Lack of Stereoselectivity in the Formation of Thietane 1,1-Dioxide Derivatives from Anancomeric Aminocyclohexenes (1)

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Two diastereoisomeric thietane 1,1-dioxides are formed in the reaction of methanesulfonyl chloride with 4-*t*-butylcyclohexanone enamines in the presence of triethylamine. Their structures and relative chemical stabilities are discussed.

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A number of papers are available in the literature about [$_{\pi}2 + _{\pi}2$] enamine sulfene cycloaddition, all concerning the mechanism of attack of sulfene, whether it is concerted or stepwise in nature (2-10). However, a less studied aspect regards the stereoselectivity in the formation of thietane 1,1-dioxide derivatives by approach of the heterocumulene to conformationally locked substrates (11,12).

The present paper deals with this particular feature, by using 4-*t*-butyl-amino-cyclohexenes (**1**) as substrates (Scheme 1). Under the conditions reported in the experimental, an approximately 1:1 mixture of two diastereoisomeric thietane 1,1-dioxides **2** and **3** are formed in all cases. Both are assigned *cis* fusion as determined by the analysis of their 200 MHz nmr spectra, two of which are reported in the Figure. The patterns relative to the protons H_C in

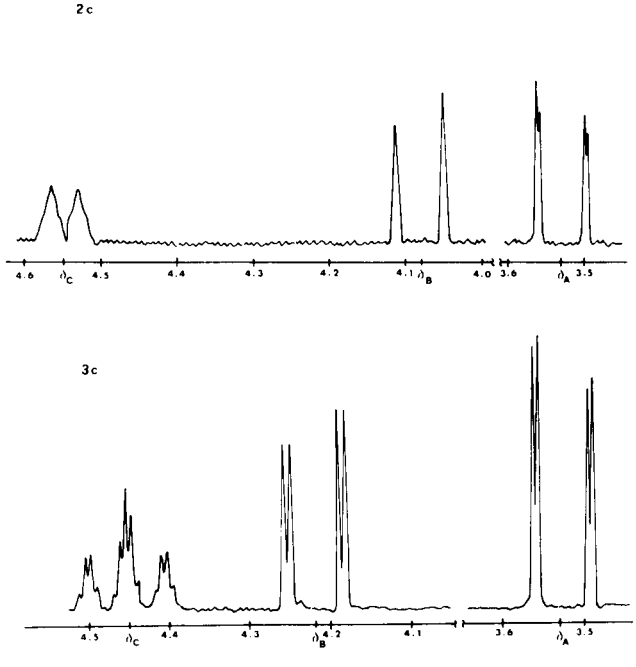


Figure The ABC patterns for **2c** and **3c**, respectively

both systems are indicative of some distortions in the tetrahedral angles introduced by the fusion. In fact the narrow signals ($J_{5,6} \cong 7$ and 0 Hz) in the range 4.37-4.55 ppm (Table) are consistent with the equatorial position of H_C in **2**, while the larger signals between 4.37 and 4.45 ppm ($J_{5,6} \cong 9$ Hz) account for the axial orientation of the same protons in **3**. The values of the vicinal coupling constants $J_{5,6}$ reflect both the flattening of the chair, as indicated by the Dreiding models, and the effect of the electronegativity of the sulfone group.

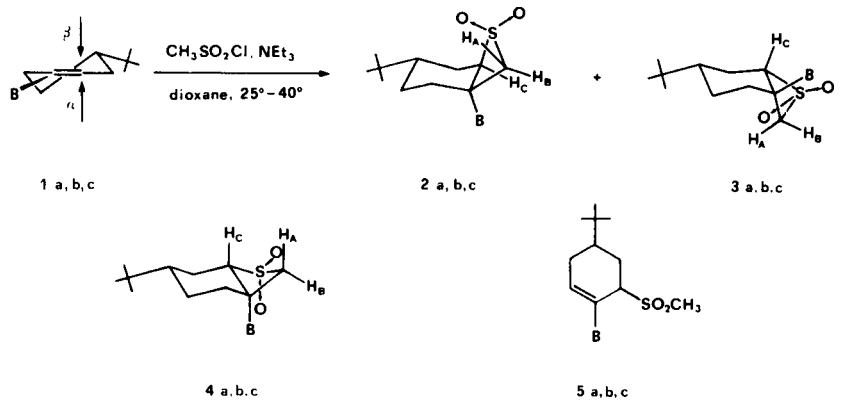
As a consequence of this attribute, compounds **2** are surely *cis* fused, while the fusion of **3** may be inferred from a comparison of the chemical shifts of their protons H_A, H_B and H_C. The range of absorptions is in accordance with expectations, as they are α to the sulfone group. Within this range however, H_C resonates downfield from the others, being bonded to a bridge carbon and *cis* to the base (12,13). This would not be the case if the fusion between the rings were *trans*, as in **4** (Scheme 1), whose H_C would be *trans* to the base and hence less deshielded.

As to the pattern of the AB systems, in all cases except for **2a** and **2b**, it can be considered an AX system, the $\Delta\nu/J$ ratio being above 9. Therefore in **3** the observed splittings can be directly related to the actual coupling constants $^4J_{AC}$ and $^4J_{BC}$. Their relative magnitudes, although small (Table), are consistent with the *trans* and *cis* four-bond coupling respectively and therefore with the assigned structure.

Since the ratio **2/3** is near 1, it is evident that they are formed by a very low stereoselective attack of sulfene from both the α and β sides of **1**, irrespective of the different basicity (14) of the amine component in the substrates.

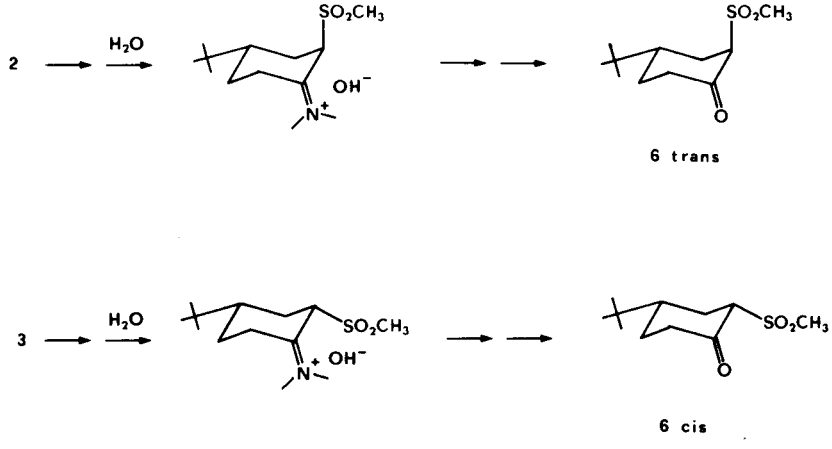
Formation of **2** and **3** is reversible as proved by isolation of the corresponding 4-methylsulfonyl morpholine, when heated with morpholine (15). However, they do not interconvert under any conditions. In fact only tars are obtained from the attempted equilibrations, together with small amounts of the hydrolysis product, *i.e.* 2-methylsulfonyl-4-*t*-butylcyclohexanone (**6**), as a mixture of *cis* and *trans* isomers. As far as hydrolysis is concerned, it has been observed that the thietane 1,1-dioxides **2** undergo hydrolysis to give the *trans* ketone on standing in air more or less easily, depending on the base, whereas **3** remains

SCHEME 1



a: B = morpholin-4-yl, b: B = piperidin-1-yl, c: B = pyrrolidin-1-yl

SCHEME 2



Table

Some ^{1}H-NMR Data for the Thietane 1,1-Dioxide Derivatives **2** and **3**

	δ_A	δ_B	δ_C	J_{AB}	J_{AC}	J_{BC}	$J_{5,6}$
2a	3.65	3.92	4.41	12.4	1.0	<0.4	7.2, <0.4
2b	3.65	3.90	4.37	12.4	1.0	<0.4	7.4, <0.4
2c	3.53	4.08	4.55	12.4	1.1	<0.4	7.0, <0.4
3a	3.55	4.23	4.40	13.4	1.2	2.0	9.0, 8.6
3b	3.59	4.16	4.37	13.4	1.1	2.0	9.0, 8.6
3c	3.53	4.22	4.45	13.5	1.2	1.8	9.8, 8,8

unchanged. This different behaviour could be related to the relatively easier formation of the immonium intermediate from **2**, with respect to **3**. The intermediate derived from **3** would suffer from strong $A^{1,3}$ strains (16) between the substituent and the base (Scheme 2).

Finally, it has been observed that under experimental conditions different from those indicated, formation of open-chain products **5** (Scheme 1) prevails over that of the heterocyclic products. Since compounds **5** are not formed by opening of **2** or **3** under the mild conditions used, this would indicate that two mechanisms must operate in the two cases (12).

EXPERIMENTAL

Melting points are uncorrected The nmr spectra were obtained on a Varian CXL-200 spectrometer in deuteriochloroform using tetramethylsilane as internal standard. The ir spectra were recorded on a Perkin Elmer 297 spectrophotometer for nujol mulls. Silica gel G (Merck) plates were used for analytical tlc, while silica (Merck, 70-230 mesh ASTM) was used as the stationary phase for chromatographic columns.

General Procedure.

To a dry dioxane solution of triethylamine and **1** in 1:1 molar ratio, methanesulfonyl chloride was added in one portion, allowing the temperature to rise from room temperature up to 40°. The mixture was stirred for 24 hours, the hydrochloride salt filtered off and the solvent removed. The oil which resulted showed no traces of unreacted enamine **1**, indicating that the reaction was complete.

1-(Morpholin-4-yl)-4-*t*-butyl-7-thiabicyclo[4.2.0]octane 7,7-Dioxide [1α,4α,6α] (**2a**). 1-(Morpholin-4-yl)-4-*t*-butyl-7-thiabicyclo[4.2.0]octane 7,7-Dioxide [1β,4α,6β] (**3a**).

The crude reaction mixture was separated by column chromatography (eluant: acetone-benzene, gradient polarity), to give **2a** (52%), R_f 0.35 (tlc, eluant: acetone-benzene 7%), mp 123-124° from 2-propanol; nmr: δ 0.86 (s, Bu-*t*, 9H), 2.54 (m, CH_2NCH_2, 4H), 3.70 (m + d, CH_2OCH_2, H-8(H_A), 5H), 3.92 (d, H-8(H_B), 1H), 4.41 (broad d, H-6 (H_C), 1H); ir: 1315-1300, 1145, 1120 cm^{-1} (SO_2).

Anal. Calcd. for $C_{15}H_{27}NSO_3$: C, 59.80; H, 8.97; N, 4.65. Found: C, 60.02; H, 9.01; N, 4.60.

The isomer **3a** was also isolated (43%), R_f 0.45, mp 130-131°, from benzene-light petroleum; nmr: δ 0.84 (s, Bu-*t*, 9H), 2.52 (m, CH_2NCH_2, 4H), 3.55 (dd, H-8(H_A), 1H), 3.68 (m, CH_2OCH_2, 4H), 4.23 (dd, H-8(H_B), 1H), 4.40 (broad dd of quartets, H-6(H_C), 1H); ir: 1320-1130 cm^{-1} (SO_2).

Anal. Calcd. for $C_{15}H_{27}NSO_3$: C, 59.80; H, 8.97; N, 4.65. Found: C, 59.97; H, 9.0; N, 4.70.

The remaining 5% was identified as the open-chain product **5a**.

1-(Piperidin-1-yl)-4-*t*-butyl-7-thiabicyclo[4.2.0]octane 7,7-Dioxide [1α,4α,6α] (**2b**). 1-(Piperidin-1-yl)-4-*t*-butyl-7-thiabicyclo[4.2.0]octane 7,7-Dioxide [1β,4α,6β] (**3b**).

The reaction products were separated by column chromatography, **2b** (52%), R_f 0.30 (tlc, eluant: acetone-benzene 4%), mp 122-123°, from 2-propanol; nmr: δ 0.84 (s, Bu-*t*, 9H), 2.44 (m, CH_2NCH_2, H-2eq, H-5eq, 6H), 3.65 (d, H-8(H_A), 1H), 3.90 (d, H-8(H_B), 1H), 4.37 (broad d, H-6(H_C), 1H); ir: 1318, 1140, 1138 cm^{-1} (SO_2).

Anal. Calcd. for $C_{16}H_{29}NSO_2$: C, 64.18; H, 9.76; N, 4.68. Found: C, 64.39; H, 9.71; N, 4.60.

The isomer **3b** was also separated (45%), R_f 0.45, mp 64-66°; nmr: δ 0.84 (s, Bu-*t*, 9H), 2.44 (t, CH_2NCH_2, 4H), 3.59 (dd, H-8(H_A), 1H), 4.16 (dd, H-8(H_B), 1H), 4.37 (broad dd, H-6(H_C), 1H); ir: 1320-1135 cm^{-1} (SO_2).

Anal. Calcd. for $C_{16}H_{29}NSO_2$: C, 64.18; H, 9.76; N, 4.68. Found: C, 64.0; H,9.68; N, 4.64.

The remaining 3% was the open-chain enamine **5b**.

1-(Pyrrolidin-1-yl)-4-*t*-butyl-7-thiabicyclo[4.2.0]octane 7,7-Dioxide [1α,4α,6α] (**2c**). 1-(Pyrrolidin-1-yl)-4-*t*-butyl-7-thiabicyclo[4.2.0]octane 7,7-Dioxide [1β,4α,6β] (**3c**).

The two isomers **2c** and **3c** were separated from the reaction mixture by column chromatography, **2c** (42%), R_f 0.20 (tlc, eluant: acetone-benzene 4%), mp 85-87°, from light petroleum; nmr: δ 8.50 (s, Bu-*t*, 9H), 2.56 (m, CH_2N, 2H), 2.66 (m, CH_2N, 2H), 3.53 (d, H-8(H_A), 1H), 4.07 (d, H-8(H_B), 1H), 4.55 (broad d, H-6(H_C), 1H); ir: 1330-1305, 1115 cm^{-1} (SO_2).

Anal. Calcd. for $C_{15}H_{27}NSO_2$: C, 63.13; H, 9.54; N, 4.91. Found: C, 63.28; H, 9.12; N, 4.74.

The isomer **3c** was also isolated, (42%), R_f 0.45, mp 124-125°, from absolute ethanol; nmr: δ 0.83 (s, Bu-*t*, 9H), 2.56 (m, CH_2N, 2H), 2.76 (m, CH_2N, 2H), 3.53 (dd, H-8(H_A), 1H), 4.22 (dd, H-8(H_B), 1H), 4.45 (dd of quartets, H-6(H_C), 1H); ir: 1330-1310, 1125-1110 cm^{-1} (SO_2).

Anal. Calcd. for $C_{15}H_{27}NSO_2$: C, 63.13; H, 9.54; N, 4.91. Found: C, 63.42; H, 9.67; N, 4.82.

The remaining 16% was identified as the open-chain enaminosulfone **5c**.

2-Methylsulfonyl-4-*t*-butylcyclohexanone (**6**).

Compound **2c** was refluxed in de-areated benzene for 48 hours. Elimination of the solvent left a viscous oil which was treated with diluted hydrochloric acid and extracted with chloroform. The solvent was evaporated and the solid residue (20%) was identified as a mixture of **6** *trans* and *cis*, mp 116-118°; nmr: δ 0.96 (s, Bu-*t*, 9H), 2.97 (s, CH_3, 0.9H), 3.11 (s, CH_3, 2.1H), 3.84 (m, H-2, 1H, $W_H \cong 16$ Hz); ir: 1710 (CO), 1300-1285, 1130-1110 cm^{-1} (SO_2).

Anal. Calcd. for $C_{11}H_{20}SO_3$: C, 56.86; H, 8.68. Found: C, 57.01; H, 8.63.

The mixture of the two diastereoisomers was crystallized from ligroin, giving the *trans* ketone **6**, mp 137-138°; nmr: δ 0.96 (s, Bu-*t*, 9H), 2.97 (s, CH_3, 3H), 3.78 (broad d, H-2, 1H, $W_H \cong 9$ Hz).

Analogous results were obtained starting from **3c**, although opening to **6** was much slower.

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REFERENCES AND NOTES

(1) Part of this investigation was presented at the 8th International Congress of Heterocyclic Chemistry, Graz, Austria, 1981.

(2) H. Ulrich, "Cycloaddition Reactions of Heterocumulenes", Academic Press, New York, 1967.

(3) L. L. Muller and J. Hamer, "1,2-Cycloaddition Reactions", Interscience, New York, 1967.

(4) G. Opitz, *Angew. Chem., Int. Ed. Engl.*, **6**, 117 (1967).

(5) W. E. Truce and L. K. Kim, *Mech. React. Sulfur Comp.*, **4**, 145 (1969).

(6) T. Nagai and N. Tokura, *Int. J. Sulfur Chem.*, **B7**, 207 (1972).

(7) W. E. Truce and J. F. Rach, *J. Org. Chem.*, **39**, 1109 (1974).

(8) L. A. Paquette, J. P. Freeman and S. Maiorana, *Tetrahedron*, **27**, 2599 (1971).

(9) M. Rivière, N. Paillous and A. Lattes, *Bull. Soc. Chim. France*, 1911 (1974).

(10) F. S. Abbott, J. E. Coates and K. Haga, *J. Org. Chem.*, **42**, 3502 (1977).

(11) J. F. Stephen and E. Marcus, *ibid.*, **34**, 2535 (1969).

(12) H. Mazarguil and A. Lattes, *Bull. Soc. Chim. France*, 3713 (1969).

(13) C. T. Goralsky and T. E. Evans, *J. Org. Chem.*, **37**, 2080 (1972).

(14) G. Stork, A. Brizzolara, H. Landesman, J. Smuszkovicz and R. Terrel, *J. Am. Chem. Soc.*, **85**, 207 (1963).

(15) R. A. Ferri, G. Pitacco and E. Valentin, *Tetrahedron*, **34**, 2537 (1978).

(16) F. Johnson, *Chem. Rev.*, **68**, 375 (1968).