, in which two sets of phenyl groups are eclipsed.[19] Conversely, **6** was assigned the structure that gave the least hindered transition state *i.e.*, **20**. Although the pyrolysis data should best be considered as an indication rather than a proof of configuration, the assignments are completely consistent with hydrogen-bonding studies and oxidation product ratios.



18



19



20

Pseudocontact shifts were studied in hopes of obtaining more evidence about configuration and conformation at sulfur.[20,21] Although **2**, **3**, **8**, and **9** and their respective benzoates gave well-resolved nmr spectra in the presence of Eu(dpm)$_3$ or Pr(dpm)$_3$, the sulfoxides **4**–**7** and their benzoates gave very broad nmr absorptions at both 60 and 100 MHz. The spectra tended to sharpen at higher temperature, but the peak position moved back to near the peak position in the absence of Eu(dpm)$_3$. The chelating character of these bifunctional compounds with Eu^{III} is presently thought to have an adverse effect upon relaxation times.

Experimental Section

Preparation of Starting Materials.—Phenyl benzyl sulfide (**10**) was prepared by literature methods, mp 39.5–40.5° (lit.[22] 44°). Oxidation by *m*-chloroperoxybenzoic acid (**15**) gave phenyl benzyl sulfoxide (**11**), mp 122.5–124.5° (lit.[22] 125°). Phenyl benzyl sulfone (**12**) was prepared by stirring 35 g (0.176 mol) of sodium benzenefulfinate with an excess of benzyl chloride in an ethanol–water solution for 24 hr. The product was filtered, washed thoroughly with water, and triturated with ethanol–methylene chloride, yielding 28 g of colorless needles, mp 147–149° (lit.[22] 144°).

Preparation of *threo*-2-Thiophenoxy-1,2-diphenyl-1-ethanol (**2**) **and 2 Benzoate.**—This material was prepared by addition of sodium thiophenoxide to *cis*-stilbene oxide, by essentially the method used by Pasto, Cumbo, and Fraser.[23] The product was difficult to crystallize. After repeated chromatographies on silica gel, a solid was obtained, mp 70–72° (lit.[23] 77–78°).

A 1.1-g portion of *threo*-**2** was treated with excess benzoyl chloride in 50 ml of ether containing 1 ml of pyridine. After standing overnight, the mixture was poured into dilute HCl and extracted twice with water. The combined aqueous extracts were extracted with ether. The combined ether layers were extracted with dilute HCl, water, and then dilute sodium carbonate solution. After drying (MgSO$_4$) and evaporation of the solvent, **2** benzoate crystallized upon long standing. This material was recrystallized from ether–pentane, giving 0.3 g (20% yield) of product, mp 70–72°. The main side product was an oily material whose nmr spectrum showed only aromatic protons.

Preparation of *erythro*-2-Thiophenoxy-1,2-diphenyl-1-ethanol (**3**) **and 3 Benzoate.**—The literature procedure[23] was again used. The product, **3**, was recrystallized three times from ether–hexane, mp 98–99.5° (43% yield).

A portion of *erythro*-**3** was benzoylated as above, yielding a solid which was recrystallized three times from ether–hexane, mp 111.0–111.3°.

Condensation of Phenyl Benzyl Sulfide[10] **and Benzaldehyde** (**13**).—To 0.44 g (0.062 g-atom) of lithium stirred under nitrogen in 30 ml of ether was added dropwise 4.7 g (0.03 mol) of bromobenzene. The reaction was started by grinding a piece of lithium in ether with bromobenzene and adding this to the above mixture. The final mixture was refluxed for 0.25 hr, after which **10** was added (5.0 g, 0.025 mol). The resulting orange solution was refluxed for 10 min, and **13** was added dropwise until the color was discharged (3.0 g, 0.028 mol). The colorless final solution was stirred overnight, then added to ice–dilute HCl. The mixture was extracted twice with ether and then with water and dried (MgSO$_4$), and the solvent was evaporated. Crystallization could not be induced; so the mixture was chromatographed on silica gel using increasing amounts of benzene in hexane and ether in benzene, as eluents. The first product obtained was benzhydrol, 3.0 g, then the mixed sulfides **2** and **3** (4.3 g, 56% yield), and finally an unidentified solid, mp 79.2–80.5° (0.2 g). The mixture of sulfides showed 60% of the threo isomer (**2**) and 40% of the erythro isomer (**3**) by nmr. These could be separated only as their benzoate esters.

In another run, the reagents were mixed as before, and aliquots of the final reaction mixture were withdrawn over a 10-hr period, worked up as above, and assayed by nmr. No variation in the ratio of **2** (59%) and **3** (41%) was noted within experimental error.

In another run, *p*-chlorobenzaldehyde (4.6 g) was added to the final reaction mixture formed from 0.01 mol of each reagent. Work-up as before yielded no identifiable *p*-chlorophenyl analogs of **2** or **3**. The nmr spectrum of the sulfide chromatography fraction, however, was exceedingly complex, and suggestive of a mixture of phenyl and *p*-chlorophenyl sulfides.

Preparation of *threo*-2-Phenylsulfinyl-1,2-diphenyl-1-ethanols (**4 and 5**).—To 3.7 g (0.012 mol) of *threo*-**2** in 20 ml of methanol was added 2.74 g (0.013 mol) of sodium metaperiodate (**14**) in about 30 ml of water.[24] Methanol was added to the resulting mixture until the cloudy solution became clear. Even though the inorganic product precipitated rapidly, the mixture was stirred for 6–8 hr. The precipitate was collected and treated twice with hot chloroform, then it was discarded. The remaining methanol solution was added to much water and extracted twice with warm chloroform. The combined chloroform solutions were extracted with water, dried (MgSO$_4$), and evaporated, and the residue was recrystallized by the triangle scheme, yielding 0.65 g of **5** (16% yield), mp 194.0–194.5°, and 1.8 g of **4** (47% yield), mp 126–126.7°.

Anal. Calcd for $C_{20}H_{18}O_2S$ (**5**): C, 74.52; H, 5.63. Found: C, 74.18, H, 5.60. Calcd for $C_{20}H_{18}O_2S$ (**4**): C, 74.52; H, 5.63. Found: C, 74.43; H, 5.30.

Oxidation of the benzoate of **2** with **15** in warm chloroform gave a mixture of *threo*-sulfoxide benzoates in the ratio of 1.75:1, in addition to a trace of **8** benzoate and unreacted starting material. Nmr of the major isomer (probably **4** benzoate) (CDCl$_3$): δ 4.69 (d, 1, J = 9.6 Hz, CHSOPh), 6.7 (d, 1, CHOBz), *ca.* 7.2 (m, Ph), and *ca.* 8.1 (m, 2, *o*-Bz). Nmr of the minor isomer (probably **5** benzoate) (CDCl$_3$): δ 4.09 (d, 1, J = 10.6 Hz, CHOSOPh), *ca.* 6.7 (d, 1, CHOBz) *ca.* 7.2 (m, Ph), and

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[18] (a) C. Walling and L. Bollyky, *J. Org. Chem.*, **29**, 2699 (1964). (b) I. D. Entwhistle and R. A. W. Johnstone, *Chem. Commun.*, 29 (1965); see also *J. Chem. Soc.*, 502 (1967). (c) D. G. Bannard-Smith and J. F. Ford, *Chem. Commun.*, 120 (1965). (d) D. W. Emerson, A. P. Craig, and I. W. Potts, Jr., *J. Org. Chem.*, **32**, 102 (1967). (e) S. I. Goldberg and M. Sahli, *Tetrahedron Lett.*, 4441 (1965).

[19] An earlier paper gives a more complete account of eclipsing effects: C. Kingsbury and D. J. Cram, *J. Amer. Chem. Soc.*, **82**, 1810 (1960).

[20] R. Fraser and Y. Wigfield, *Chem. Commun.*, 1471 (1970), and references cited therein.

[21] K. K. Andersen, P. Card, and J. J. Uebel, Abstracts, 161st National Meeting of the Amerian Chemical Society, Los Angeles, Calif., 1971, No. ORGN 143.

[22] H. W. Clapham and H. Hepworth, *J. Chem. Soc.*, **119**, 1189 (1921).

[23] D. J. Pasto, C. Cumbo, and J. Fraser. *J. Amer. Chem. Soc.*, **88**, 2194 (1966).

[24] N. J. Leonard and C. R. Johnson, *J. Org. Chem.*, **27**, 282 (1962).

ca. 8.1 (m, *o*-Bz). On a preparative scale, the two benzoates, mp 143–147°, defied separation.

Preparation of *erythro*-2-Phenylsulfinyl-1,2-diphenyl-1-ethanols (6 and 7) and Benzoate Derivatives.—By essentially the procedure of Leonard and Johnson[24] (see above), *erythro*-**3** (5.0 g, 0.016 mol) was oxidized with **14** (3.75 g, 0.018 mol) yielding **7**, 4.1 g (71% yield), mp 190–193°, recrystallized from pyridine, mp 204.2–205.4°, and **6**, 0.5 g (9% yield), mp 140–143°, recrystallized from methylene chloride–ether, mp 154.5–155.2°.

Anal. Calcd for $C_{20}H_{18}O_2S$ (**7**): C, 74.52; H, 5.63. Found: C, 75.03; H, 5.80. Calcd. for $C_{20}H_{18}O_2S$ (**6**): C, 74.52; H, 5.63. Found: C, 74.22; H, 5.48.

erythro-**3** was oxidized with **15** and the product ratio was determined by nmr integration (average of several traces) over the characteristic resonances[6] of **6** and **7**. The relative product yields were 85% **7** and 15% **6**. In a large-scale run beginning with 0.9 g (0.00294 mol) of **3**, 0.7 g (74% yield) of **7** was isolated, mp 195–196°. The minor isomer was difficult to isolate in this case. Esterification of the alcohols was complicated by other reactions. The esters were prepared by placing *erythro*-**3** benzoate (3.0 g, 0.007 mol) into 40 ml of cold chloroform, and adding **15** (1.2 g, 0.0073 mol) in 20 ml of cold chloroform in increments. The final mixture was heated for *ca.* 5 min, cooled, extracted twice with dilute Na_2CO_3 and once with water, dried ($MgSO_4$), and evaporated, and the residue was recrystallized by the triangle scheme yielding 0.65 g of **6** benzoate (20% yield), mp 180–181°, and 0.85 g of **7** benzoate (27% yield), mp 169.8–171.2°. An unknown material, 0.45 g, mp 134–136°, whose nmr spectrum showed no alkyl protons, and starting material, 0.4 g, were also isolated. *erythro*-**3** benzoate could not be oxidized with $NaIO_4$ in our hands. The high-melting sulfoxide–benzoate formed **6**, and the low-melting benzoate formed **7**, when treated with potassium hydroxide in ethanol, with the usual work-up.

Anal. Calcd for $C_{27}H_{22}O_3S$ (**7** benzoate): C, 76.03; H, 5.20. Found: C, 75.98; H, 5.23. Calcd for $C_{27}H_{22}O_3S$ (**6** benzoate): C, 76.03; H, 5.20. Found: C, 76.23; H, 5.13.

Condensation of Phenyl Benzyl Sulfoxide (11) with Benzaldehyde.—The calculated quantity of commercial *n*-butyllithium (in this case 12 ml) was added to a slurry of 6.0 g (0.027 mol) of **11**, stirred under nitrogen in 105 ml of dry ether. The mixture was gently heated for 0.5 hr in an attempt to dissolve all of the **11** (in later runs tetrahydrofuran was used with better success). To the orange solution, benzaldehyde (2.2 g, 0.021 mol) was added dropwise, and the mixture was stirred for *ca.* 10 hr. The mixture was poured into ice-dilute HCl. The solid which formed (**5** and **7**) was filtered, washed with water, and air dried. The ether layer was washed with water, dried ($MgSO_4$), and evaporated, yielding 4.7 g of an oil. The nmr spectrum of the oil showed a complex mixture of **11**, benzaldehyde, butyl-containing materials, and **4**. Crystallization was induced with some difficulty. The precipitates were separated by the triangle scheme of recrystallization, yielding 1.1 g (17% yield) of **7**, mp 202–203°, 1.05 g (17% yield) of **5**, mp 193–194°, 0.6 g (9.3% yield) of **4**, mp 124–125°, and 1.3 g of a substance, mp *ca.* 90°, whose nmr spectrum showed it to be a mixture of **4**, **6**, and starting material. From this was isolated 0.05 g of **6**, mp 146–147°, and 0.055 g of **4**, plus 0.7 g of a material whose nmr showed it to contain 78% **4** and 22% **6**.

In another run, 5.0 g (0.023 mol) of **11** was treated with phenyllithium and then benzaldehyde, and the reaction mixture was worked up immediately. The initial precipitate, 1.23 g, was almost pure **7**. The ether solution was worked up as before, and yielded 0.74 g of a material (mp *ca.* 170°) whose nmr spectrum was similar to **5**. Recrystallization from hot chloroform gave pure **5**, mp 193–194°. The remainder was chromatographed on Florisil. With 50% benzene in hexane, the intramolecularly hydrogen bonded isomer **4** and benzhydrol were eluted. Using benzene with a trace of ether as eluent, **4** and **6** were eluted, and these were separated by crystallization. With ether as eluent, a mixture of **5** (0.10 g), **7** (0.03 g), and **4** (0.68 g) were eluted. The latter mixture was separated by recrystallization. A total of 1.26 g (17% yield) of **7**, 0.72 g (9.7% yield) of **5**, 0.34 g (4.6% yield) of **6**, and 1.56 g (21% yield) of **4** were obtained from all sources. In another run, relative yields of 40% **4**, 10% **5**, 15% **6**, and 35% **7** were observed by nmr analysis.

The *p*-chlorophenyl analogs of **4** and **7** (termed **4′** and **7′**) were prepared by condensing the lithium salt of **11** (0.046 mol) with *p*-chlorobenzaldehyde (6.0 g, 0.043 mol). The reaction was worked up as before and the crude product was recrystallized by the triangle scheme. The first material to be isolated, 1.4 g, mp 238–240°, was *p*-chlorobenzoic acid, then 0.8 g of **7′**, mp 185–187°, and finally 1.4 g of the mixed isomers analogous to **16** and **17**, mp 144–149°. The remainder was chromatographed on Florisil, yielding 0.2 g of *p*-chlorobenzyl alcohol, mp 68.5–69.5°, 0.8 g of **4′**, mp 145–146°, and 0.4 g of mixed sulfoxides, mp >173°. The latter, upon recrystallization, yielded some **7′** and small amounts of a third sulfoxide (probably **5′**) which could not be completely separated from **7′**. The fourth sulfoxide (**6′**) was not observed. The sulfoxides **7′** and **4′** were recrystallized to purity, mp 198.5–199.0° and 148.0–149.0°, from chloroform and from methylene chloride–ether, respectively.

Anal. Calcd for $C_{20}H_{17}ClO_2S$ (**7′**): C, 67.31; H, 4.80. Found: C, 67.19; H, 4.63. Calcd for $C_{20}H_{17}ClO_2S$ (**4′**): C 67.31; H, 4.80. Found: C, 67.05; H, 4.70.

Crossover Run.—To a mixture of lithium metal (0.39 g, 0.056 g-atom) stirred under nitrogen in ether, 3.6 g of bromobenzene (0.023 mol) was added and the reaction was induced to begin by crushing a piece of lithium in the mixture. To the phenyllithium solution, **11** (5.0 g, 0.023 mol) was added with a long period of stirring to dissolve as much **11** as possible. To the orange solution, benzaldehyde (about 1.1 g) was added until the solution became colorless. An aliquot of this solution showed no apparent reaction with water. To this mixture 3.2 g of *p*-chlorobenzaldehyde (0.023 mol) was added and the mixture was stirred for 10 hr. The usual work-up was followed. The organic precipitate, *ca.* 1 g, mp >140°, was a mixture of sulfoxides which defied separation. The combined organic materials were chromatographed on Florisil. The first material isolated was **4**, 0.3 g (4% yield), mp 122–123°, then **4′**, 0.1 g (1% yield), mp 145°, mmp with authentic **4′**, 148–149°. Later fractions gave a solid, mp 182°, whose nmr spectrum suggested the presence of **7′**. After repeated recrystallizations, a small amount of **7′** was isolated, *ca.* 0.05 g, mp 199°. Later fractions gave *p*-chlorobenzyl alcohol, 0.8 g, and an inseparable mixture of sulfoxides.

Preparation of 2-Phenylsulfinyl-1,2-diphenylethanone (16).—Commercial *n*-butyllithium (12.1 ml, *ca.* 0.029 mol) was added by syringe to **11** (6.0 g, 0.0271 mol) in 30 ml of ether. The resulting milky orange solution was stirred for 15 min, then methyl benzoate (4.1 g, 0.028 mol) was added dropwise. The resulting mixture was poured onto dilute HCl–ice, extracted twice with water, dried ($MgSO_4$), and evaporated. Recrystallization afforded 1.5 g (20% yield) of **16**, mp 150–151°. The second isomer, **17**, was unaccountably very difficult to purify, although eventually 0.2 g, mp 137–139°, was obtained (somewhat contaminated with **16**). Chromatography of the remaining oil yielded starting materials and an unknown solid material, mp 188–190°.

Anal. Calcd for $C_{20}H_{16}O_2S$ (**16**): C, 74.97; H, 5.03. Found: C, 74.98; H, 5.07.

The above ketone **16** (0.40 g) was dissolved in the minimum tetrahydrofuran (*ca.* 40 ml) and *ca.* 0.2 g of $LiAlH_4$ was added with stirring. Saturated aqueous sodium sulfate solution was added to decompose excess hydride; very dilute HCl was then added and the organic layer was taken up in methylene chloride, dried ($MgSO_4$), and evaporated. The nmr spectrum of the residue showed **6** to be the only observable sulfoxide. Isolation yielded 0.135 g (30% yield) of **6** and a noncrystallisable oil smelling of thiophenol. It runs at lower temperature, the reaction was much cleaner with only **6** and occasionally a trace of **5** being isolated. Control experiments showed that **4**–**7** were about equally unstable to the reaction conditions.

Preparation of 2-Phenylsulfonyl-1,2-diphenyl-1-ethanols (8 and 9).—The condensation was run in a manner analogous to the sulfide and sulfoxide condensations. In several runs the red color of the anion faded before **15** could be added and no product resulted. The lack of solubility of phenyl benzyl sulfone (**13**) was also troublesome. In a run beginning with 5.0 g (0.0216 mol) of **13**, the nmr spectrum showed 35% starting material, 50% threo product, **8**, and 15% erythro product, **9**. The erythro product cocrystallized with **13** and was difficult to isolate, but 4.3 g of **8** was easily obtained (58% yield), mp 118.2–118.7°.

Anal. Calcd for $C_{20}H_{18}O_3S$ (**8**): C, 70.98; H, 5.36. Found: C, 70.94; H, 5.39.

The threo sulfone benzoate was formed by oxidation of **2** benzoate with 2 equiv of **15**, mp 197–198°.

Anal. Calcd for $C_{27}H_{22}O_4S$ (**8** benzoate): C, 73.30; H, 5.02. Found: C, 73.31; H, 5.13.

The erythro sulfide benzoate resisted oxidation to the sulfone. The sulfide–alcohol **3** could be oxidized with **15** at 65° to yield *erythro*-**9**, mp 129.5–131.0°.

Anal. Calcd for $C_{20}H_{18}O_3S$: C, 70.88; H, 5.36. Found: C, 70.93; H, 5.34.

In a crossover run, the anion of **13** was prepared as before (22 mmol). To this material benzaldehyde was added until no color remained. To this mixture, *p*-chlorobenzaldehyde (2.0 g) was added and the mixture was stirred for 3 hr. Chromatography on Florisil gave **16**, **1** (0.4 g), and several fractions of mixed **8'** and **13**. With pure benzene as eluent, **8'**, 0.15 g, mp 151–152° was isolated, which was identical with authentic material prepared separately.

Procedure for the Pyrolyses.—Equal quantities (*ca.* 0.050 g) of two of the four sulfoxides, **4–7**, were dissolved in *ca.* 1 ml of DMSO in an nmr tube and placed in an oil bath at 119 ± 3° A trace of pyridine was added to absorb any acid formed. The nmr tube was withdrawn at invervals and the diminishment of the characteristic nmr signals[6] of **4–7** was followed by nmr integration (the average of 3–5 traces in each of eight points was taken). As **4–7** diminished, the spectrum of deoxybenzoin appeared, identical with that of authentic material.

Registry No.—**2** benzoate, 32120-62-0; **3**, 10277-57-3; **3** benzoate, 32120-64-2; **4**, 28455-74-5; **4'**, 32120-77-7; **5**, 28455-94-9; **6**, 28455-75-6; **6** benzoate, 32120-68-6; **7**, 32120-69-7; **7** benzoate, 32120-70-0; **7'**, 28455-78-9; **8**, 28520-74-3; **8** benzoate, 32120-73-3; **8'**, 32120-74-4; **9**, 28520-75-4; **16**, 32120-75-5; **17**, 32120-76-6.

Substituent Effects on the Half-Wave Potentials of Chalcones in Dimethylformamide

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The reduction half-wave potentials of two series of substituted *trans*-chalcones (I) have been determined in dimethylformamide. One series contains substituents in ring A, included in this series are five ortho-substituted compounds, and the other contains substituents in ring B. The first polarographic reduction wave was studied and it was shown to be a one-electron, diffusion-controlled process. Polarographic data and preliminary cyclic voltametric data indicate that the electrochemical reduction involves rapid chemical reaction of the one-electron transfer product. A very good linear free-energy relationship for substituents in ring A, excluding the ortho substituents, was obtained between $E_{1/2}$ and σ ($r = 0.997$). The linear free-energy relationship for substituents in ring B obtained between $E_{1/2}$ and σ was virtually as good ($r = 0.985$). The $E_{1/2}$ values for the ortho substituents in ring A were positively displaced by about 35 mV from their para isomers. The ortho isomers show a good linear relationship when $E_{1/2}$ is plotted against σ_p ($r = 0.982$). The $E_{1/2}$ data were also treated with the Swain–Lupton expression and generally poorer correlations were obtained with it than those obtained with the Hammett expression. Comparisons of these linear free-energy relationships with others previously reported for the chalcone system are made.

A number of linear free-energy relationships have been established for several α,β-unsaturated ketone systems,[3] including the chalcones. The effect of substituents on ultraviolet spectra,[4] basicities,[5] carbonyl stretching frequencies of chalcones,[6] and dipole moments[7] of chalcone types have been reported. The results of a wide variety of investigations on the effect of substituents on the polarographic half-wave potentials for the reduction of carbonyl compounds have been reported for numerous systems.[8a] Furthermore, there are many examples of correlation of their half-wave potentials with Hammett substituent constants.[8a] For example, good correlations of reduction half-wave potentials with Hammett σ constants were observed for acetophenones[9] and benzophenones.[10]

The effect of substituents on the reduction half-wave potentials of chalcones and chalcone analogs in aqueous media has been reported.[11] The electrochemical reduction mechanism of chalcone in aqueous alcohol mixtures has been studied extensively and is well summarized in a recent publication.[12] The reduction process involves several chemical reactions, is dependent upon hydrogen ion activity, and is further complicated by the formation of organomercury compounds. Electrochemical studies in nonaqueous solvents on chalcone also have been reported;[13] however, a systematic study of substituent effects in a nonaqueous medium has not been carried out. In acetonitrile and in dimethylformamide, chalcone is reduced to a carbanion radical which undergoes rapid polymerization.[13] No evidence is reported for the other reactions which were observed in aqueous solvents. The absence of the more complicated chemical reactions in nonaqueous media should lead to more reliable relationships between half-wave potentials and structure. The elucidation of the structure–reactivity–potential relationship of this relatively simple α,β-unsaturated ketone system will enhance the understanding of the reduction of this system and provide a model for other similar but more complex systems, some

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[1] This work represents a partial fulfillment of the requirements for the B.S. degree with honor by M. L. A.

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