[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF NOTRE DAME]

Seven-Membered Heterocycles. I. Synthesis of Benzo[b]thiepin 1,1-Dioxide and 1-Phenylsulfonyl-4-phenyl-1,3-butadiene

VINCENT J. TRAYNELIS AND RICHARD F. LOVE[1]

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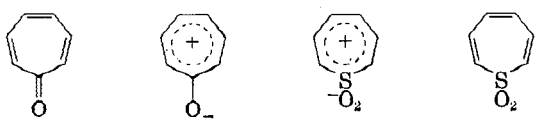
The synthesis of benzo[b]thiepin 1,1-dioxide from homothiachromanone is reported along with the preparation of 1-phenylsulfonyl-4-phenyl-1,3-butadiene. Spectral properties of these materials indicate that, qualitatively, conjugation is extended by the sulfone group; however, this effect does not appear to involve to any appreciable extent the sulfur oxygen bond.

Several groups of investigators have recently reported the synthesis of unsaturated seven-membered sulfur heterocycles. These compounds, both sulfides and sulfones, have been prepared to test the presence of aromatic properties in such systems. In the case of sulfones(II) an analogy to tropone(I) can be cited where the sulfonyl group by electron attraction and possible participation of its vacant *d* orbitals can help delocalize the 6 π electrons over seven atoms. The question of

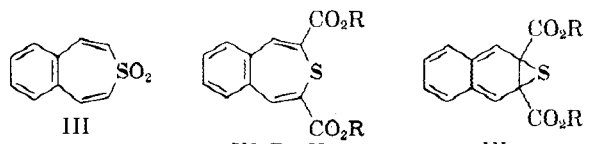


I II

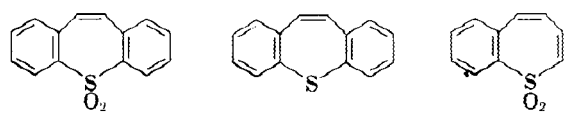
the importance of this stabilization in the absence of planarity has been raised.[2-4]

An attempt to synthesize the parent sulfone, thiepin-1,1-dioxide (II), has been reported by Maerov[2] while Overberger and Katchman[4] have described the preparation of useful intermediates toward the synthesis of II. The final step in Maerov's synthetic scheme gave a substance which was unstable and lost weight upon standing. Apparently II, if really obtained by Maerov, is not resonance stabilized.

Truce and Lotspeich[3] have described the synthesis of benzo[d]thiepin-3,3-dioxide (III) a stable solid. After a brief study of the chemical properties of III, they conclude that III possessed about the same resonance energy as *w*-stryryl methyl sulfone. Scott[5] reported the preparation of benzo[d]-thiepin-2,4-dicarboxylic acid (IV) and observed that upon mild heating sulfur was eliminated with the formation of 2,3-naphthalenedicarboxylic acid. Upon reinvestigation and extension of this work, Dimroth and Lenke[6] found that after esterification of IV the corresponding diester V was remarkably more stable than the acid. On the basis of ultraviolet spectra in sulfuric acid, the formation of an unusual dibromide, and other considerations, Dimroth suggested this system possessed some resonance stabilization.[7] However, the structural assignment for IV has been questioned by Schonberg and Fayez,[8] who interpret the properties of Scott's acid in terms of structure VI.



III IV. R = H V. R = CH_3, C_2H_5 VI.



VII VIII IX

In the dibenzo[b,f]thiepin system Bergmann and Rabinovitz[9] have described the synthesis of both the sulfone VII and the sulfide VIII; while Loudon, Sloan and Summers[10] reported the conversion of various derivatives of VIII to substituted phenanthrenes by a thermal elimination of sulfur.

We have outlined the synthesis of benzo[b]thiepin-1,1-dioxide (IX) in a preliminary communication.[11] In this paper we wish to describe the details of that synthesis and structure proof, in addition to the preparation of 1-phenylsulfonyl-4-phenyl-1,3-butadiene.

(1) Socony Mobil Fellow 1956–1957; Eastman Kodak Fellow 1957–1958. Abstracted from part of the Ph.D. dissertation of R. F. Love, submitted June 1960.

(2) S. B. Maerov, Ph.D. dissertation, University of Washington, 1954.

(3) W. E. Truce and F. J. Lotspeich, *J. Am. Chem. Soc.*, 78, 848 (1956).

(4) C. G. Overberger and A. Katchman, *J. Am. Chem. Soc.*, 78, 1965 (1956).

(5) G. P. Scott, *J. Am. Chem. Soc.*, 75, 6332 (1953).

(6) K. Dimroth and G. Lenke, *Chem. Ber.*, 89, 2608 (1956).

(7) The name used by Dimroth and co-workers[6] for these esters suggests aromatic properties, dimethyl 4,5-benzothiatropilidene dicarboxylate (2,7).

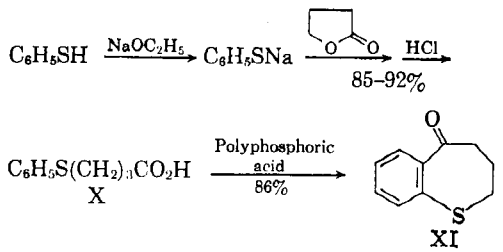
(8) A. Schonberg and M. B. E. Fayez, *J. Org. Chem.*, 23, 104 (1958).

(9) E. D. Bergmann and M. Rabinovitz, *J. Org. Chem.*, 25, 828 (1960).

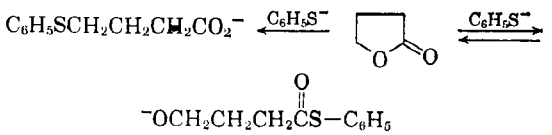
(10) J. D. Loudon, A. D. B. Sloan, and L. A. Summers, *J. Chem. Soc.*, 3814 (1957).

(11) V. J. Traynelis and R. F. Love, *Chemistry and Industry*, 439 (1958).

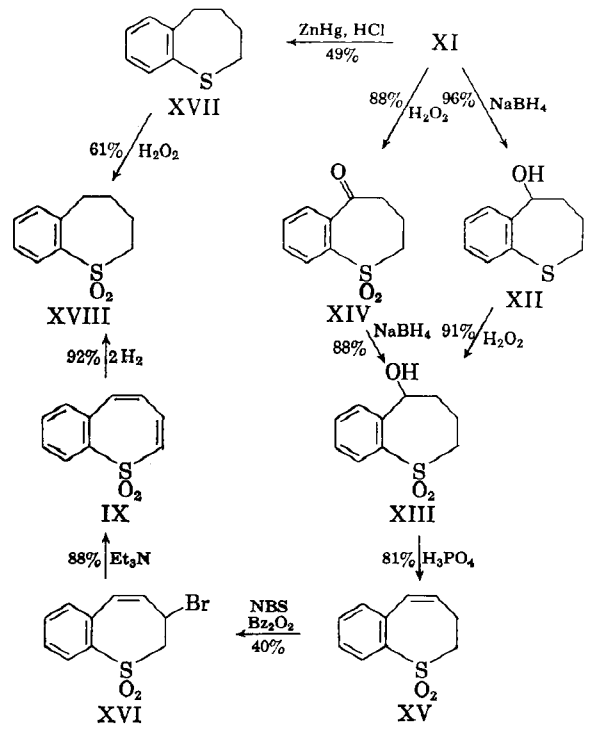
The starting material for the synthesis of IX was the known 5-oxo-2,3,4,5-tetrahydrobenzo[b]thiepin (XI)[12,13] (homothiachromanone), which had been prepared by a Friedel-Crafts cyclization of the acid chloride obtained from γ-phenylmercaptobutyric acid (X). We have repeated these reactions; however, a more convenient method which gives higher yields involves the polyphosphoric acid cyclization of X. The starting γ-phenylmercaptobutyric acid is available by a modification of Reppe's reaction[14] of sodium thiophenoxide and γ-butyrolactone. This reaction appears to involve an alkyl-oxygen fission with an ester that normally



hydrolyzes by acyl-oxygen fission.[15] One explanation of this result involves a rapid but reversible ring opening by acyl-oxygen fission in competition with an irreversible alkyl-oxygen fission which gives the sodium salt of X.



The ketone XI was reduced by sodium borohydride and gave 5-hydroxy-2,3,4,5-tetrahydrobenzo[b]thiepin (XII) in 95% yield. Oxidation of XII with 30% hydrogen peroxide produced, in 91% yield, 5 - hydroxy - 2,3,4,5 - tetrahydrobenzo[b]thiepin-1,1-dioxide (XIII). An alternate route to XIII involved the oxidation of XI to 5-oxo-2,3,4,5-tetrahydrobenzo[b]thiepin - 1,1 - dioxide (XIV) (88%) followed by reduction with sodium borohydride (88%). Dehydration of XIII was accomplished with about 95% phosphoric acid, prepared by the addition of the calculated quantity of phosphorus pentoxide to 85% phosphoric acid, and gave an 81% yield of 2,3-dihydrobenzo[b]thiepin-1,1-dioxide (XV). The yields in this reaction were sensitive to the purity of the starting alcohol (XIII) and size run. The final double bond was introduced by allylic bromination of XV with *N*-bromo-succinimide and benzoyl peroxide which gave 3-bromo-2,3-dihydrobenzo[b]thiepin-1,1-dioxide (XVI) in 40% yield, followed by dehydrobromination with triethylamine. Reaction in the last case was immediate and gave 92% of triethylamine hydrobromide, m.p. 246°, and 88% of pale yellow crystalline benzo[b]thiepin-1,1-dioxide (IX), m.p. 139–140°.



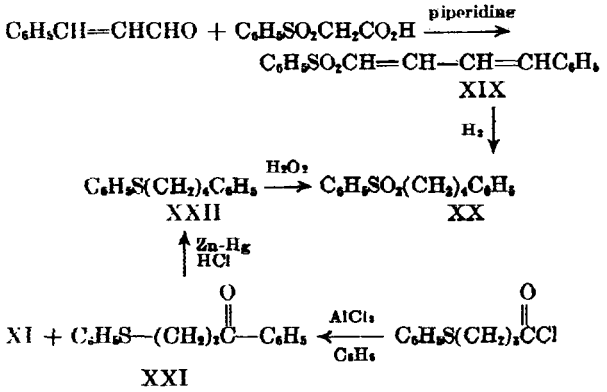
The structure of benzo[b]thiepin-1,1-dioxide was established by catalytic hydrogenation using either Raney nickel at moderate pressure or platinum oxide at atmospheric pressures. When the latter conditions were employed in a semimicro hydrogenation apparatus, IX absorbed quantitatively two moles of hydrogen and gave 92% of 2,3,4,5-tetrahydrobenzo[b]thiepin - 1,1 - dioxide (XVIII). Comparison of the infrared spectrum, melting point and mixture melting point of this material with an authentic sample prepared from homothiachromanone (XI) by a Clemmenson reduction followed by oxidation with hydrogen peroxide, established the structure of the reduction product.

Structural assignments of the intermediate products, XII, XIII, XIV, XV, XVI were based on analytical data, ultraviolet and infrared spectra, and the nature of the reaction by which each was prepared. The infrared spectra of compounds XII and XIII showed the presence of the hydroxyl stretching frequency 2.85–2.92 μ, while structures XIII, XIV, XV and XVI exhibited characteristic sulfone bands 7.5–7.8 μ and 8.5–8.9 μ. The ultraviolet absorption spectra of XV (λ_{max} 250 mμ, log ε 4.14; λ_{max} 291 mμ, log ε 3.74) and XVI (λ_{max} 260 mμ, log ε 3.86; λ_{max} 294 mμ, log ε 3.78) were similar and indicated conjugation of the olefin with the

(12) P. Cagniant and A. Deluzarche, *Compt. rend.*, **223**, 677 (1946).
(13) W. E. Truce and J. P. Milionis, *J. Am. Chem. Soc.*, **74**, 974 (1952).
(14) W. Reppe, *Ann.*, **596**, 194 (1955).
(15) F. A. Long and L. Friedman, *J. Am. Chem. Soc.*, **72**, 3692 (1950).

aromatic ring.[16] Chemical evidence for compounds XV and XVI has also been obtained. Quantitative hydrogenation of XV in the presence of platinum oxide at atmospheric pressure showed the absorption of only one mole of hydrogen and gave XVIII. The presence of an allylic halogen in compound XVI was demonstrated by its reactivity with alcoholic silver nitrate and sodium iodide in acetone.

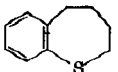
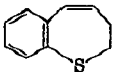
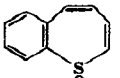
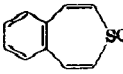
The synthesis of 1-phenylsulfonyl-4-phenyl-1,3-butadiene (XIX) was undertaken to provide the open chain analog of benzo[b]thiepin-1,1-dioxide for comparison of spectral and chemical properties. A base-catalyzed condensation of cinnamaldehyde with phenylsulfonylacetic acid produced lustrous, faintly yellow leaflets of 1-phenylsulfonyl-4-phenyl-1,3-butadiene (40%). Its structure was established by reduction to 1-phenylsulfonyl-4-phenylbutane (XX) and comparison with an authentic sample. The independent synthesis of XX involved initially a Friedel-Crafts reaction of γ-phenylmercaptobutyryl chloride and benzene, which gave both γ-phenylmercaptobutyrophenone (XXI) (30%) and XI. After a Clemmenson reduction (68%) of XXI, the resulting 4-phenylbutyl phenyl sulfide (XXII) was converted (76%) to the corresponding sulfone XX by treatment with hydrogen peroxide.



The ultraviolet absorption spectra of benzo[b]-thiepin-1,1-dioxide, 1-phenylsulfonyl-4-phenyl-1,3-butadiene, and some related compounds both from this work and the literature appear in Table I. When one compares the 230 mμ band of 1-phenylsulfonyl-4-phenyl-1,3-butadiene to the 223 mμ band of 1-phenyl-1,3-butadiene or the 225 mμ band of phenyl vinyl sulfone, the bathochromic shift indicates an extension in conjugation whether this be an effect of the sulfonyl group on the phenylbutadiene moiety or *vice versa*. Likewise, the 305 mμ absorption in XIX shifting considerably from 280 mμ band in phenylbutadiene supports the conclusion that the sulfonyl group extends conjugation. A choice of model compounds for comparison with benzo[b]thiepin-1,1-dioxide is more difficult; however, the ultraviolet spectrum of IX is considerably different from its 2,3,4,5-tetrahydro derivative XVIII (which resembles an alkyl phenyl sulfone) and its 2,3-dihydro derivative XV (which resembles styrene and 1-phenylpropene). The strong absorption at 234 mμ in IX may be due to a new conjugated system and it is interesting to note that the isomeric benzo[d]thiepin-3,3-dioxide[3] also absorbs strongly at 232 mμ.

TABLE I

ULTRAVIOLET ABSORPTION SPECTRA IN 95% ETHANOL

Compound		λ_{max}, mμ	log ε
$C_6H_5SO_2CH{=}CH_2$[a]		225	4.1
		267	3.02
$C_6H_5SO_2CH{=}CHC_6H_5$[b]		275	4.41
$C_6H_5SO_2(CH{=}CH)_2C_6H_5$ (XIX)		230	4.22
		305	4.47
$C_6H_5SO_2(CH{=}CH)_2C_6H_5$ (XIX) (in cyclohexane)		229	4.21
		304	4.65
$CH_2{=}CH{-}CH{=}CH{-}C_6H_5$[c]		223	4.09
		280	4.47
$C_6H_5SO_2(CH_2)_4C_6H_5$ (XX)		225	3.01
		254	2.85
		259	2.98
		265	3.04
		272	2.94
	(XVIII)	(222)[d]	4.06
		(227)[d]	3.90
		262	3.51
		269	3.56
		277	3.54
	(XV)	224	3.9
		250	3.99
		291	3.74
	(IX)	221	4.16
		234	4.13
		290	3.99
"	in cyclohexane	233	4.10
		288	3.97
	(III)	232	4.5
		268	3.9

[a] See ref. 17. [b] See ref. 18. Only the K-band absorption was reported. [c] See ref. 19. [d] Inflection point. [e] See ref. 3.

The ultraviolet absorption maxima of IX and XIX were essentially the same in 95% ethanol and cyclohexane. As no change was likewise observed for the K band absorption of methyl phenyl sulfone, diphenyl sulfone, and phenyl β-styryl sulfone in these solvents,[18] IX and XIX appear no different than these conjugated sulfones. Unlike conjugated aromatic ketones, which exhibit an appreciable solvent effect,[18] these unsaturated sulfones must have the same energy differences be-

(16) The ultraviolet absorption spectrum of styrene has the following bands: λ_{max} 211 mμ, log ε 4.20; λ_{max} 244 mμ, log ε 4.08; λ_{max} 282 mμ, log ε 2.65. [B. H. Eccleston, J. H. Coleman, and H. G. Adams, *J. Am. Chem. Soc.*, 72, 3867 (1950)] and for 1-phenylpropene: λ_{max} 251 mμ, log ε 4.23; λ_{max} 284 mμ, log ε 2.98; λ_{max} 293 mμ, log ε 2.78 [M. S. Newmann and H. C. Demo, *J. Am. Chem. Soc.*, 73, 3649 (1951)].

(17) C. C. Price and H. Morita, *J. Am. Chem. Soc.*, 75, 4747 (1953).

(18) V. Baliah and Sp. Shanmuganathan, *J. Phys. Chem.*, 62, 255 (1958).

(19) E. A. Braude, *Ann. Repts.*, 42, 126 (1945).

tween ground and excited states in both polar and nonpolar solvents. This could imply that the nature of the S=O bond and charge on oxygen does not undergo any marked change when going from the ground to the excited state.

Examination of the symmetric and asymmetric stretching vibrations in the infrared spectrum of the sulfones listed in Table II also indicates that conjugation has little effect on the S=O bond. The initial report of this observation with simpler molecules was made by Barnard, Fabian, and Koch.[20]

In summary while conjugative interactions involving the sulfonyl group in IX and XIX most likely occur, they do not implicate to any appreciable extent the sulfur oxygen bonds. The exact contribution that these interactions make toward increased stability in benzo[b]thiepin-1,1-dioxide must await further test.

TABLE II

SULFONE BANDS IN THE INFRARED SPECTRA

Compound	ν in Cm.$^{-1}$[a] Sym.	Asym.
2,3,4,5-Tetrahydrobenzo[b]-thiepin-1,1-dioxide (XVIII)	1157	1324
2,3-Dihydrobenzo[b] thiepin-1,1-dioxide (XV)	1164	1321
Benzo[b]thiepin-1,1-dioxide (IX)	1153	1327
4-Phenylbutyl phenyl sulfone (XX)	1151	1324
1-Phenylsulfonyl-4-phenyl-1,3-butadiene (XIX)	1149	1325

[a] Measurements were made in carbon tetrachloride and where splitting was observed, the most intense band was recorded.

EXPERIMENTAL[21]

γ-Phenylmercaptobutyric acid (X). *Method A.* A modification of the procedure described by Reppe[14] was employed. γ-Butyrolactone (45 g., 0.52 mole) was added in one portion to a solution of sodium thiophenoxide prepared from sodium (12.5 g., 0.50 g.-atom), 150 ml. of ethanol, and thiophenol (55 g., 0.50 mole). After 4 hr. of reflux, the ethanol was removed, the resulting white pasty mass broken up and kept overnight in a vacuum oven at 115–120°. The crude product was dissolved in water, filtered, and acidified with dilute hydrochloric acid. The precipitate was collected, dried and after crystallization from petroleum ether (b.p. 60–80°) gave 83.5 g. (85%) of γ-phenylmercaptobutyric acid, m.p 68–69° (lit.,[14] m.p. 69°).

Method B. To a solution of potassium ethoxide prepared from potassium (7.8 g., 0.20 g.-atom) and 50 ml. of absolute ethanol was added a solution of thiophenol (22 g., 0.20 mole) in 150 ml. of diethyl carbitol. After the ethanol was removed by distillation, γ-butyrolactone (18 g., 0.21 mole) in 100 ml. of diethyl carbitol was added slowly and the resulting slurry heated with rapid stirring for 3 hr. at 170–175°. To the cooled reaction mixture was added 300 ml. of water and the solution washed with two 300-ml. portions of ether. The aqueous solution was acidified with hydrochloric acid; after the resulting precipitate was collected and dried, crystallization from petroleum ether (b.p. 60–80°) gave 36 g. (92%) of γ-phenylmercaptobutyric acid, m.p. 68–69°.

The *amide* was prepared by the method described in Shriner and Fuson[22] and after recrystallization from petroleum ether (b.p. 60–80°) melted at 95–96° (lit.,[13] m.p. 96–96.5°).

5-Oxo-2,3,4,5-tetrahydrobenzo[b]thiepin (XI) (*Homothiachromanone*). *Method A.* The initial preparation according to the procedure of Cagniant[13] and Truce[13] involved the conversion of γ-phenylmercaptobutyric acid (9.8 g., 0.05 mole) through the acid chloride to homothiachromanone (6.1 g., 68%), b.p. 119–121° (1.5 mm.), n_D^{20} 1.6220 [lit.,[13] b.p. 119.5–120° (1.5 mm.), n_D^{20} 1.6228] *via* a Friedel-Crafts ring closure carried out in tetrachloroethane.

Method B. After phosphorus pentoxide (740 g., 5.2 moles) was added with rapid stirring and cooling to 500 ml. of phosphoric acid (85%) in a 2-l. three-necked flask fitted with a dropping funnel and mechanical stirrer and the mixture heated at 100° for 2 hr., a melt of γ-phenylmercaptobutyric acid (98 g., 0.5 mole) was added over 45 min. to this polyphosphoric acid at 90°. The stirred mixture was maintained at 90–95° for an additional 45 min., cooled, poured onto 2000 g. of crushed ice and extracted with 300 ml. of benzene. After the extract was washed with water, 5% sodium hydroxide solution, water, and dried over anhydrous sodium sulfate, the solvent was removed and distillation of the residue gave 1.1 g. of forerun, n_D^{20} 1.6228 and 77.5 g. (86%) of colorless 5-oxo-2,3,4,5-tetrahydrobenzo[b]thiepin, b.p. 119–120° (1.5 mm.), n_D^{20} 1.6232.

The *semicarbazone* was prepared in the usual manner and after recrystallization from aqueous ethanol melted at 220–222° (lit.,[13] m.p. 222°).

5-Hydroxy-2,3,4,5-tetrahydrobenzo[b]thiepin (XII). A solution of 5-oxo-2,3,4,5-tetrahydrobenzo[b]thiepin (25 g., 0.14 mole) in 75 ml. of 95% ethanol was added dropwise to a solution of sodium borohydride (2.63 g., 0.07 mole) in 40 ml. of 25% aqueous ethanol maintained at 10–15°. After the reaction mixture was refluxed for 30 min., the volume of the solvent was reduced to 20–30 ml. under reduced pressure and the resulting slurry poured onto a mixture of 200 g. of crushed ice and 20 ml. of concd. hydrochloric acid. The alcohol was filtered and crystallization from cyclohexane gave 24.3 g. (95%) of 5-hydroxy-2,3,4,5-tetrahydrobenzo[b]-thiepin, as fine white needles, m.p. 70–71°.

Anal. Calcd. for $C_{10}H_{12}OS$: C, 66.62; H, 6.71. Found: C, 66.40; H, 6.76.

The *p-nitrobenzoate* was prepared in the usual way and after recrystallization from 95% ethanol melted at 149–150°.

Anal. Calcd. for $C_{17}H_{15}NO_4S$: C, 61.99; H, 4.59. Found: C, 62.32; H, 4.50.

The *acetate* ester was prepared by refluxing 5-hydroxy-2,-3,4,5-tetrahydrobenzo[b]thiepin (5.0 g., 0.027 mole) in 10 ml. of acetic anhydride. Distillation gave 5.55 g. (90%) of a colorless liquid which solidified on cooling and crystallization from petroleum ether (b.p. 60–80°) produced 5.3 g. (86%) of pure acetate ester, m.p. 71–72°.

Anal. Calcd. for $C_{12}H_{14}O_2S$: C, 64.83; H, 6.38. Found: C, 64.88; H, 6.21.

5-Oxo-2,3,4,5-tetrahydrobenzo[b]thiepin-1,1-dioxide (XIV). A solution of 5-oxo-2,3,4,5-tetrahydrobenzo[b]thiepin (12 g., 0.068 mole), 60 ml. of glacial acetic acid and 37 ml. of 30% hydrogen peroxide was allowed to stand overnight, warmed on a steam bath 1 hr. and poured into 300 ml. of

(20) D. Barnard, J. M. Fabian, and H. P. Koch, *J. Chem. Soc.*, 2442 (1949).

(21) All melting points and boiling points are uncorrected. The microanalysis were carried out by Midwest Microlab Inc., Indianapolis, Ind. Infrared spectra were determined with a Perkin-Elmer model 21 or a Baird Associates infrared spectrophotometer by R.F.L. and Anthony Saraceno.

(22) R. L. Shriner and R. C. Fuson, *Systematic Identification of Organic Compounds*, 3rd ed., J. Wiley and Sons, Inc., New York, 1948.

water. The resulting solid was collected and after recrystallization from ethanol gave 12.4 g. (88%) of white platelets, m.p. 155–156°.

Anal. Calcd. for $C_{10}H_{10}O_3S$: C, 57.13; H, 4.79. Found: 57.28; H, 4.87.

5-Hydroxy-2,3,4,5-tetrahydrobenzo[b]thiepin-1,1-dioxide (XIII). *Method A.* To a solution of 5-hydroxy-2,3,4,5-tetrahydrobenzo[b]thiepin (25 g., 0.14 mole) in acetone (70 ml.) and glacial acetic acid (20 ml.) was added 50 ml. of 30% hydrogen peroxide over a period of 1 hr. After the mixture remained at room temperature 6 hr. and was refluxed 1 hr., the acetone was removed under diminished pressure and 100 ml. of water added. The precipitate was collected, dried and crystallized from acetone to give 25.7 g. (91%) of 5 - hydroxy - 2,3,4,5 - tetrahydrobenzo[b]thiepin - 1,1 - dioxide, m.p. 139–141°.

Method B. A solution of ketone XIV (5.0 g., 0.024 mole) in freshly distilled dioxane (50 ml.) was added with stirring to a solution of sodium borohydride (0.500 g., 0.0132 mole) in 50% aqueous dioxane (20 ml.). After 1 hr. at room temperature, the mixture was refluxed for 30 min., cooled and the solvent removed under reduced pressure. The residue was treated with 50 ml. of 5% hydrochloric acid and the liberated alcohol collected, dried and recrystallized from acetone to afford 4.43 g. (88%) of 5-hydroxy-2,3,4,5-tetrahydrobenzo[b]thiepin-1,1-dioxide, m.p. 140–141°. An analytical sample was obtained after one recrystallization from benzene and two from acetone, m.p. 141–142°.

Anal. Calcd. for $C_{10}H_{12}O_3S$: C, 56.58; H, 5.70. Found: C, 56.74; H, 5.79.

The *acetate* ester was prepared from 5-hydroxy-2,3,4,5-tetrahydrobenzo[b]thiepin-1,1-dioxide (2.0 g., 0.0094 mole) and acetyl chloride (10 ml., 0.14 mole) with 30 min. reflux time. The acetyl chloride was removed by distillation and the residue dissolved in hot ethyl acetate. Large crystals (1.89 g.) separated upon cooling and after recrystallization from ethyl acetate gave 1.62 g. (68%) of the acetate ester, m.p. 144.5–145.5°.

Anal. Calcd. for $C_{12}H_{14}O_4S$: C, 56.68; H, 5.55. Found: C, 56.77; H, 5.84.

2,3-Dihydrobenzo[b]thiepin-1,1-dioxide (XV). 5-Hydroxy-2,3,4,5-tetrahydrobenzo[b]thiepin-1,1-dioxide (5.0 g., 23.5 mmoles) was dissolved in a solution of phosphorus pentoxide (20 g., 0.14 mole) in 85% orthophosphoric acid (50 ml.). After the mixture was heated with swirling on a steam bath for 30 min. and poured onto 300 ml. of ice water, the product was filtered and dried *in vacuo*. Crystallization from carbon tetrachloride gave 3.86 g. (81%) of 2,3-dihydrobenzo[b]thiepin-1,1-dioxide, m.p. 104–106°. An analytical sample was prepared by recrystallization from cyclohexane, m.p. 106–107°.

Anal. Calcd. for $C_{10}H_{10}O_2S$: C, 61.83; H, 5.19. Found: C, 62.02; H, 5.39.

The *dibromide* was prepared by the addition of bromine (1.7 g., 10.5 mmoles) to a solution of the above olefin (XV) (2.0 g., 10.3 mmoles) in 30 ml. of glacial acetic acid. Upon gentle warming the bromine color was discharged and the crystalline precipitate which formed was separated by filtration. Recrystallization from benzene gave 2.69 g. (73%) of 4,5-dibromo-2,3,4,5-tetrahydrobenzo[b]thiepin-1,1-dioxide, m.p. 195–196°.

Anal. Calcd. for $C_{10}H_{10}Br_2O_2S$: C, 33.92; H, 2.85; Br, 45.15. Found: C, 33.95; H, 2.97; Br, 45.26.

3-Bromo-2,3-dihydrobenzo[b]thiepin-1,1-dioxide (XVI). A mixture of 2,3-dihydrobenzo[b]thiepin-1,1-dioxide (4.0 g., 0.0206 mole), recrystallized *N*-bromosuccinimide (3.67 g., 0.0206 mole), dried Celite (4.0 g.), benzoyl peroxide (0.58 g., 2.0 mmoles), and 300 ml. of dry carbon tetrachloride was refluxed for 6 hr., then cooled to room temperature and filtered. The solid was extracted with 50 ml. of hot ethanol, which upon evaporation gave an orange colored residue. This residue was treated with 25 ml. of chloroform, filtered, and gave 0.96 g. (47%) of succinimide, m.p. 122–124°.

The filtrate of the original reaction mixture was evaporated under reduced pressure and the solid residue recrystallized from ethyl acetate to afford 2.24 g. (40%) of 3-bromo-2,3-dihydrobenzo[b]thiepin-1,1-dioxide, m.p. 142–144°. An analytical sample, m.p. 144–145°, was obtained after two recrystallizations from an ethyl acetate-petroleum ether (b.p. 30–60°) mixture.

Anal. Calcd. for $C_{10}H_9BrO_2S$: C, 43.97; H, 3.32. Found: C, 44.32; H, 3.64.

Benzo[b]thiepin-1,1-dioxide (IX). Triethylamine (0.75 g., 7.42 mmoles) was added to a solution of 3-bromo-2,3-dihydrobenzo[b]thiepin-1,1-dioxide (2.0 g., 7.34 mmoles) in 40 ml. of benzene. After remaining at room temperature for 2 hr., the reaction mixture was filtered and gave 1.24 g. (92%) of triethylamine hydrobromide, m.p. 246°. The filtrate was reduced to about 20 ml. volume and 10 ml. of petroleum ether (b.p. 30–60°) added. The solid was isolated and recrystallization from ethanol gave 1.41 g. (88%) of benzo[b]thiepin-1,1-dioxide, m.p. 139–140°. An analytical sample was prepared by crystallizations from benzene and from ethanol, m.p. 140–141°.

Anal. Calcd. for $C_{10}H_8O_2S$: C, 62.48; H, 4.19. Found: C, 62.56, 62.51; H, 4.30, 4.44.

2,3,4,5-Tetrahydrobenzo[b]thiepin (XVII). By following the procedure of Truce and Milionis,[13] 5-oxo-2,3,4,5-tetrahydrobenzo[b]thiepin (8.0 g., 38 mmoles) was converted *via* a Clemmenson reduction to 3.6 g. (49%) of 2,3,4,5-tetrahydrobenzo[b]thiepin, b.p. 103–105° (3 mm.), n_D^{20} 1.6052 (lit.,[13] b.p. 103–104° (3 mm.), $n_D^{29.5}$ 1.5996).

2,3,4,5-Tetrahydrobenzo[b]thiepin-1,1-dioxide (XVIII). A solution of 2,3,4,5-tetrahydrobenzo[b]thiepin (1.0 g., 5.6 mmoles) in 10 ml. of glacial acetic acid and 5 ml. of 30% hydrogen peroxide was refluxed 4 hr. After cooling, the mixture was poured into 50 ml. of water and the solid filtered and dried. Recrystallization from petroleum ether (b.p. 60–80°) gave 0.73 g. (61%) of white crystalline product, m.p. 77–78° (lit.,[13] m.p. 77–78°).

Hydrogenation of benzo[b]thiepin-1,1-dioxide. A solution of benzo[b]thiepin-1,1-dioxide (217 mg., 1.13 mmoles) in 20 ml. of 95% ethanol and 16 mg. of platinum oxide catalyst was exposed to hydrogen at atmospheric pressure in a semi-micro hydrogenation apparatus.[23] The theoretical amount of hydrogen was absorbed in about 6 hr. After the solution was filtered, the catalyst washed with 95% ethanol, the combined filtrates were evaporated under a stream of nitrogen and gave 203 mg. (92%) of 2,3,4,5-tetrahydrobenzo[b]thiepin-1,1-dioxide, m.p. 77–78°. A mixture melting point with a sample of authentic material as prepared above showed no depression and the infrared spectra of the two samples were identical.

Phenylmercaptoacetic acid. After a solution of chloroacetic acid (18.9 g., 0 20 mole) in 220 ml. of 5% sodium carbonate was added with rapid stirring to a solution of thiophenol (22.0 g., 0.20 mole), sodium hydroxide (8.0 g., 0.20 mole) and 100 ml. of 95% ethanol, the reaction mixture was stirred 3 hr. at room temperature, heated 30 min. on a steam bath, cooled and acidified. The isolated product was recrystallized from petroleum ether (b.p. 60–80°) and gave 27.7 g. (82%) of phenylmercaptoacetic acid, m.p. 61–62° (lit.,[24] m.p. 63–64°).

Phenylsulfonylacetic acid. Phenylmercaptoacetic acid (25.0 g., 0.15 mole) was dissolved in 100 ml. of glacial acetic acid and treated over a 3-hr. period with three 20-ml. portions of 30% hydrogen peroxide. After standing overnight, solvent was evaporated under reduced pressure and the residue recrystallized from an equal portion of chloroform and acetic acid to give 17.8 g. (60%) of phenylsulfonylacetic acid, m.p. 111–112° (lit.,[25] m.p. 111.5–112.5°).

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(23) For diagram of apparatus see, A. A. Baldoni, Ph.D. dissertation, Univ. of Notre Dame, 1951, p. 54.

(24) O. Behaghel, *J. prakt. Chem.*, [2] 114, 299 (1926).

(25) R. Otto, *J. prakt. Chem.*, [2] 30, 341 (1884).

1-Phenylsulfonyl-4-phenyl-1,3-butadiene (XIX). Employing the procedure of Chodroff and Whitmore,[26] a solution of phenylsulfonylacetic acid (10.0 g., 0.05 mole), 30 ml. of anhydrous pyridine, cinnamaldehyde (7.76 g., 0.06 mole), and 0.6 ml. of piperidine was heated on a steam bath for 6 hr. The resulting dark red liquid was poured onto a mixture of 35 ml. of concd. hydrochloric acid and 100 g. of ice. The precipitate was isolated and upon crystallization from 100 ml. of methanol gave 5.59 g. (41%) of faintly yellow, lustrous flakes, m.p. 95–97°. An analytical sample was prepared by two further crystallizations from 95% ethanol to give nearly white 1-phenylsulfonyl-4-phenyl-1,3-butadiene, m.p. 97–98°.

Anal. Calcd. for $C_{16}H_{14}O_2S$: C, 71.08; H, 5.22. Found: C, 70.89; H, 5.38.

γ-Phenylmercaptobutyrophenone (XXI). γ-Phenylbutyryl chloride prepared from 75.0 g. (0.38 mole) of the corresponding acid (X) and 60 ml. (0.75 mole) of thionyl chloride was taken up in 200 ml. of dry benzene and added dropwise to a slurry of 80.0 g. (0.60 mole) of aluminum chloride in 250 ml. of benzene at 5–10°. After the mixture was stirred at room temperature for 3 hr. and poured onto 2500 g. of ice, the organic phase was separated, washed with water, 5% sodium hydroxide solution, water, and dried over anhydrous sodium sulfate. The benzene was removed and distillation of the residue gave 52.4 g. of a yellow oil, b.p. 115–180° (0.8 mm.). Redistillation through an 8-inch Vigreux column gave three fractions: I, 11.6 g., b.p. 114–130° (1.0 mm.), n_D^{20} 1.6162; II, 4.4 g., b.p. 130–165° (1.0 mm.), n_D^{20} 16115; III, 34.3 g., b.p. 165–180° (1.0 mm.), n_D^{20} 1.6109. The last fraction was again distilled through a 60-cm. jacketed column, packed with glass helices, and gave 29.1 g. (30%) of γ-phenylmercaptobutyrophenone, b.p. 168–171° (0.7 mm.). The contaminant in the earlier fractions was the cyclic ketone X. A solid was obtained by cooling a solution of the above oil in absolute ethanol to −20°. In this manner 5.0 g. of liquid gave 4.1 g. of crystalline XXI, m.p. 36–38°.

Anal. Calcd. for $C_{16}H_{16}OS$: C, 74.98; H, 6.29. Found: C, 75.01; H, 6.38.

The *semicarbazone* was prepared and after recrystallization from ethanol melted at 126–127° (lit.,[12] m.p. 122°).

1-Phenylmercapto-4-phenylbutane (XXII). A mixture of 150 g. of amalgamated zinc, 200 ml. of concd. hydrochloric acid, 200 ml. of glacial acetic acid, 150 ml. of toluene, and 20.0 g. (0.078 mole) of γ-phenylmercaptobutyrophenone was refluxed vigorously for 40 hr. At intervals of 8, 12, and 30 hr., 60-ml. increments of concd. hydrochloric acid were added. When cooled, the toluene layer was separated and washed with water, saturated sodium bicarbonate solution, water, and dried over anhydrous sodium sulfate. The solvent was removed at atmospheric pressure and the residue distilled through an eight inch asbestos wrapped column to give 12.9 g. (68%) of a pale yellow oil, b.p. 157–160° (1.2 mm.), n_D^{20} 1.5910. An analytical sample was obtained after two distillations of the above material and was colorless 4-phenylbutyl phenyl sulfide b.p. 153–154° (1.0 mm.), n_D^{20} 1.5929.

Anal. Calcd. for $C_{16}H_{18}S$: C, 79.29; H, 7.49. Found: C, 79.26; H, 7.58.

1-Phenylsulfonyl-4-phenylbutane (XX). A solution of 1-phenylmercapto-4-phenylbutane (1.0 g., 41 mmoles), glacial acetic acid (12 ml.) and 30% hydrogen peroxide (5 ml.) was warmed on the steam bath 1 hr., then poured into 50 ml. of water. The precipitate was collected, dried *in vacuo*, and crystallized from petroleum ether (b.p. 60–80°) to give 0.85 g. (76%) of the sulfone, m.p. 65–66°.

Anal. Calcd. for $C_{16}H_{18}O_2S$: C, 70.04; H, 6.61. Found: C, 70.05; H, 6.59.

Hydrogenation of 1-phenylsulfonyl-4-phenyl-1,3-butadiene. A Paar hydrogenation apparatus was charged with 1-phenylsulfonyl-4-phenyl-1,3-butadiene (1.0 g., 3.7 mmoles), methanol (140 ml.) and a catalytic amount of Raney nickel and was shaken under a hydrogen atmosphere (50 p.s.i.) for 1 hr. After the catalyst was filtered and washed with methanol, the filtrate was evaporated under a stream of dry air and gave 0.93 g. (91%) of 1-phenylsulfonyl-4-phenylbutane, m.p. 65–66°. A mixture melting point with a sample of authentic material as prepared above showed no depression and the infrared spectra of the two samples were identical.

An alternate attempt to reduce the above compound using platinum oxide as catalyst and hydrogen at atmospheric pressure was unsuccessful. Only incomplete reduction occurred.

Spectra. The ultraviolet spectra were determined using a Perkin-Elmer Spectracord and Beckman DU instruments. Approximately 10^{-5} molar solutions in 95% ethanol and cyclohexane were used and the data are listed in Table I.

The infrared absorption frequencies listed in Table II were measured using the Perkin-Elmer Model 21 spectrophotometer fitted with sodium chloride optics. Sample solutions were prepared in Spectral grade carbon tetrachloride and cells of 0.050-cm. thickness were used. The absorption bands were frequency calibrated against a film of polystyrene which in turn had been checked against water vapor absorption.

NOTRE DAME, IND.

(26) S. Chodroff and W. F. Whitmore, *J. Am. Chem. Soc.*, 72, 1073 (1950).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF BRITISH COLUMBIA]

Synthesis in the Pyridine Series. I. The Synthesis of 3,4-Dimethyl-5-isopropylpyridine. A General Approach to 3,4,5-Trialkylated Pyridines

JAMES P. KUTNEY AND ROGER C. SELBY

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The synthesis of 3,4-dimethyl-5-isopropylpyridine has been achieved. Modifications of the synthetic scheme provide a general synthetic approach to new and difficultly accessible 3,4,5-trialkylated pyridines.

In connection with the structural elucidation of a new alkaloid isolated from a Chilean plant, it became necessary to consider the identity of several 3,4,5-trialkylpyridine derivatives. The particular compounds which were necessary for our study were the two possible dimethylisopropylpyridines, namely, 3,4-dimethyl-5-isopropylpyridine and 3,5-dimethyl-4-isopropylpyridine. Investigation of the literature soon revealed that 3,4,5-trialkylpyridines are not readily available and in particular, com-