of white powder, m.p. 132–134°. The pure hydrated quaternary salt was obtained as small, shiny platelets from ethanol–ether, m.p. 136° dec.

Anal. Calcd. for $C_{22}H_{34}N_2O_6S_2$: C, 54.29; H, 7.04; N, 5.76; S, 13.18. Found: C, 54.24; H, 6.94; N, 5.69; S, 13.13.

Attempted Quaternization of X. 3′-Morpholinospiro[5-norbornene-2,2′-thietane] 1′,1′-Dioxide *p*-Toluenesulfonate (X·*p*-TsOH).—A solution of 5.4 g. (0.02 mole) of purified X (containing about 5% of an isomeric substance, m.p. 118–121°) and 4.1 g. (0.022 mole) of methyl *p*-toluenesulfonate in 50 ml. of ethanol was refluxed for 4 hr. After cooling, ether was added to the cloud point and the contents were cooled. There was obtained 6.6 g. (75.0 %) of a white solid, m.p. 204–209°. Two recrystallizations of this material from ethanol–ether gave the pure *p*-toluenesulfonic acid salt, m.p. 217–218°.

Anal. Calcd. for $C_{20}H_{27}NO_6S_2$: C, 54.40; H, 6.16; N, 3.17; S, 14.52. Found: C, 54.40; H, 6.08; N, 3.35; S, 14.60.

A 1.0-g. sample of this salt was dissolved in water and the aqueous solution was treated with a slight excess of sodium hydroxide solution. The cloudy suspension was extracted several times with 10-ml. portions of methylene chloride. The combined organic layers were washed with water, dried, filtered, and evaporated. The resulting white solid was recrystallized from ethanol to give 550 mg. of pure X, m.p. 128–129°.

4-Methyl-4-{spiro[5-norbornene-2,2′-thietane]-3′-yl}morpholinium *p*-Toluenesulfonate 1′,1′-Dioxide (XXII).—A mixture of 13.5 g. (0.05 mole) of X (m.p. 118–121°) and 13.0 g. (0.07 mole) of methyl *p*-toluenesulfonate was heated on a steam bath for 4 hr. The solution which first formed slowly deposited a crystalline solid. The resulting solid mass was recrystallized from ethanol–ether and dried to give 8.7 g. (39.7%) of white solid, m.p. 241–242° dec. The pure quaternary salt was obtained as small white platelets from 95% ethanol–ether, m.p. 244° dec.

Anal. Calcd. for $C_{21}H_{29}NO_6S_2$: C, 55.36; H, 6.41; N, 3.08; S, 14.08. Found: C, 55.34; H, 6.41; N, 2.98; S, 14.19.

Acknowledgment.—The author wishes to acknowledge helpful discussions with Dr. G. Slomp concerning certain aspects of the n.m.r. spectra.

α-Halosulfones. III. The Steric Course of the Cycloaddition of Chlorosulfene to Enamines[1]

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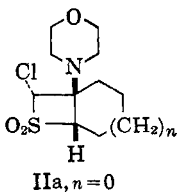
Received March 20, 1964

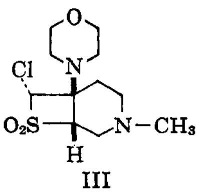
The cycloaddition of chlorosulfene to various morpholine enamines has been studied. The assignment of stereochemistry to the resulting chloro morpholino thietane dioxides has been deduced from their n.m.r. spectra.

Although chloroketene is not yet known, we were prompted to study the possibility of preparing chlorosulfene (I) and to examine the steric course of its addition to certain enamines.[3,4] Addition of chloromethanesulfonyl chloride to an equimolar mixture of triethylamine and the morpholine enamines of cyclopentanone, cyclohexanone, and cycloheptanone in dioxane solution gave rise to single crystalline substances which have been formulated as the chloro morpholino thietane dioxides IIa–c on the basis of elemental analysis, and infrared and nuclear magnetic resonance spectra (see Table I). A similar reaction with 1-methyl-4-morpholino-1,2,5,6-tetrahydropyridine, however, gave both of the possible isomeric cycloadducts, III and IV. In another example, treatment of the morpholine enamine of 5-norbornene-2-carboxaldehyde with chlorosulfene yielded a mixture of the two isomers V and VI.

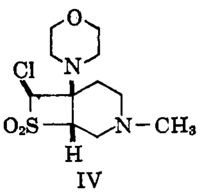
$$\mathrm{ClCH{=}SO_2} \underset{\mathrm{I}}{\longleftrightarrow} \mathrm{Cl\bar{C}H{-}SO_2^+}$$



IIa, $n = 0$
b, $n = 1$
c, $n = 2$



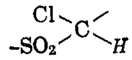
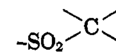
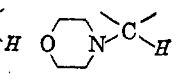
III



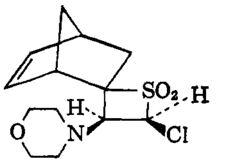
IV

TABLE I

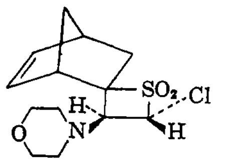
PARAMETERS OF N.M.R. SPECTRA IN DEUTERIOCHLOROFORM SOLUTION (δ-UNITS)

Compd.			
IIa	5.71 (J = 2.5)[a]	4.54[b]	...
IIb	5.49 (J = 1.5)[a]	4.27[b]	...
IIc[c]	...	...	...
III	5.58 (J = 2.0)[a]	4.35[b]	...
IV	5.22 (J = 2.0)[a]	4.50[b]	...
V	5.80 (J = 9)[d]	...	3.42 (J = 9)[d]
VI	5.50 (J = 5)[d]	...	3.04 (J = 5)[d]

[a] Triplet; the appearance of this proton as a triplet in all the compounds reported herein is most fascinating. The first impulse is to attribute the splitting to a 1,3-transannular interaction with the proton at that position. However, in similar systems wherein the relation of these two protons may be considered roughly identical, an unsplit signal in the δ 5.29–5.48 region is reported for this hydrogen.[4] Whatever the causative agent, more specific examples of related systems must be studied before definite claims can be made. [b] Broad doublet with small additional splitting. [c] Spectrum could only be obtained in dimethyl sulfoxide. [d] Doublet.



V



VI

Consideration of the n.m.r. spectra of compounds IIa–c and III (Table I) has led to the conclusion that

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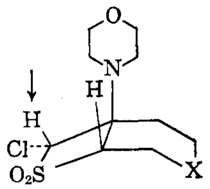
[1] For parts I and II, see L. A. Paquette, *J. Am. Chem. Soc.*, **86**, 4085, 4089 (1964).

[2] Department of Chemistry, The Ohio State University, Columbus 10, Ohio.

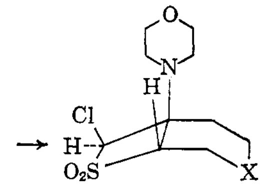
[3] For recent evidence regarding the intermediacy of sulfenes, see I. J. Borowitz, *J. Am. Chem. Soc.*, **86**, 1146 (1964); J. F. King and T. Durst, *ibid.*, **86**, 287 (1964); W. E. Truce, R. W. Campbell, and J. R. Norell, *ibid.*, **86**, 288 (1964).

[4] After the completion of this work, Truce and Norell [*ibid.*, **85**, 3231 (1963)] independently reported the cycloaddition of chlorosulfene to ketene diethyl acetal.

these substances possess identical over-all stereochemistry. In contrast, the n.m.r. spectrum of the thietane dioxide IV showed that the proton on carbon-bearing chlorine had undergone a large upfield shift. In a generalized structure such as VII, the proximate presence of the heterocyclic moiety to the proton in question would be expected to produce a substantial deshielding effect on the latter. In the isomeric structure VIII, this same proton is effectively removed from this area of strong deshielding and would therefore resonate at higher field. Using this line of reasoning, we have assigned compound III (and, by extrapolation, compounds IIa–c) to the isomer whose proton on carbon-bearing chlorine appears at δ 5.58 and structure IV to the isomer whose like proton resonates at 5.22.



VII



VIII

Compounds V and VI furnished n.m.r. spectra in which the magnitude of the coupling constants of the two thietane dioxide ring protons in each substance permitted over-all stereochemical assignments to be made. Thus, in isomer V the dihedral angle of the two protons on the hetero four-membered ring is approximately 0° and therefore would be expected to produce a coupling constant of 8–10 c.p.s.[5] On the other hand, isomer VI possess the same two protons in about an 110–120° relationship to each other, a situation which should give rise to a coupling constant of 3–5 c.p.s. In actuality, the coupling constants were found to be 9 and 5 c.p.s., respectively. Although the Karplus relationship has been found not to apply *accurately* to four-membered ring systems,[6] such a clear-cut choice of alternatives, wherein both of the two possibilities are available for study, cannot but lead to a secure solution of the present stereochemical problem.

In conclusion, brief mention should be made about the *apparent* stereospecificity observed in the formation of IIa–c. Should steric factors intervene in the course of the reaction, it is obvious that thietane dioxides of type VII should predominate over their isomeric counterparts VIII. However, the observation that both isomers are formed in the case of the heterocyclic and bicyclic enamines either belies this conclusion or supports the concept of the intervention of more subtle effects (influence of piperidine ring nitrogen, puckering of the spiro thietane dioxide ring, etc.) in these examples. However, the possibility cannot be overlooked that in the cycloaddition reaction with the carbocyclic enamines only the major isomer was isolated and the second was lost in the work-up procedure by precipitation as its hydrochloride salt along with triethylamine hydrochloride.

Experimental[7]

7-Chloro-1-morpholino-6-thiabicyclo[3.2.0]heptane 6,6-Dioxide (IIa).—To a stirred solution of 30.6 g. (0.20 mole) of 1-morpholinocyclopentene and 20.2 g. (0.20 mole) of triethylamine in 150 ml. of dioxane was added dropwise a solution of 29.8 g. (0.20 mole) of chloromethanesulfonyl chloride[8] with external cooling to maintain the temperature at approximately 30°. When the addition was completed, the mixture was allowed to stand overnight at room temperature. The precipitated triethylamine hydrochloride was separated by filtration and washed well with ether. The combined filtrates were evaporated under reduced pressure and the resulting dark oil was purified by rapid passage through a column of Woelm basic alumina. Elution with ether–hexane (1:1) afforded a colorless oil which crystallized on trituration with aqueous ethanol. There was obtained 19.7 g. (37.2%) of grayish solid, m.p. 121–128°. Two recrystallizations of this material from aqueous ethanol gave pure white platelets, m.p. 131–133°, ν^{Nujol} 1321 and 1110 cm.$^{-1}$ (SO_2).

Anal. Calcd. for $C_{10}H_{16}ClNO_3S$: C, 45.19; H, 6.07; N, 5.27; S, 12.07. Found: C, 45.23; H, 6.14; N, 5.14; S, 11.99.

8-Chloro-1-morpholino-7-thiabicyclo[4.2.0]octane 7,7-Dioxide (IIb).—A solution of 33.4 g. (0.02 mole) of 1-morpholinocyclohexene and 20.2 g. (0.20 mole) of triethylamine in 150 ml. of dioxane was treated with 29.8 g. (0.20 mole) of chloromethanesulfonyl chloride as described above. Rapid passage of the crude dark oil through a column of Woelm basic alumina (elution with ether–hexane, 1:1) gave a colorless oil which crystallized on trituration with aqueous ethanol. There was obtained 22.8 g. (40.8%) of IIb, m.p. 144–153°. Two recrystallizations of this material from ethanol gave pure white blades, m.p. 155–157°, ν^{Nujol} 1323 and 1141 cm.$^{-1}$ (SO_2).

Anal. Calcd. for $C_{11}H_{18}ClNO_3S$: C, 47.22; H, 6.48; Cl, 12.67; N, 5.01; S, 11.46. Found: C, 47.18; H, 6.32; Cl, 12.79; N, 4.79; S, 11.61.

9-Chloro-1-morpholino-8-thiabicyclo[5.2.0]nonane 8,8-Dioxide (IIc).—Reaction of 36.2 g. (0.20 mole) of 1-morpholinocycloheptene on the same scale by a procedure identical with that above afforded 20.6 g. (35.6%) of white solid, m.p. 121–131°. Two recrystallizations of this solid from ethanol gave pure IIc, m.p. 131–133°, ν^{Nujol} 1319 and 1165 cm.$^{-1}$ (SO_2).

Anal. Calcd. for $C_{12}H_{20}ClNO_3S$: C, 49.05; H, 6.86; Cl, 12.07; N, 4.77. Found: C, 48.96; H, 7.45; Cl, 11.97; N, 4.50.

7-Chloro-6-morpholino-3-methyl-8-thia-3-azabicyclo[4.2.0]octane 8,8-Dioxides (*trans*-III and *cis*-IV).—A solution of 36.4 g. (0.20 mole) of 1-methyl-4-morpholino-1,2,5,6-tetrahydropyridine and 20.2 g. (0.20 mole) of triethylamine in 150 ml. of dioxane was treated with 29.8 g. (0.20 mole) of chloromethanesulfonyl chloride as described above. After standing overnight the mixture was diluted with 1.5 l. of water and made slightly basic with dilute sodium hydroxide solution. The mixture was extracted with methylene chloride and the organic phase was dried, filtered, and evaporated. The residual light brown oil was fractionally crystallized from ethanol–ether to give 10.0 g. of the more insoluble isomer IV, m.p. 142–146°. Several recystallizations of this material from ethanol gave white needles, m.p. 153–155° dec., ν^{Nujol} 1328 and 1160 cm.$^{-1}$ (SO_2).

Anal. Calcd. for $C_{11}H_{19}ClN_2O_3S$: C, 44.81; H, 6.49; Cl, 12.03; S, 10.88. Found: C, 45.10; H, 6.46; Cl, 12.26; S, 10.80.

Concentration of the mother liquor from the above crystallization afforded 13.0 g. (total yield 23.0 g., 39.2%) of the more soluble isomer III, m.p. 147–149°. Pure III was obtained as white blades from ethanol, m.p. 149°, ν^{Nujol} 1325 and 1192 cm.$^{-1}$ (SO_2).

Anal. Found: C, 45.13; H, 6.99; Cl, 12.40; S, 10.83.

4′-Chloro-3′-morpholinospiro[5-norbornene-2,2′-thietane] 1′,1′-Dioxides (XIX and XX).—A solution of 47.8 g. (0.25 mole) of the morpholine enamine of 5-norbornene-2-carboxaldehyde[9] and 25.3 g. (0.25 mole) of triethylamine in 200 ml. of dioxane was treated with a solution of 37.3 g. (0.25 mole) of chloromethanesulfonyl chloride as described above. The resulting black oil was passed through a column of Florisil[10] for rapid purification (elution with ether). There was obtained a gum which slowly crystallized, 36.9 g. (48.7%). Fractional crystallization of this material

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[5] M. Karplus, *J. Chem. Phys.*, **30**, 11 (1959).

[6] M. Karplus, *J. Am. Chem. Soc.*, **85**, 2871 (1963).

[7] The author is indebted to Dr. William A. Struck and his associates of the Physical and Analytical Chemistry Department of The Upjohn Co. for the microanalytical and spectral data.

[8] H. Brintzinger, H. Koddebusch, K. Kling, and G. Jung, *Chem. Ber.*, **85**, 455 (1952).

[9] L. A. Paquette, *J. Org. Chem.*, **29**, 2851 (1964).

[10] Florisil is a magnesia-silica gel adsorbent manufactured by the Floridin Co., Tallahassee, Fla.

from ethanol afforded isomer V (least soluble) as white prisms, m.p. 162–164°.

Anal. Calcd. for $C_{13}H_{18}ClNO_3S$: C, 51.39; H, 5.97; N, 4.61; S, 10.55. Found: C, 50.86; H, 5.36; N, 4.18; S, 10.66.

From the mother liquors of the above recrystallizations there was isolated the more soluble isomer VI as a white granular powder, m.p. 125–126°.

Anal. Found: C, 51.70; H, 6.09; N, 4.50; S, 10.76.

Nuclear Acylation of Arylamines

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Aromatic carboxylic acids react with arylamines in polyphosphoric acid solution at 180–200° to furnish aminobenzophenones in appreciable yield. Diphenylamine, triphenylamine, and 2-aminobiphenyl yield heterocyclic bases. Substituted benzanilides are converted to aminobenzophenones by the hot reagent. Mechanisms to account for the results are proposed.

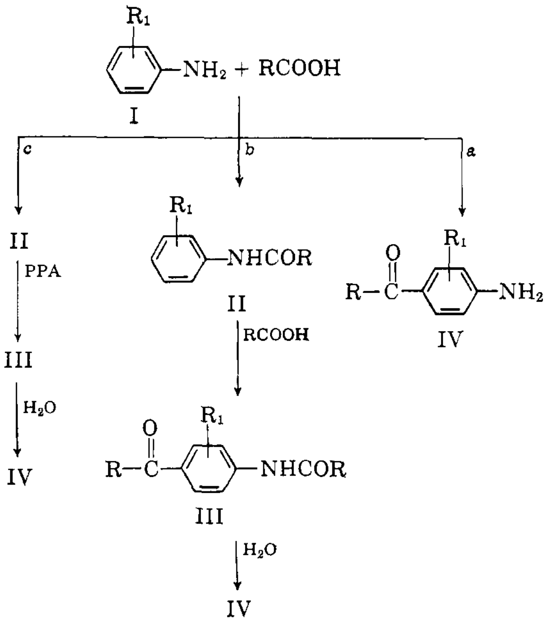
Whereas the intermolecular nuclear acylation reactions in polyphosphoric acid (PPA) of phenols, phenolic ethers, esters, and a variety of aromatic compounds have been extensively studied, little is known of a similar reaction of arylamines.[1–3] Only an occasional such amino ketone synthesis employing PPA has been reported.[4–6] The ring positions in the aromatic amines (I) are said to be unreactive towards carboxylic acids in the presence of PPA[4] and the usual product of reaction is an N-acylated arylamine (II).[7]

It has been found here that equimolar amounts of arylamine (I) and carboxylic acid condense to furnish aminobenzophenones (IV, R = aryl) in 5–55% yields (Table I) on heating with excess PPA at 180–200°. In some instances, 4-aminobenzophenone for example, the yield was improved (65–70%) by employing a molar excess of benzoic acid in the reaction with aniline. The unsubstituted and *ortho*-substituted arylamines gave 30–55% yields of amino ketones where the acyl group preferentially entered in the *para* position, but yields were lower (5–20%) for the *para*-substituted arylamines.[8]

The anilides (II) on treatment with carboxylic acid and excess PPA readily underwent nuclear acylation to N-acylaminobenzophenones (III). Moreover, heating benzanilide (0.01 mole) with either benzoic acid (0.01 or 0.02 mole) or benzoic anhydride[9] (0.01 mole) in PPA at 150° for 30 min. gave comparable yields (60–70%) of 4-aminobenzophenone.

The synthesis of IV directly from arylamine (I) and carboxylic acid is explicable by more than one reaction process: (a) a direct Friedel–Crafts type nuclear acylation of the arylamine to IV; (b) a similar reaction of anilide (II) derived in a preferential and preliminary step from the amine and carboxylic acid, to III; and (c) a PPA-catalyzed transformation of the initially formed II to III as discussed below. (See Scheme I.)

SCHEME I



It is suggested that the amino ketones (IV) listed in Table I, arose principally by routes b and c, and that nuclear acylation of the respective arylamines occurred, if at all, only to a minor extent.[10] The arylamines (I), unlike the relatively less basic anilides (II), would presumably be extensively and effectively protonated in PPA solution and consequently would resist nuclear acylation.[11] The availability in acid solution of an appreciable number of nonprotonated anilide (II) molecules, would allow for a rapid and facile reaction. Consistent with this view is the observation that benzoic anhydride (or benzoic acid) failed to acylate dimethylaniline in the presence of PPA, but the much weaker base triphenylamine reacted readily with benzoic acid to furnish what appears to be 9,10-diphenylacridinium hydroxide (V) in 20% yield. The carbinol (V) may

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[1] F. D. Popp and W. E. McEwen, *Chem. Rev.*, **58**, 377 (1958).

[2] F. Uhlig and H. R. Snyder, "Advances in Organic Chemistry: Methods and Results," Vol. 1, Interscience Publishers, Inc., New York, N. Y., 1960, p. 35.

[3] J. Marthe and S. Munavalli, *Bull. soc. chim. France*, 2679 (1963).

[4] H. R. Snyder and C. T. Elston, *J. Am. Chem. Soc.*, **77**, 364 (1955).

[5] R. A. Abramovitch, D. H. Hey, and R. A. J. Long, *J. Chem. Soc.*, 1781 (1957).

[6] F. D. Popp, *J. Org. Chem.*, **27**, 2658 (1962).

[7] H. R. Snyder and C. T. Elston, *J. Am. Chem. Soc.*, **76**, 3039 (1954).

[8] A similar substitution pattern was observed by Dippy and Moss [*J. Chem. Soc.*, 2205 (1952)] when treating monobenzoyl anilides with benzoy chloride in the presence of zinc chloride.

[9] The nuclear acylation of II with benzoic anhydride and PPA was also reported by D. A. Denton and H. Suschitzky [*ibid.*, 4741 (1963)] before the present investigation was completed.

[10] Although aniline and benzoic acid are reported not to condense to benzanilide in PPA solution,[7] the anilide and also 4-benzaminobenzophenone were in fact isolated after reaction in about 20% yield (see Experimental). The N-acylation procedure of Snyder and Elston[7] may, in other instances as well, lead to a mixture of anilide (II) and N-acylated aminobenzophenone (III).

[11] The nature of the actual C-acylating agent is not known; a conjugate acid, $RCOOH_2^+$, or an oxocarbonium ion, RCO^+, derived from the carboxylic acid, RCOOH, merit consideration.