

KINETIC AND EQUILIBRIUM CONTROL IN THE FORMATION OF
GEM-DISULFOXIDE EPIMERS

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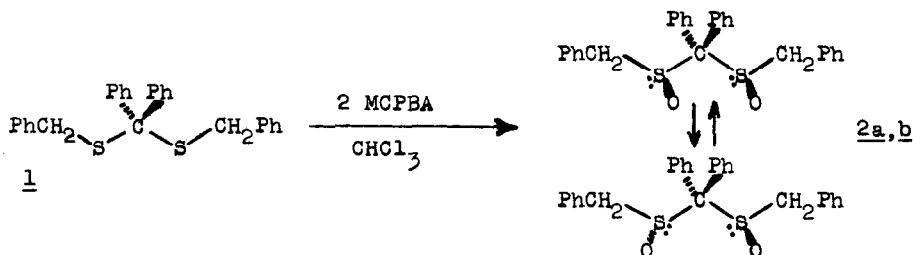
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We wish to report the first example of equilibrium control of the ratio of disulfoxide epimers formed by the oxidation of gem-disulfides (thio-acetals). Benzophenone bis(benzylthio) acetal (1) was rapidly and quantitatively converted at 0-4° into a mixture of the epimeric disulfoxides, 2a and 2b, in a ratio that continued to change progressively even well after the oxidation was completed. Spontaneous interconversion of these epimers was also observed in a chloroform solution originally containing only one epimer. These observations suggest that kinetic and equilibrium control are responsible for the proportions of 2a and 2b in the reaction mixtures.



These results are very surprising in view of those recently reported by Tsuchihashi¹ who concluded that the epimer ratios of a series of unsubstituted-methylene disulfoxides, RS(O)CH₂S(O)R', prepared from the monosulfoxides, depend only on kinetic control. The methylene disulfoxides showed no tendency to epimerize, an observation apparently in agreement with other reports describing the preparation and isolation of similar disulfoxide epimers.²⁻⁴

Conversions of 1 into 2 with 2 MCPBA in CHCl₃ at 0-4° were virtually completed within 3 min,⁵ and epimers 2a and 2b were easily distinguishable by their respective CH₂ AB quartets.⁶ The reaction mixtures were washed with aq NaHSO₃ and NaHCO₃ or treated with dry NH₃ and the organic layer was con-

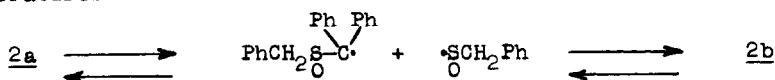
centrated to an oil; trituration with pentane-Et₂O provided white crystals of 2 (85-90%), mp 98-100°, nmr, δ^{CDCl_3} 7.80-7.00 (m, Ph), 3.84 and 3.37 (AB q, $J = 12.5$ Hz, CH₂ of 2a) and 4.02 and 3.34 (AB q, $J = 12.5$ Hz, CH₂ of 2b). Examination (nmr) of the reaction mixtures indicated that 2a and 2b were present in a ratio of 42:58 after 3 min at 0-4°, 35:65 after 10 min at 0-4°, 28:72 after 30 min at 25°, and 25:75 after 70 min at 25°.

Epimer 2a (10-15%) was isolated when the reaction was terminated within a few minutes and the product was recrystallized (CHCl₃-Et₂O) without delay; mp 101-102°; ir, $\nu_{\text{max}}^{\text{CCl}_4}$ 1055, 1074 and ν_{KBr} 1050, 1070 (d, vs, S-O str; there was no O-S-O absorption of the corresponding sulfone⁵); nmr, δ^{CDCl_3} 7.80-7.60, 7.60-7.40, 7.35-7.00 (3 groups of complex multiplets, 20 H, Ph) and 3.84 and 3.37 (AB q, $J = 12.5$ Hz, 4 H, CH₂).⁷

Epimer 2b (10-15%) was isolated when work-up was delayed and recrystallization was allowed to proceed over an extended period; nmr, δ^{CDCl_3} 7.80-7.40, 7.35-7.00 (2 groups of multiplets, 20 H, Ph) and 4.02 and 3.34 (AB q, $J = 12.5$ Hz, 4 H, CH₂); mp and ir were identical with those of 2a.⁷

A CDCl₃ solution of one pure epimer in a closed nmr tube gradually indicated the formation of the other epimer. Oxidation of 1, 2a, or 2b quantitatively provided the same disulfone, mp 204° (dec).⁵

The equilibration of 2 may be compared to the racemization of benzylic sulfoxides. Mislow has shown that benzyl tolyl sulfoxide undergoes racemization at 135° via a homolytic dissociation-recombination mechanism, and the activation energy for the racemization, 44 kcal/mol, was equated with the upper limit of the bond dissociation energy, $D(\text{PhCH}_2\text{—SOTol})$.^{8a} On the other hand, alkyl and aryl sulfoxides, whose carbon-sulfur bond dissociation energies are in the neighborhood of 56-69 kcal/mol, generally require temperatures above 200° for racemization, and the process occurs by pyramidal inversion without bond scission.^{8b} Since benzylic carbon-sulfur bonds have bond dissociation energies 12-25 kcal/mol lower than those of the corresponding alkyl carbon-sulfur bonds,⁹ the bond dissociation energies of benzhydrylic carbon-sulfur bonds should be lowered to a greater degree. For 2, therefore, the bond dissociation energy, $D(\text{PhCH}_2\text{SOCPh}_2\text{—SOCH}_2\text{Ph})$, should be in the neighborhood of 20-30 kcal/mol, and homolytic dissociation-recombination would reasonably account for the observed equilibration of 2a-2b at 0-25°. In contrast, the bond dissociation energies of unsubstituted-methylene disulfoxide epimers, $D(\text{RSOCH}_2\text{—SOR}')$, should be considerably larger, and their equilibration by either mechanism would proceed too slowly to be recognized at moderate temperatures.



Equilibration of 2 by the homolytic processes is also supported by observations not compatible with other mechanisms: 1) Equilibration in CHCl_3 was significantly faster in the presence of MCPBA, a free-radical progenitor; 2) After standing for several days (25°), reaction mixtures of 2 exhibited new resonances in the CH_2 region which could be associated with dimerization products formed slowly from the equilibrating species,¹⁰ and 3) Although pure 2b melted sharply at $101\text{--}102^\circ$, it was transformed into an intractable pink viscous oil when dissolved in CCl_4 and heated at 80° for 15–30 min, a result suggesting that free-radical reactions involving CCl_4 were initiated during the equilibration.^{10, 11}

The meso and dl assignments reported for the unsubstituted-methylene disulfoxide epimers have been based on the non-equivalence and equivalence, respectively, of the methylene protons.^{1–4} The absence of these corresponding protons in 2 precludes the direct application of this technique. However, tentative assignments of 2a-meso and 2b-dl were deduced through an extension of this technique. Thus, of the two epimers, 2a exhibited the more complex phenyl-proton resonance, an observation which was associated with the non-equivalent gem-diphenyls of the meso structure.¹² In support of these assignments, our data (extrapolated, $t \rightarrow 0$) suggest that 2a may be the kinetically preferred epimer; in all of the kinetically controlled oxidations reported by Tsuchihashi,¹ the meso (erythro) disulfoxide predominated. A detailed investigation of these phenomena is in progress.¹³

NOTES AND REFERENCES

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3. M. Cinquini, S. Colonna, and F. Taddei, Boll. Sci. Fac. Chim. Ind. Bologna, 27, 231 (1969).
4. R. Louw and H. Niewenhuyse, Chem. Commun., 1561 (1968).
5. C. Y. Meyers, L. L. Ho, A. Ohno, and M. Kagami, Tetrahedron Lett., 4751 (1973).
6. The two equivalent CH_aH_b groups (diastereotopic protons with respect to S-O) within each epimer are different for 2a and 2b.
7. Elemental analysis was correct for structure 2.
8. (a) E. G. Miller, D. R. Rayner, H. T. Thomas, and K. Mislow, J. Amer. Chem. Soc., 90, 4861 (1968); (b) D. R. Rayner, A. J. Gordon, and K. Mislow,

- ibid., 90, 4854 (1968).
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10. These observations parallel those of Mislow who similarly accounted for the formation of other products during the thermal racemization of benzyl tolyl sulfoxide, especially when carried out in p-xylene (ref 8a).
11. (a) Radical-chain reactions of CCl_4 are especially rapid (see C. Walling, "Free Radicals in Solution," John Wiley and Sons, New York, 1957, Chapter 6); (b) It is significant that homolytic dissociation would also account for certain characteristics exhibited by species related to 2; e.g., the cleavage reactions of 1 (ref 5), and our observation that trityl phenyl sulfoxide apparently undergoes oxidation (to the sulfone) faster than it is formed from the sulfide and MCPBA (C. Y. Meyers and M.-L. Hsu, to be published); (c) Rapid dissociation-recombination would also account for the surprisingly low and virtually identical melting points of 2a, 2b, and their mixtures.
12. The phenyl-proton resonance of 2a resembles that of benzhydryl benzyl sulfoxide which possesses non-equivalent gem-diphenyls. In contrast, benzhydryl benzyl sulfide and sulfone, as well as 1 and its sulfone, whose respective gem-diphenyls are equivalent, exhibit much simpler phenyl-proton resonance (cf. C. Y. Meyers and G. J. McCollum, Tetrahedron Lett., 289 (1973) and ref 5).
13. Support by National Science Foundation Grant GF-3676 and the Japan Society for the Promotion of Science is gratefully acknowledged.