

Distinct Difference of Chemical Behaviors between 5H,7H-Dibenzo-
[b,g][1,5]dithiocin 12-Oxide and Thiazocine S-Oxide

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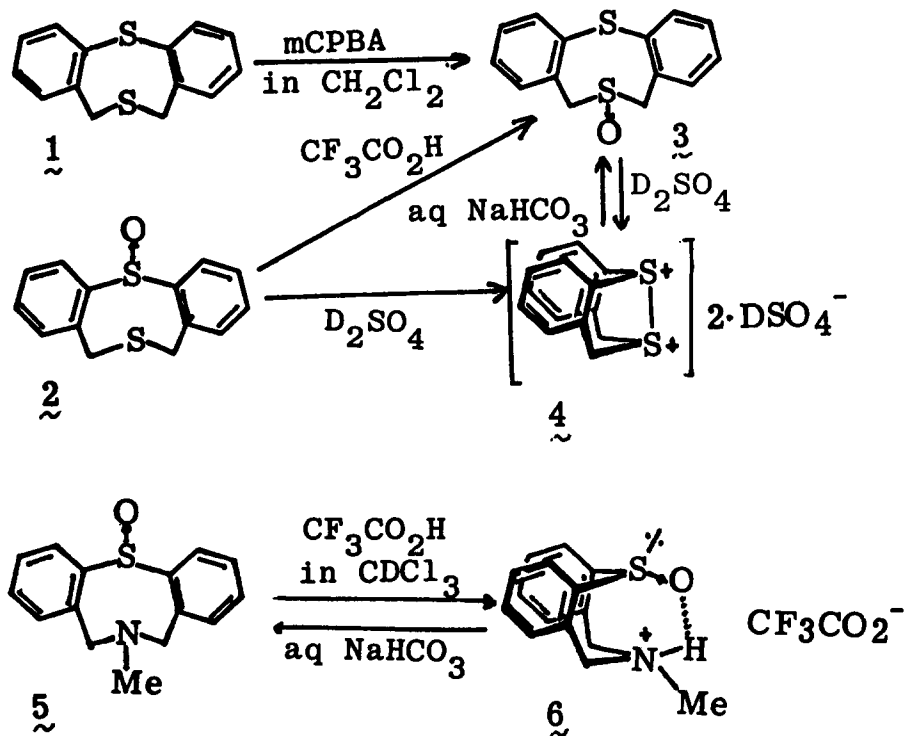
5H,7H-Dibenzo[b,g][1,5]dithiocin 12-oxide (2) rearranged into 6-oxide (3) in the presence of $\text{CF}_3\text{CO}_2\text{H}$. The corresponding thiazocine S-oxide (5) was only protonated at the amino group under the same conditions. Furthermore, methylation of 2 afforded S-methylated product (7) in contrast to O-methylated product in 5.

In connection with our investigations on the formation of a hypervalent bond in dibenzothiazocine system,¹ the regioselective preparation and the conformational properties of the title compound came in point. Many kinds of heterocyclic analogue of dibenzo[a,d]cyclooctadiene skeleton have been prepared mainly for detailed conformational analyses.² This letter describes the distinct difference of chemical behaviors between the title dithiocin and azocine in connection with the conformational features.

5H,7H-Dibenzo[b,g][1,5]dithiocin (1) was prepared by the procedure reported by Ollis et al.^{2a} Oxidation of 1 with an equimolar amount of m-chloroperbenzoic acid (mCPBA) afforded 6-oxide (3) exclusively. Another oxide (2) was obtained by an alternative way via cyclization of the corresponding bis(o-bromomethylphenyl) sulfoxide with sodium sulfide hydrate in methanol solution in 82 % yield.

Standing of 2 in CDCl_3 solution in the presence of excess $\text{CF}_3\text{CO}_2\text{H}$ afforded 3 exclusively and smoothly at room temperature via apparent 1,5-oxygen shift by intra- and/or intermolecular mechanism. The same product (3) was also obtained after quenching the solution of 2 dissolved in concentrated sulfuric acid with aqueous sodium hydrogen carbonate at low temperature. Quantitative formation of dithiodication (4) was observed in D_2SO_4 starting from both 2 and 3, however, this fact does not necessarily

imply the presence of $\underline{4}$ during the migration.³ The result is very different from that of 5H,7H-dibenzo[b,g][1,5]thiazocine 12-oxide ($\underline{5}$) where just protonation occurs at the amino group as shown in $\underline{6}$.⁴



Methylation of $\underline{2}$ with Meerwein's reagent ($\text{Me}_3\text{O}^+\text{SbCl}_6^-$) furnished S-methylated product ($\underline{7}$). Structural determination of $\underline{7}$ is based on the ^1H NMR and IR spectral data (see Table I). The benzyl protons appear as an AB quartet at δ 4.77 and 5.35 ($J = 14.1$ Hz) in CD_3CN solution. In the IR spectrum, the characteristic absorption was observed at $\nu_{\text{max}} = 1030$ and 1070 cm^{-1} assignable to stretching vibration of the sulfoxide group.

There are some interesting structural problems in these dibenzodithiocin derivatives concerning the conformation of eight-membered ring. The elucidation of conformational properties of such a ring system was possible as a result of distinctive differences in the ^1H NMR spectra of the boat-chair and twist-boat conformers. The methylene peak of one of the conformers shows a distinct AB quartet due to rigidity of the conformation, while the other has a singlet like peak due to flexibility of the conformation at room temperature. The former signals are assigned to the boat-chair conformer and the latter to the twist-boat conformer according to the literature.^{2,5} The characteristic ^1H NMR spectral data for benzyl protons are apparent in Table I. The ^1H NMR spectra of $\underline{2}$ and $\underline{7}$ do not show

any temperature dependence from $-30\text{ }^{\circ}\text{C}$ to $70\text{ }^{\circ}\text{C}$, which indicates that these compounds exist as a single conformer in CDCl_3 solution. In the ^1H NMR spectra of $\underline{2}$ and $\underline{7}$, ortho protons to the sulfoxide group appear at δ ca. 8; the downfield shift relative to the other aromatic protons is a direct consequence of the deshielding anisotropy by the sulfoxide group. This is supported by the same ^1H NMR feature of $\underline{5}$ and $\underline{8}$, the structure of which has been determined by X-ray analysis.^{1a,b} Therefore, the most favorable and preferential conformer in $\underline{2}$ and $\underline{7}$ can be concluded as the boat-chair conformer and the sulfoxide group is close to benzene rings as shown below (not $\underline{7}'$). Although there are two geometric isomers for $\underline{7}$ concerning the configuration at the two sulfur atoms, only a single isomer was produced by methylation. Judging from the steric hindrance, attack of an electrophile from quasi-equatorial direction is preferred as shown. This is supported by X-ray structure analysis of $\underline{7}$, although further refinement is still necessary ($r = 0.150$).

Here it is noticeable that methylation of $\underline{2}$ resulted only in S-methylation ($\underline{7}$), whereas dibenzothiazocine 12-oxide ($\underline{5}$) reacted to give O-methylated compound ($\underline{8}$) exclusively under the same conditions.^{1a} The difference of chemical behavior between the title compounds can be explained by considering their favorable conformer at the ground state in solution. Thus, the sulfoxide group of $\underline{5}$ is reactive to an electrophile due to transannular participation of the amino function to the electron deficient sulfoxide group resulting in the twist-boat conformer,¹ in contrast to that of $\underline{2}$ where the boat-chair conformer is preferred to the twist-boat conformer.

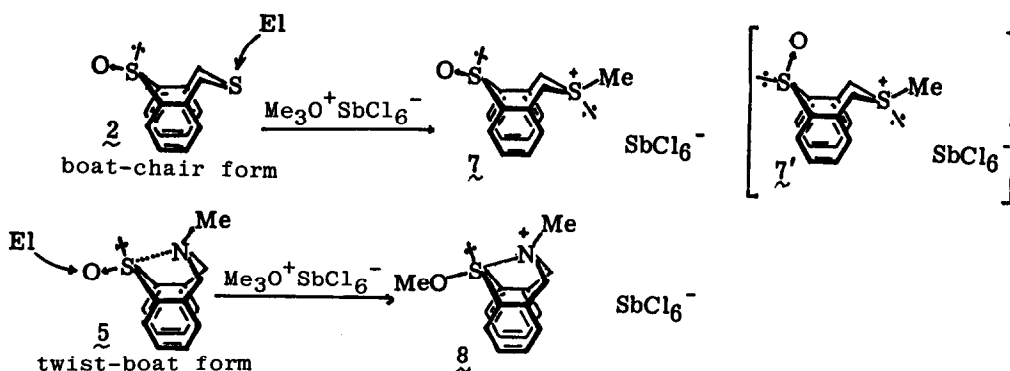


Table I. Physical Data of New Compounds⁶ and their Related Compounds.

compd.	mp (°C)	solvent	¹ H NMR (δ)		aromatic	IR (KBr) (ν _{max} , cm ⁻¹)
			Me	CH ₂		
2	202.5-204.5	CDCl ₃	-	3.88, 4.55 (ABq, J=15 Hz, 4H) ^b	7.00-7.50 (m, 6H) 8.00-8.12 (m, 2H)	1070, 1035
3	184.5-187	CDCl ₃	-	3.88, 3.95 (ABq, J=13 Hz) ^a 4.19, 5.61 (ABq, J=12.5 Hz) ^b	7.17-7.59 (m, 8H)	1055, 1045
4 ^c		D ₂ SO ₄	-	5.26, 5.55 (ABq, J=15.6 Hz, 4H) ^{a, e}	7.10-7.80 (m, 8H)	
5 ^d	113-115	CDCl ₃	2.56 (s, N-Me)	3.88 (s, 4H) ^a	6.98-7.67 (m, 6H) 8.08-8.35 (m, 2H)	1065, 1015
6 ^c		CDCl ₃ + CF ₃ CO ₂ H	2.50 (d, J=5 Hz)	4.80 (dd, J=5, 14 Hz, 2H), 4.83 (d, J=14 Hz, 2H) ^a	7.27-7.63 (m, 6H) 8.00-8.33 (m, 2H)	
7	178-181.5	CD ₃ CN	3.20 (s, S-Me)	4.77, 5.35 (ABq, J=14.1 Hz) ^b	7.50-7.73 (m, 6H) 8.03-8.18 (m, 2H)	1070, 1030
8 ^d	148-151	CD ₃ CN	2.77 (s, N-Me) 3.92 (s, O-Me)	4.25 (s, 4H) ^a	7.35-7.80 (m, 6H) 7.92-8.15 (m, 2H)	1445, 993

^a, twist-boat form. ^b, boat-chair form. ^c, not isolated. ^d, Ref. 1a and 1b. ^e, DSS as an internal standard.

References and Notes

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- (3) Detailed mechanistic study is now in progress. (a) Furukawa et al. proposed such a dithiodication intermediate in 1,5-oxygen rearrangement in 1,5-dithiocin 1-oxide; N. Furukawa, A. Kawada, and T. Kawai, *J. Chem. Soc., Chem. Commun.* 1151 (1984). Very recently they observed the same dibenzo-dithiodication (4) in D₂SO₄ solution; private communication. (b) W. K. Musker, T. L. Wolford, and P. B. Roush, *J. Am. Chem. Soc.* **100**, 6416 (1978).
- (4) N. J. Leonard and A. E. Yethon, *Tetrahedron Lett.* 4259 (1965).
- (5) Even though the conformation of dibenzodithiodication (4) must be twist-boat or boat-boat, considerably separated AB quartet (J = 15.6 Hz) was observed. This should be due to the rigidity of the conformation, resulting from the formation of a bond between both sulfur atoms.
- (6) Analytical and spectral data for all new compounds were fully compatible with the given assignments.

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