Thiocarbonyls. VIII. The Question of *gem*-Dithiol Formation in Aralkyl Ketones[1]

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The formation of a stable crystalline *gem*-dithiol on treatment of dibenzyl ketone with hydrogen sulfide and hydrogen chloride led to an investigation of the reactions of a number of related compounds under these conditions. Four different classes of compounds have been isolated depending on the structure of the starting ketone. 1,3-Di-*p*-chlorophenyl-2-propanone and 1,3-di-*p*-methoxyphenyl-2-propanone were the only other ketones which gave *gem*-dithiols. Phenyl-2-propanone, 1,5-diphenyl-3-pentanone, and 2-indanone formed trithianes. 1,1-Diphenyl-2-propanone, 2-tetralone, and 2-phenylcyclohexanone gave α,β-unsaturated sulfides. 1,1,3-Triphenyl-2-propanone and 1-phenyl-2-indanone gave enethiols.

Trithianes are usually expected as products of the acid-catalyzed addition of hydrogen sulfide to ketones and aldehydes.[3] A variety of other products have been reported,[4] but these have generally been treated as exceptional cases. Among the aliphatic ketones studied, acetone and methyl ethyl ketone give trithianes,[3] while cyclopentanone and cyclohexanone give moderately stable monomers in the form of enethiols,[5] and by way of the eneamines, without acid catalysis, *gem*-dithiols.[6]

TABLE I

RESULTS OF ADDITION OF HYDROGEN SULFIDE TO ARALKYL KETONES

Starting material	Product type	Product isolated
1,3-Di-*p*-chlorophenyl-2-propanone	*gem*-Dithiol	1,3-Di-*p*-chlorophenylpropane-2,2-dithiol
1,3-Di-*p*-methoxyphenyl-2-propanone	*gem*-Dithiol	1,3-Di-*p*-methoxyphenylpropane-2,2-dithiol
1,3-Di-*p*-nitrophenyl-2-propanone	No reaction	
Phenyl-2-propanone	1,3,5-Trithiane	Trithiophenylacetone
1,5-Diphenyl-3-pentanone	1,3,5-Trithiane	Trithiodibenzylacetone
2-Indanone	1,3,5-Trithiane	Trithio-2-indanone
Cycloheptanone	1,3,5-Trithiane	Trithiocycloheptanone
1,1-Diphenyl-2-propanone	α,β-Unsaturated sulfide	Bis-1,1-diphenyl-2-propenyl sulfide
2-Tetralone	α,β-Unsaturated sulfide	Bis(3,4-dihydro-2-naphthyl) sulfide
2-Phenylcyclohexanone	α,β-Unsaturated sulfide	Bis-2-phenyl-1-cyclohexenyl sulfide
1,1,3-Triphenyl-2-propanone	Enethiol	1,1,3-Triphenylpropene-2-thiol
1-Phenyl-2-indanone	Enethiol	3-Phenylindene-2-thiol

Benzophenone and substituted benzophenones give highly colored monomeric thiones.[3] Campaigne and Moss[7] found that 1-indanone, 1-tetralone, and their 3-methyl derivatives give trithianes while 2-methyl-1-indanone and 2-methyl-1-tetralone give bis-2-methyl-3-indenyl sulfide and bis-2-methyl-3,4-dihydronaphthyl sulfide, respectively, presumably by addition of the initially formed enethiol to a second molecule of the ketone. Campaigne[4] has proposed a reaction scheme which accounts for the formation of the various types of products in the reaction of hydrogen sulfide with aldehydes or ketones. Figure 1 shows a modified version of this scheme.

This study was initiated by the discovery that 1,3-diphenyl-2-propanone (dibenzyl ketone) yields a stable crystalline *gem*-dithiol on treatment with hydrogen sulfide and hydrogen chloride.[8] Previously, *gem*-dithiols had been prepared only by the action of hydrogen sulfide on aldehydes and ketones at high pressures (36–8500 atm.) in the absence of catalysts.[9] A broad survey of compounds related in various ways to 1,3-diphenyl-2-propanone was undertaken in hopes of finding additional compounds capable of forming *gem*-dithiols under mild conditions. All of the compounds were treated in essentially the same manner, with hydrogen sulfide and hydrogen chloride in methanol or ethanol at 0–5°. The results are summarized in Table I. The addition of the gases generally was continued until a solid product was formed.

Under these conditions, 1,3-di-*p*-chlorophenyl-2-propanone and 1,3-di-*p*-methoxyphenyl-2-pro-

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[1] This work was supported by a grant, No. G-9855, from the National Science Foundation to Indiana University. For paper no. VII of this series see E. Campaigne, W. B. Reid, Jr., and J. D. Pera, *J. Org. Chem.*, **24**, 1229 (1959).

[2] Taken from a thesis submitted by B. E. Edwards to Indiana University in partial fulfillment of the requirements for the degree of Doctor of Philosophy, June, 1962.

[3] E. Campaigne, *Chem. Rev.*, **39**, 1 (1946).

[4] E. Campaigne, "Organic Sulfur Compounds," Vol. 1, N. Kharasch, ed., Pergamon Press, New York, N.Y. 1961, p. 134.

[5] D. C. Sen, *J. Indian Chem. Soc.*, **13**, 268 (1936).

[6] C. Djerassi and B. Tursch, *J. Org. Chem.*, **22**, 1041 (1962).

[7] E. Campaigne and R. C. Moss, *J. Am. Chem. Soc.*, **76**, 1269 (1954).

[8] G. A. Berchtold, B. E. Edwards, E. Campaigne, and M. Carmack, *ibid.*, **81**, 3148 (1959).

[9] T. L. Cairns, G. L. Evans, A. W. Larchar, and B. C. McKusick, *ibid.*, **74**, 3982 (1952).

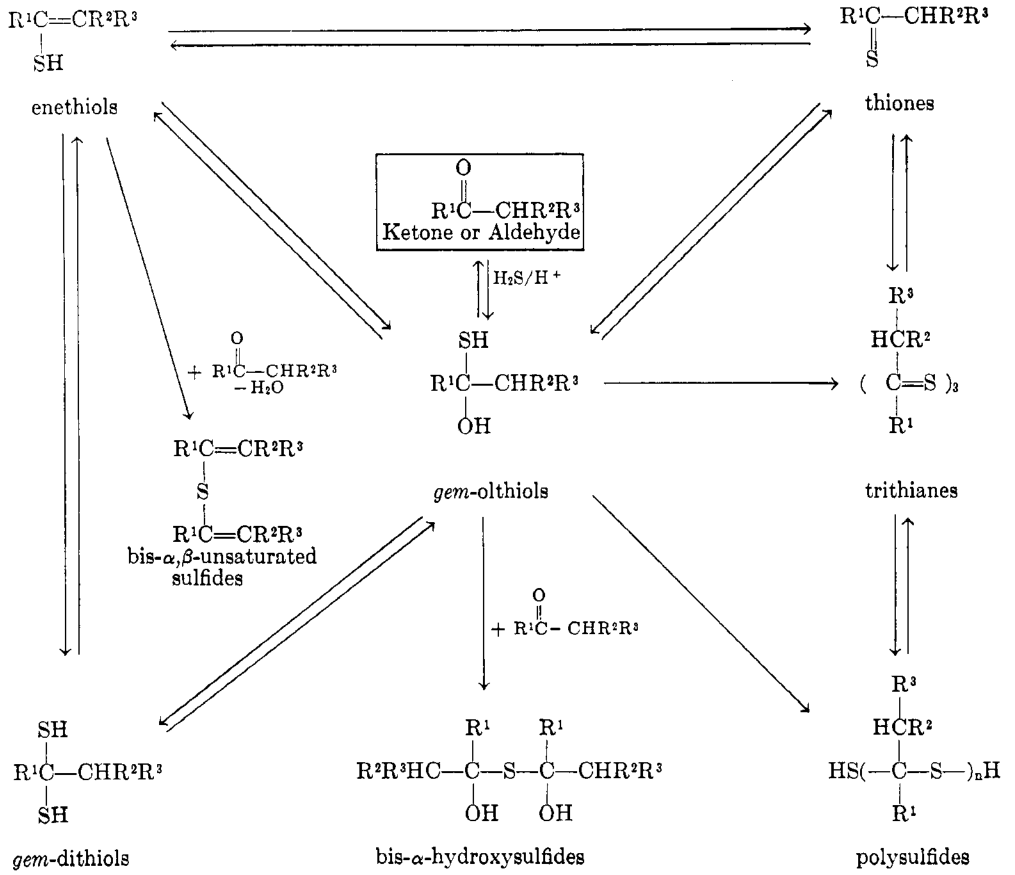
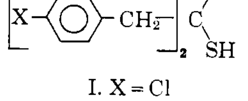


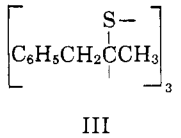
Fig. 1.—Addition of H_2S to ketones or aldehydes.

panone were initially converted to red solutions, from which the corresponding *gem*-dithiols, I and II, precipitated as white solids. 1,3-Di-*p*-nitrophenyl-2-propanone was completely unreactive under the standard conditions.

Phenyl-2-propanone initially gave a pale pink, very viscous oil, which remained unchanged when let stand in the reaction mixture in a refrigerator for as long as a month. However, if the solvent was decanted and the oil allowed to stand in the contact with the air, it soon solidified to a white solid which was shown to be a trithiane, 2,4,6-tribenzyl-2,4,6-trimethyl-1,3,5-trithiane (III).

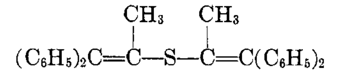


I. X = Cl
II. X = OCH_3



III

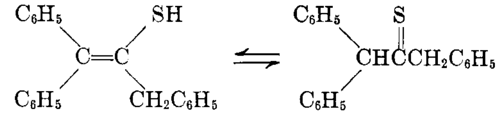
The 1,1-diphenyl-2-propanone solution turned red almost immediately upon addition of hydrogen sulfide, but after about one-half hour, the solution was again colorless, and after one hour it was bright blue. Various attempts to isolate the blue material led only to starting material. After 8 hours of continuous addition of the gases, a white solid appeared, and after ten hours, the blue color had disappeared, leaving a white solid which was identified as bis-1,1-diphenyl-2-propenyl sulfide (IV).



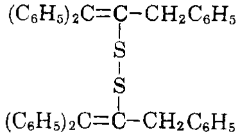
$$(C_6H_5)_2C{=}\overset{CH_3}{C}{-}S{-}\overset{CH_3}{C}{=}C(C_6H_5)_2$$

IV

1,1,3-Triphenyl-2-propanone gave initially a pink solution which faded to colorless as a white solid was deposited from the reaction mixture. Elemental analysis and molecular weight determination showed the product to be the monomer, V. The infrared spectrum of V shows a weak sulfhydryl band at 2577 cm.$^{-1}$, and the n.m.r. spectrum indicates that it exists essentially completely in the enethiol form, Va. The —CH_2— resonance appears at $\tau = 6.20$ and the —SH at $\tau = 7.24$. No signal corresponding to benzhydryl hydrogen was observed, and intergration of the spectrum showed the ratio of —SH to —CH_2— to be very near 1:2. Treatment of V with lead acetate gave a yellow lead salt, which was oxidized with iodine to give the disulfide, VI. Treatment of V with 2,4-dinitro-

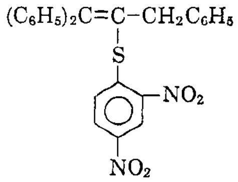


Va Vb



$(C_6H_5)_2C{=}C(CH_2C_6H_5)-S-S-C(CH_2C_6H_5){=}C(C_6H_5)_2$

VI



VII

chlorobenzene in alcoholic potassium hydroxide gave the corresponding sulfide, VII.

1,5-Diphenyl-3-pentanone was found to give the corresponding trithiane, as did 2-indanone and cycloheptanone. 2-Tetralone and 2-phenylcyclohexanone behaved like 1,1-diphenylacetone readily forming α,β-unsaturated sulfides. The product from 2-tetralone was dehydrogenated to the known β-naphthyl sulfide.

1-Phenyl-2-indanone apparently gave an enethiol like that formed from 1,1,3-triphenylacetone. However, this material was characterized only by conversion to its 2,4-dinitrophenyl sulfide. The product was a high boiling oil which showed sulfhydryl absorption in the infrared, but its sulfur analysis was lower than required by the enethiol, and the molecular weight higher. These results might be explained by dimerization or polymerization reactions involving loss of hydrogen sulfide from the enethiol.

As suggested by the reaction scheme shown in Fig. 1, the consequences of treating an aralkyl ketone with hydrogen sulfide are not simple. Structurally related phenylacetones may yield any one of four different types of product (Table I). Although structural similarities in each group of products are apparent, the differences between groups are slight, and the selective formation of *gem*-dithiols under these conditions remains unique to dibenzyl ketones. The path of these reactions must involve a delicate balance of steric and electronic factors. The initial red color observed in most of the reactions is probably due to formation of the monomeric thione, but it is not possible to say whether the thione is a true intermediate, or a by-path along the way. Minor components of the reaction mixtures were not isolated, as they were generally very viscous oils, probably polymeric sulfides.

It is of interest to note that the physical constants reported in the literature for 1,3-di-*p*-nitrophenyl-2-propanone differ considerably from those found in this study. Manchot and Krische[10] first reported that nitration of 1,3-diphenyl-2-propanone gave the dinitro derivative, m.p. 105°. Manchot and Zahn[11] noted that repeated recrystallization gave a product melting at 120°, but that lower melting fractions from the mother liquors all gave proper analyses for dinitro derivatives. In our hands, chromatography of the nitration product gave the di-*p*-nitro ketone melting at 140–141°, in low recovery. The material seemed to react with alumina, and lower melting fractions were not further studied. The oxime of this dinitro ketone melts at 155–156° (reported[10] 133°).

Experimental

Hydrogen sulfide and hydrogen chloride gases were obtained in cylinders from The Matheson Co., Inc. Melting points are capillary, corrected. Infrared spectra were determined in potassium bromide mulls, and ultraviolet spectra in cyclohexane solutions. N.m.r. spectra were obtained in solvents noted using a Varian Associates Model HR 60 high resolution spectrometer with the assitance of Mr. Art Clause. Peak positions were determined relative to internal TMS by the usual side band technique. Microanalyses were carried out by Midwest Microlabs, Inc. Molecular weights were determined using a Mechrolabs vapor pressure osmometer, Model 301A, in solvents noted.

1,3-Di-*p*-chlorophenylpropane-2,2-dithiol (I).—A solution of 0.85 g. (2.9 moles) of 1,3-di-*p*-chlorophenyl-2-propanone[12] in 30 ml. of absolute methanol was added dropwise to 20 ml. of absolute methanol saturated with hydrogen sulfide and hydrogen chloride at 0° with continuous stirring and addition of the gases. The solution turned pink almost immediately. The temperature was maintained at 0–5° for 4.5 hr. after which the flask was stoppered and stored in a refrigerator overnight. The resulting solid was collected on a fritted glass funnel and dried in a vacuum desiccator over sodium hydroxide, yielding 0.96 g. (95%), m.p. 90–107°. Eight recrystallization from *n*-hexane–benzene gave 0.20 g. of I as white needles, m.p. 121–124° dec., ν_{max} 2551 cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{14}Cl_2S_2$: C, 54.71; H, 4.28; S, 19.47. Found: C, 54.94; H, 4.44; S, 19.61.

1,3-Di-*p*-methoxyphenylpropane-2,2-dithiol (II).—Hydrogen sulfide and hydrogen chloride gases were passed into a stirred solution of 2.02 g. (7.5 mmoles) of 1,3-di-*p*-methoxyphenyl-2-propanone[12] in 50 ml. of absolute methanol at 5°. The solution quickly turned pink. The addition of the gases was continued with stirring at 0–5° for 4 hr. at which time a white solid had appeared in the flask. The flask was stoppered and refrigerated overnight. The white solid was collected on a fritted glass funnel and dried in a vacuum desiccator over sodium hydroxide. The crude yield was 1.49 g. (62%), m.p. 63–64°. An analytical sample was prepared by recrystallization from *n*-pentane, m.p. 65–66°, ν_{max} 2571, 2532 cm.$^{-1}$, n.m.r. (CS_2) τ 7.82.

Anal. Calcd. for $C_{17}H_{20}O_2S_2$: C, 63.71; H, 6.29; S, 20.01. Found: C, 63.73; H, 6.31; S, 19.79.

Trithiophenylacetone (III).—A solution of 14.85 g. of phenylacetone in 50 ml. of 95% ethanol was saturated with hydrogen chloride at 0–5°. Hydrogen sulfide and hydrogen chloride were then passed into the solution with stirring for 6 hr. at 0–5°. The pink solution was stoppered and stored in a refrigerator 6 weeks. The solvent was then decanted from the pink gummy material adhering to the flask. After standing for serveral days exposed to the air, all of the material changed to a white solid, m.p. 60–70°, 13.7 g. (82%). The solid was recrystallized from glacial acetic acid and finally from ethanol to give a white solid, m.p. 89–90°.

Anal. Calcd. for $(C_9H_{10}S)_3$: S, 21.34; mol. wt., 450. Found: S, 21.24; mol. wt., (CCl_4) 455. N.m.r. (CCl_4): phenyl H, τ = 2.80; benzyl H, τ = 6.67, 6.75 (intensity 2:1); methyl H, τ = 8.29, 8.32 (intensity 1:2).

Bis-1,1-diphenyl-2-propenyl Sulfide (IV).—A stirred solution of 5 g. of 1,1-diphenyl-2-propanone in 50 ml. of absolute methanol at 0–5° was saturated with hydrogen sulfide and hydrogen chloride. The solution turned red. After 30 min. of addition of the gases, the solution was again

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[10] W. Manchot and P. Krische, *Ann.*, **337**, 170 (1904).

[11] W. Manchot and C. Zahn, *ibid.*, **345**, 331 (1906).

[12] S. Chiaverelli, G. Settimj, and H. M. Alves, *Gazz. Chim. Ital.*, **87**, 109 (1957).

colorless and shortly it turned blue. After 8 hr., a white solid appeared in the reaction flask and at 10 hr. the blue color had disappeared. The solid was collected on a fritted glass filter, washed with cold methanol, and dried in a vacuum desiccator over sodium hydroxide. The crude product, 3.5 g., melted at 104–107°. Recrystallization from cyclohexane–hexane gave a sample melting at 132–133°, λ_{max} 300 mμ (log ϵ 4.10).

Anal. Calcd. for $C_{30}H_{26}S$: C, 86.07; H, 6.28; S, 7.65; mol. wt., 418. Found: C, 86.41; H, 6.48; S, 7.65; mol. wt. ($CHCl_3$), 415.

1,1,3-Triphenylpropene-2-thiol (V).—Thirty milliliters of absolute methanol was saturated with hydrogen sulfide and hydrogen chloride at 0°. A solution of 2.86 g. (0.01 mole) of 1,1,3-triphenyl-2-propanone[13] in 40 ml. of absolute methanol was added to the stirred solution with continued addition of the gases. The solution turned pink almost immediately, and, within 30 min., a white solid began to separate. After 6 hr. at 0°, the flask was stoppered and refrigerated overnight. The resulting white granular solid was collected on a fritted glass funnel and dried in a vacuum desiccator over sodium hydroxide, yielding 2.53 g., m.p. 88–90°. The mother liquor was concentrated to one half its original volume under nitrogen, resaturated with hydrogen sulfide and hydrogen chloride, and refrigerated overnight. On filtration, an additional 0.18 g., m.p. 88–90°, was obtained. The total crude yield was 90%. An analytical sample was prepared by recrystallization from *n*-hexane, m.p. 90–91°, ν_{max} 2577 cm.$^{-1}$, n.m.r. ($CDCl_3$) τ 6.20, 7.24.

Anal. Calcd. for $C_{21}H_{18}S$: C, 83.40; H, 6.00; S, 10.60; mol. wt., 302. Found: C, 83.36; H, 6.06; S, 10.20; mol. wt. (CCl_4), 300, 302.

Bis-1,1,3-triphenyl-2-propenyl Disulfide (VI).—Treatment of a sample of V in ethyl acetate with ethanolic lead acetate gave a yellow lead salt, soluble in ethyl acetate, insoluble in ethanol or water, m.p. 75–80°. Oxidation of 0.08 g. (0.2 mmole) of this salt in ethyl acetate with iodine gave 18 mg. of VI, m.p. 214–214.5° after recrystallization from ethanol benzene.

Anal. Calcd. for $C_{42}H_{34}S_2$: C, 83.78; H, 5.68; mol. wt., 603. Found: C, 83.74; H, 5.75; mol. wt. ($CHCl_3$), 600.

1,1,3-Triphenyl-2-(2′,4′-dinitrophenylthio)propene (VIII).—To 200 mg. (0.67 mmole) of V in 3 ml. of absolute ethanol was added 40 mg. (0.7 mmole) of potassium hydroxide in 3 ml. of absolute ethanol and 135 mg. (0.67 mmole) of 2,4-dinitrochlorobenzene in 2 ml. of absolute ethanol. A yellow precipitate appeared almost immediately. The mixture was boiled for 10 min. on the steam bath, the volume being maintained by the addition of benzene. The mixture was centrifuged quickly, the hot supernatant transferred to a clean tube and allowed to crystallize. Further recrystallization from chloroform–methanol gave 270 mg. (86%) of the sulfide as yellow granules, m.p. 204–205°.

Anal. Calcd. for $C_{27}H_{20}O_4N_2S$: C, 69.21; H, 4.30; S, 6.84. Found: C, 69.05; H, 4.37; S, 6.79.

Trithio-1,5-diphenyl-3-pentanone.—To 30 ml. of absolute methanol, saturated with hydrogen sulfide and hydrogen chloride at 0°, was added 2.4 g. (0.01 mole) of 1,5-diphenyl-3-pentanone[14] with stirring. The solution turned peach colored almost immediately. After 6 hr. the flask was stoppered and placed in a refrigerator overnight. The resulting orange solution was decanted from a white waxy solid deposited in the flask. The solution was concentrated under nitrogen and finally dried under vacuum to give 2.32 g. of very viscous oil which was not further examined. The waxy solid was recrystallized from *n*-hexane to give 0.20 g. of fine needles, m.p. 160–160.5°.

Anal. Calcd. for $(C_{17}H_{18}S)_3$: C, 80.26; H, 7.13; S, 12.61; mol. wt., 763. Found: C, 80.73; H, 7.17; S, 12.29; mol. wt. (CCl_4), 740.

Trithio-2-indanone.—Hydrogen sulfide and hydrogen chloride were passed into a solution of 3.67 g. (0.028 mole) of 2-indanone[15] in 50 ml. of absolute methanol cooled in a salt–ice bath. The solution was maintained at 0–5° for 3 hr. with stirring and continuous addition of the gases. The flask, containing a white solid, was stoppered and refrigerated overnight. The solid was collected on a fritted glass funnel and dried in a vacuum desiccator over sodium hydroxide. The crude yield was 4.10 g., m.p. 110–170°. A sample recrystallized from cyclohexane for analysis melted at 206.5–208°.

Anal. Calcd. for $(C_9H_8S)_3$: C, 72.92; H, 5.44; S, 21.65; mol. wt., 444. Found: C, 73.00; H, 5.62; S, 21.37; mol. wt. ($CHCl_3$), 460.

3-Phenylindene-2-thiol.—Hydrogen sulfide and hydrogen chloride were passed into a solution of 4.08 g. (0.19 mole) of 1-phenyl-2-indanone[15] in 40 ml. of absolute methanol at 0–5° with stirring. After 3 hr. the flask, containing a yellow solution and a yellowish gum, was stoppered and refrigerated for 5 days. At the end of this time, there having been no apparent change in the mixture, the supernatant liquid was decanted, leaving the gummy yellow residue in the flask. The residue was dissolved in benzene, then dried at aspirator vacuum and finally at 0.5 mm. to give 1.54 g. of yellow gum. Chromatography of this material on 50 g. of 100-mesh silicic acid in *n*-hexane–ether gave a yellow band, a center cut of which was taken for analysis. In an earlier experiment, it was found that the gum could be distilled in a molecular still at *ca.* 150° (0.5 mm.) without loss of sulfhydryl absorption in the infrared. However, the samples became increasingly colored on distillation.

Anal. Calcd. for $C_{15}H_{12}S$: S, 14.28; mol. wt., 224. Found: S, 11.94; mol. wt., 337; ν_{max} 2545 cm.$^{-1}$.

The oil gave an orange salt on treatment with lead acetate solution, m.p. 130–140°, and decolorized iodine in ethanol.

3-Phenyl-2-(2′,4′-dinitrophenylthio)indene.—A mixture of 0.99 g. of the above yellow oil, 0.90 g. of 2,4-dinitrofluorobenzene, and 0.06 g. of potassium fluoride[16] was heated gently on a steam bath for 30 min. The orange mass was extracted with hot benzene and the benzene extract concentrated and chromatographed on 60 g. of 100-mesh silicic acid in benzene. Assay of the eluted fractions by thin-layer chromatography on silicic acid directed the isolation of 64 mg. of a yellow powder which was recrystallized from *n*-hexane–benzene to m.p. 178–179°.

Anal. Calcd. for $C_{21}H_{14}O_4N_2S$: C, 64.60; H, 3.61; N, 7.17; mol. wt., 390. Found: C, 64.83; H, 3.74; N, 7.31; mol. wt. ($CHCl_3$), 380.

Bis-3,4-dihydro-2-naphthyl Sulfide.—A solution of 4.41 g. (0.03 mole) of 2-tetralone[17] in 40 ml. of absolute methanol was cooled to 0° in a salt–ice bath with stirring and hydrogen sulfide and hydrogen chloride were passed into the solution for 2 hr. The solution first turned pink, then a white solid appeared. The flask was stoppered and refrigerated overnight. The solid was collected on a fritted glass filter, and dried in a vacuum desiccator over sodium hydroxide. The yield was 4.0 g. (79%), m.p. 141–142°, λ_{max} mμ (log ϵ); 322 (4.21), 303 (4.20), 275.5 (4.10).

Anal. Calcd. for $C_{20}H_{18}S$: C, 82.71; H, 6.25; S, 11.04; mol. wt., 290. Found: C, 82.95; H, 6.48; S, 10.87; mol. wt. (CCl_4), 285.

Bis-2-naphthyl Sulfide.—To 1.45 g. (5 mmoles) of bis-3,4-dihydro-2-naphthyl sulfide was added 20 ml. of dry toluene and 2.5 g. (10.2 mmoles) of chloranil, all under dry nitrogen. The solution was protected with a drying tube and refluxed for 8 hr., then cooled, and poured into 100 ml. of *n*-pentane. The white granular precipitate was washed with water, then extracted with boiling *n*-hexane and the extract combined with the reaction mother liquor and dried

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(13) A. Orékhoff, *Bull. soc. chim. France*, **25**, 108 (1919).

(14) J. M. Conia and P. Gosselin, *ibid.*, 836 (1961).

(15) A. T. Blomquist and E. J. Moriconi, *J. Org. Chem.*, **26**, 3761 (1961).

(16) N. N. Vorozhtsov, Jr., and G. G. Iakobson, *J. Gen. Chem. USSR* (Engl. Transl.), **28**, 40 (1958).

(17) J. A. Barltrop and J. E. Sexton, *J. Chem. Soc.*, 1038 (1952).

over magnesium sulfate. The resulting solution was passed through a column of neutral alumina (1 × 5 cm.) to give 0.5 g. of white crystalline material. Further recrystallization gave white granules, m.p. 149–150°.[18]

Bis-2-phenyl-1-cyclohexenyl Sulfide.—To 2.63 g. (1.53 mmoles) of 2-phenylcyclohexanone (prepared by oxidation of the 2-phenylcyclohexanol[19]) in 30 ml. of absolute methanol at 0–5° were added hydrogen sulfide and hydrogen chloride gases with stirring. Within 10 min. the solution turned pink, then became cloudy. After 6 hr. the gases were stopped and the flask stoppered and refrigerated for 2 days. The solution was evaporated to dryness at the aspirator under nitrogen, 20 ml. benzene added, and the solution again evaporated to leave 2.6 g. of a waxy white solid. This material was chromatographed on a column of 90 g. of 100-mesh silicic acid made up in *n*-hexane and eluted with cyclohexane–5% ether. The purified product, 1.6 g. (61%) melted at 91–92°, λ_{max} 280 mμ (log ϵ 3.97).

Anal. Calcd. for $C_{24}H_{26}S$: C, 83.18; H, 7.56; S, 9.25; mol. wt., 346.5. Found: C, 83.18; H, 7.64; S, 9.20; mol. wt. ($CHCl_3$), 346.

Trithiocycloheptanone.—Hydrogen sulfide and hydrogen chloride were passed into a solution of 11.2 g. (0.1 mole) of cycloheptanone in 40 ml. of absolute methanol at 0–5° in a salt–ice bath. The solution began to turn peach colored in a few moments, then clouded. After 3 hr. the gases were stopped, and the flask was stoppered and refrigerated overnight. The resulting white granular solid was collected on a fritted glass funnel, washed with cold methanol, and dried in a vacuum desiccator over sodium hydroxide, yielding 12 g. (94%) of trithiocycloheptanone, m.p. 73–75°. A sample recrystallized for analysis from *n*-hexane melted at 75–76°.

Anal. Calcd. for $(C_7H_{12}S)_3$: C, 65.56; H, 9.44; S, 25.00; mol. wt., 385. Found: C, 65.54; H, 9.35; S, 25.24; mol. wt. ($CHCl_3$), 385.

1,3-Di-*p*-nitrophenyl-2-propanone.—1,3-Diphenyl-2-propanone was nitrated by the method of Manchot and Zahn[11] to give 11 g. of a product melting at 105–110°. This material was dissolved in benzene and chromatographed on a column of 300 g. of alumina in cyclohexane. Elution with benzene returned about half of the material in fractions melting between 120 and 140°. The alumina turned brown on contact with the nitro compound. A fraction melting at 137–139°, 2.4 g., was refractionated on 100 g. of Woelm Grade 1 Neutral alumina. The brown color appeared again when the nitro compound contacted the alumina. Benzene elution gave fractions totaling 1 g. A center fraction melted at 140–141° after three recrystallizations from ethanol.

Anal. Calcd. for $C_{15}H_{12}O_5N_2$: N, 9.33. Found: N, 9.36.

The oxime of this ketone was prepared and found to melt at 155–156° (lit., m.p. 133°).[10]

Anal. Calcd. for $C_{15}H_{13}O_5N_3$: N, 13.33. Found: N, 13.20.

Oxidation with dichromate, permanganate, chromic oxide, and nitric acid gave varying yields of *p*-nitrobenzoic acid plus, in some runs, a lower melting nitro acid which was shown by comparison of its infrared spectrum with that of an authentic sample, and further oxidation to *p*-nitrobenzoic acid, to be *p*-nitrophenylacetic acid. No other isomeric nitro acids were detected among the oxidation products by infrared examination.

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The Synthesis and Properties of Some Simple 1,4-Dihydropyridines

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A simple analogue of the dihydropyridine system present in the coenzyme DPNH, 1,4,4-trimethyl-1,4-dihydropyridine, has been synthesized by the reaction of β,β-dimethylglutaraldehyde and methylamine and characterized by elemental analysis, reduction to a known compound, and n.m.r., infrared, and ultraviolet [$\lambda\lambda_{max}$ 2708 (ϵ 3200); 2305 (ϵ 7500) in isooctane] spectra. Its basicity, measured by the method of Hall, was appreciably lower than that expected (pK_a 7.4 *vs.* 10.45 for the corresponding tetrahydropyridine), implying a stabilization energy of *ca.* 4 kcal./mole for the 1,4-dihydropyridine system and suggesting that the 1,4-dihydropyridine ring system is flat. Thus, the stereochemical preference for side A or side B in enzymatic reactions of carbonyl compounds with DPNH must be due to asymmetry of the transition state permitted by the "active sites" of the enzymes concerned. A few reactions of the 1,4,4-trimethyl-1,4-dihydropyridine were studied and some 1-aryl-1,4-dihydropyridines were prepared and characterized.

The dihydropyridine ring system is of considerable interest because of its presence in the coenzyme, diphosphopyridine nucleotide (DPNH). The coenzyme has been firmly established as a 1,4-dihydropyridine.[2–4] Very little reliable information is available on the properties of unsubstituted (or alkyl-substituted) 1,4- or 1,2-dihydropyridines. In this paper, we report the synthesis and properties of 1,4,4-trimethyl-1,4-dihydropyridine as well as a series of 1-aryl-1,4-dihydropyridines. The 4,4-dimethyl grouping prevents facile isomerization to the isomeric 1,2-dihydropyridine.[5]

Results

Synthesis.—The lithium aluminum hydride reduction of the bis-*N*-methylanilide of β,β-dimethylglutaric acid according to Weygand and coworkers[6] yielded a solution of β,β-dimethyl-

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