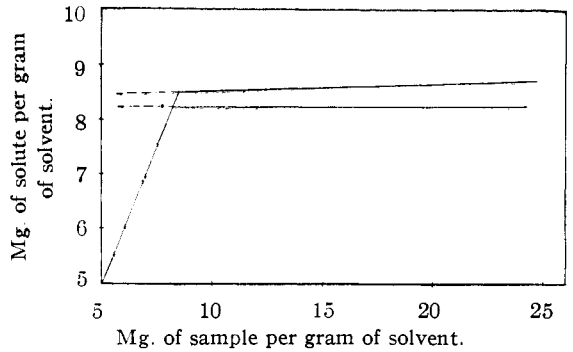


Fig. 1.—Solubility analysis of samples B (sloped line) and C (horizontal line).

and γ-isomers and that the reaction products of the azide with penicillamine and of III with penicillamine methyl ester may be mixtures of α- and γ-glutamyl derivatives instead of the substance constituting the title of their paper.

Experimental

N-Phenylacetyl-L-glutamic acid was prepared and dehydrated exactly as described.[1] The anhydro derivative was ammonolyzed exactly as described and the crude product melted at 131–136° (A). Several recrystallization of this material from acetone–petroleum ether (b.p. 60–80°) gave a product melting at 144–146° (B), as described. Pure material, m.p. 148–149° (C) was obtained as the insoluble residue in the equilibrated ampoules of (B) which were used in the solubility analysis.

Anal. Calcd. for $C_{13}H_{16}N_2O_4$: C, 59.09; H, 6.06; N, 10.60. Found: Sample A: C, 60.33; H, 6.83; N, 10.12. Sample B: C, 58.75; H, 6.33; N, 10.88. Sample C: C, 59.09; H, 6.36; N, 10.54.

A mixture of 1.06 g. (4 millimoles) of sample, 4 cc. of pyridine and 4 cc. of acetic anhydride was refluxed until gas evolution ceased, the envolved gas being collected over water saturated with carbon dioxide. The volumes of carbon dioxide evolved, corrected for the blank on the apparatus, probably accurate within ±5 cc. were: sample A, 28 cc.; sample B, 9 cc.; sample C, none.

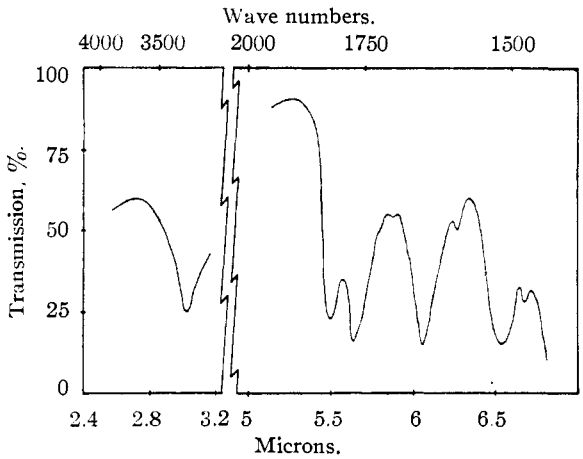


Fig. 2.—Infrared spectrum of anhydrophenacetylglutamic acid.

Solubility analyses were done in purified acetone, using about 8 g. of solvent in sealed glass ampoules which were constantly tumbled in a thermostatically controlled water-bath at 25.0 ± 0.1° for at least 44 hours. Approximately 2.5-g. aliquots of equilibrated solution were used for determination of the amount of dissolved sample. The purity of sample A was sufficiently low that the material gave erratic results of no analytical value in this determination. The values found and plotted in Fig. 1 are considered to be accurate within ±0.15 mg./g.

NEW YORK 11, N. Y.

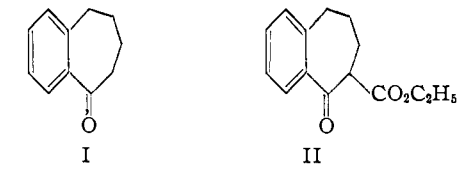
NOTES

Synthesis of Dimethyl 6,7,8,9-Tetrahydro-5H-cycloheptabenzene-5-acetate-6-propionate[1,2]

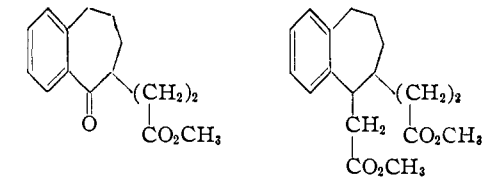
BY A. G. ANDERSON, JR., AND HELEN FRANCES GREEF

RECEIVED APRIL 28, 1952

In the search for synthetic routes to compounds related to colchicine, we have carried out some model studies starting with 6,7,8,9-tetrahydro-5H-cycloheptabenzen-5-one (I). In the course of this work dimethyl 6,7,8,9-tetrahydro-5H-cycloheptabenzene-5-acetate-6-propionate (IV) has been synthesized. IV is of interest as a model compound in that an acyloin condensation of this diester followed by bromination and dehydrobromination according to known procedures[3] would afford a third ring having a tropolone structure and the resultant ring system would then be quite similar to that present in colchicine.



I II



III IV

Carboethoxylation of I with diethyl carbonate in the presence of sodium hydride[4] gave ethyl 6,7,8,9-tetrahydro - 5H - cycloheptabenzen - 5 - one - 6 - carboxylate (II) in 72% yield. The sodium salt of II was prepared by reaction with sodium hydride in anhydrous dioxane. Treatment of this salt with

(1) From the Ph.D. Thesis of Helen Frances Greef.

(2) Supported in part by State of Washington Initiative 171 funds for research in biology and medicine.

(3) D. J. Cram and J. D. Knight, THIS JOURNAL, **73**, 4136 (1951).

(4) F. S. Swamer and C. R. Hauser, *ibid.*, **72**, 1352 (1950).

methyl β-bromopropionate gave an extremely viscous material which could not be obtained analytically pure but gave no test with ferric chloride and was presumed to be largely methyl 6,7,8,9-tetrahydro-5H-cycloheptabenzen-5-one-6-carboethoxy-6-propionate. This crude material was treated with methanolic barium hydroxide[5] and the resultant acid, which decomposed on attempted purification by distillation, esterified directly with diazomethane to give methyl 6,7,8,9-tetrahydro-5H-cycloheptabenzen-5-one-6-propionate (III) as a viscous oil in 60% yield from II. Hydrolysis of the crude intermediate diester with a mixture of acetic and hydrochloric acids or with alcoholic potassium hydroxide resulted in lower yields of III and the formation of tarry by-products.

A Reformatsky reaction of III with methyl bromoacetate followed by dehydration of the crude product and then catalytic hydrogenation afforded IV in 28% over-all yield from III. The low yield realized was not unexpected as it has been previously observed[6] that hindered ketones give poor yields in the Reformatsky reaction.

Experimental[7]

Ethyl 6,7,8,9-Tetrahydro-5H-cycloheptabenzen-5-one-6-carboxylate (II).—A solution of 160 g. (1.0 mole) of 6,7,-8,9-tetrahydro-5H-cycloheptabenzen-5-one (I), prepared as previously described,[8] in 300 ml. of di-*n*-butyl ether (dried over sodium hydride) was added dropwise with vigorous stirring over a period of two to three hours to a gently refluxing mixture of 48 g. (2.0 moles) of sodium hydride in 100 ml. of the dry di-*n*-butyl ether and 240 ml. of freshly distilled diethyl carbonate (b.p. 124–126°). After the addition was complete, the mixture was refluxed for six hours, during which time the mixture was kept fluid by the occasional addition of further quantities of dry solvent, and then allowed to stand overnight. After cooling to 10°, unreacted sodium hydride was destroyed by the addition of 100 ml. of alcohol and the cold mixture was then neutralized by the addition of dilute hydrochloric acid under an atmosphere of nitrogen. After separation of the layers and extraction of the aqueous layer several times with ether, the combined organic layers were washed with saturated salt solution until neutral and then dried over sodium sulfate. Distillation gave 166.5 g. (72%) of II as a yellow oil (b.p. 125–134° at 1 mm., $n^{25.5}$D 1.5623) which gave an intense purple color with 5% ferric chloride solution. The ultraviolet absorption spectrum of an ethanolic solution showed maxima in mμ at 246 (ε 6500) and 290 (ε 13,000).

Anal. Calcd. for $C_{14}H_{16}O_3$: C, 72.34; H, 7.00. Found: C, 72.41; H, 6.97.

Methyl 6,7,8,9-Tetrahydro-5H-cycloheptabenzen-5-one-6-propionate (III).—A solution of 156.6 g. (0.67 mole) of the aforementioned keto ester (II) in 500 ml. of purified dioxane[9] was added dropwise with stirring over a period of two to three hours to a gently refluxing mixture of 16.1 g. (0.67 mole) of sodium hydride in 100 ml. of purified dioxane. The resultant mixture was refluxed for an additional hour. To this hot mixture was then added dropwise a solution of 112 g. (0.67 mole) of methyl β-bromopropionate in 200 ml. of purified dioxane. After stirring and refluxing overnight, the mixture was cooled and the precipitated sodium bromide separated by filtration. Removal of the volatile substances from the filtrate by distillation under reduced pressure left 273.5 g. of a viscous yellow oil which gave no test with 5% ferric chloride solution but could not be purified by distillation. A mixture of 15.9 g. of this oil, presumed to contain mainly methyl 6,7,8,9-tetrahydro-5H-cycloheptabenzen-5-one-6-carboethoxy-6-propionate, 78 g. of barium hydroxide octahydrate, 260 ml. of water and 125 ml. of methanol was refluxed vigorously for 20 hours.[5] Most of the methanol was then removed by distillation under reduced pressure and the cooled residue was acidified with dilute hydrochloric acid. The yellow oil which separated was dissolved in ether, the solution dried over sodium sulfate, and the solvent evaporated. The extremely viscous acidic yellow oil which remained (11 g.), and which decomposed on attempted purification by distillation, was taken up in 500 ml. of dry ether. This solution was cooled to 0° in an ice-bath and to it was added with stirring a cold solution of approximately 0.15 mole of diazomethane in ether. Excess diazomethane was destroyed by the addition of a few ml. of acetic acid. Distillation gave 8.56 g. (60% from II) of methyl 6,7,8,9-tetrahydro-5H-cycloheptabenzen-5-one-6-propionate (III) as a viscous yellow oil, b.p. 160–170° at 1 mm., $n^{25.5}$D 1.5344.

Anal. Calcd. for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 73.39; H, 7.39.

Dimethyl 6,7,8,9-Tetrahydro-5H-cycloheptabenzene-5-acetate-6-propionate (IV).—A mixture of 40 g. of twenty-mesh zinc, 44 g. (0.18 mole) of III, 27.5 g. (0.18 mole) of methyl bromoacetate and a crystal of iodine in 100 ml. of dry toluene was heated under reflux for three hours with the addition of 20 g. of zinc and 9.2 g. of methyl bromoacetate at one-hour intervals. After the last addition, the heating was continued for six more hours. The mixture was cooled to 0° and 100 g. of ice and 15 ml. of acetic acid added. After separation of the layers and extraction of the organic layer several times with ether, the combined organic layers were washed successively with 1% ammonium hydroxide (10–15 times), water, and a saturated sodium chloride solution, and then dried over sodium sulfate. To the brown, viscous oil which remained after removal of the solvents under reduced pressure was added 40 g. of fused, anhydrous potassium bisulfate and the mixture was heated (oil-bath) at 150–160° for one hour. The organic product was extracted from the solid material with ether, the solution dried, and the solvent removed by evaporation. The dark oil which remained was dissolved in 100 ml. of absolute methanol and treated with hydrogen at 30–40 lb. pressure in the presence of 1–2 g. of Raney nickel catalyst. After removal of the catalyst and solvent, distillation *in vacuo* gave 15.5 g. (28% from III) of IV as a viscous yellow oil, b.p. 170–180° at 0.8 mm., $n^{25.5}$D 1.5201.

Anal. Calcd. for $C_{18}H_{24}O_4$: C, 71.03; H, 7.95. Found: C, 69.86; H, 7.64.

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(5) G. Buchi and O. Jeger, *Helv. Chim. Acta*, **32**, 538 (1949).

(6) E. C. Horning, M. G. Horning and E. J. Platt, THIS JOURNAL, **72**, 2731 (1950).

(7) Melting points and boiling points are uncorrected.

(8) A. G. Anderson, Jr., and H. F. Greef, THIS JOURNAL, **74**, 5124 (1952).

(9) A. I. Vogel, "Practical Organic Chemistry," Longmans, Green and Co., New York, N. Y., 1948, p. 175.

The Synthesis of C^{14}-Labeled "Squalene"[1]

BY WILLIAM G. DAUBEN AND H. LEON BRADLOW

RECEIVED APRIL 19, 1952

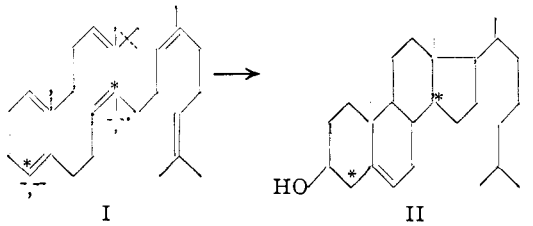
The present concern in the metabolic fate of polyisoprenoid compounds[2] has revived the interest in the early hypothesis of Robinson[3] on the possibility of a direct conversion of the triterpene squalene (I) to cholesterol (II). A convenient way to test this suggestion would be to employ squalene uniquely labeled with C^{14}. The location of the label in the terpene should be such that if a conversion of the type described by Robinson occurred, the labeled atom could singly and easily be removed

(1) The term "squalene" is used to indicate that the product, although a triterpene with six double bonds, is not identical with the naturally occurring compound but is a mixture of double bond isomers (see text).

(2) "Ciba Foundation Conference on Isotopes in Biochemistry," J. and A. Churchill, Ltd., London, 1951, p. 24 ff.; K. Bloch, "Recent Progress in Hormone Research," Vol. VI, Academic Press, Inc., New York, N. Y., p. 111 ff.

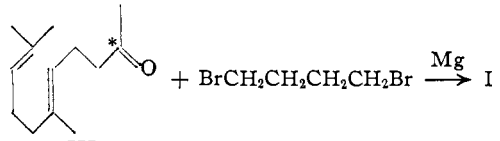
(3) R. Robinson, *J. Chem. Soc. Ind. (London)*, **53**, 1062 (1934).

from the sterol. The placement of the C^{14} at carbon atom four in cholesterol would meet this requirement and such a labeled "squalene" has been prepared. Experimental evidence in support of the postulated conversion has recently been reported by Langdon and Bloch[4] who employed a randomly labeled squalene from natural sources.



I II

The synthesis of squalene has been reported twice. In 1931, Karrer and Helfenstein[5] prepared the compound by allowing farnesyl bromide to react with either magnesium or potassium in a Wurtz reaction and their yield was only 7%. More recently, Schmitt[6] has synthesized squalene in 38%



III

yield by means of a Barbier reaction between geranylacetone (dihydropseudoionone), III, and tetramethylene bromide in the presence of magnesium. The method of Karrer and Helfenstein was not investigated because of the low yield in the condensation reaction and the difficulty in preparing pure farnesyl bromide.

The labeled geranylacetone, the required marked intermediate, was prepared by a modification of the method of Carroll[7] using dilute aqueous alcoholic sodium hydroxide for the ketonic cleavage of the labeled ethyl geranylacetoacetate. The usual barium hydroxide method[8] was found to give inconsistent results, whereas the preceding method consistently gave 90% yields. The carbonyl labeled ethyl acetoacetate was prepared by acylation of the magnesium derivative of ethyl *t*-butyl malonate and pyrolysis of the resulting ester.[9] The previously reported procedure of Sakami, Evans and Gurin[10] involving the condensation of ethyl bromoacetate and ethyl acetate in the presence of magnesium was found to proceed erratically. The labeled geranylacetone, prepared above, was allowed to react with tetramethylene bromide and magnesium. When the resulting squalene was isolated directly from the reaction mixture, as described by Schmitt,[5] the infrared spectrum of the distillate showed the presence of a hydroxyl band at 2.92 μ. Treatment of this material with phosphorus tribromide and collidine gave the pure hydrocarbon. The infrared spectrum of the product is shown in Fig. 1. It is of interest to note the presence of bands at both 11.25 and 12.0 μ. Such bands are characteristic of the type of structures[11] $RR'C{=}CH_2$ and $RR'C{=}CHR''$, respectively. A previous report from this Laboratory[12] has shown that natural squalene has only the trialkylethylene structure present but that squalene obtained by purification through the solid hexahydrochloride has both types of structure present. In Fig. 1 it can be seen that the spectra of synthetic and regenerated squalene are identical in all respects. Earlier work[11] has indicated that regenerated squalene has 20–40% of the double bonds present as the unsymmetrical dialkylethylene type and a similar calculation gives about the same result for the C^{14}-labeled material. Thus, synthetic squalene differs from the naturally occurring triterpene in regard to the types of double bonds present.

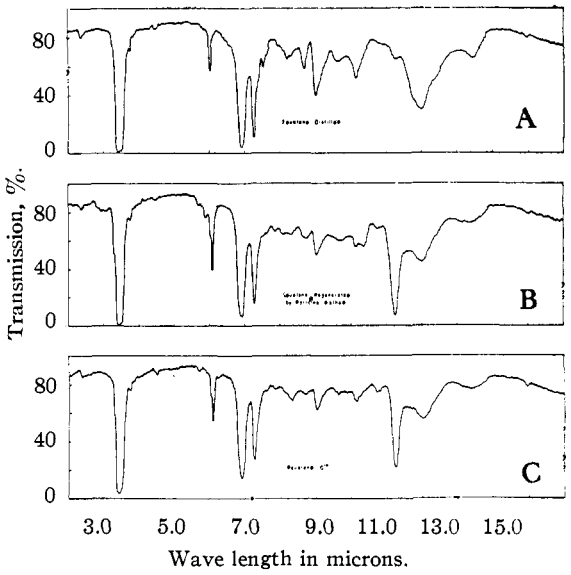


Fig. 1.—Infrared spectra: A, squalene distilled; B, squalene regenerated by pyridine method; C, squalene C^{14}.

It has previously been reported,[12] that squalene can be chromatographed on "Quilon" treated paper using methanol as the developing solvent. It was found that natural squalene gave a single spot with an average R_f value of 0.71 and that regenerated squalene showed two spots, a very strong zone with a value of 0.71 and a second weak one with a value of 0.86. When the C^{14}-labeled material was chromatographed under the same conditions, it also showed two spots with the identical R_f values of the regenerated terpene. Radioautography of the papers showed only two spots and these were identical with those detected by iodine. When the labeled squalene was run together with C^{14}-labeled cholesterol, identical results were obtained as those reported earlier using color tests for identification of the spots.

The authors wish to express their appreciation to Miss Mildred Gee for assistance and to Dr. David

(4) R. G. Langdon and K. Bloch, THIS JOURNAL, **74**, 1869 (1952).
(5) P. Karrer and A. Helfenstein, *Helv. Chim. Acta*, **14**, 78 (1931).
(6) J. Schmitt, *Ann.*, **547**, 115 (1941).
(7) M. F. Carroll, *J. Chem. Soc.*, 704 (1940).
(8) L. Ruzicka, *Helv. Chim. Acta*, **6**, 492 (1928).
(9) D. S. Breslow, E. Baumgarten and C. R. Hauser, THIS JOURNAL, **66**, 1286 (1944).
(10) W. Sakami, W. E. Evans and S. Gurin, *ibid.*, **69**, 1110 (1947).
(11) H. W. Thompson and D. H. Whiffen, *J. Chem. Soc.*, 1412 (1948).
(12) W. G. Dauben, L. B. Bradlow, N. K. Freeman, D. Kritchersky and M. Kirk, THIS JOURNAL, **74**, 4321 (1952).

Kritchevsky for the determination of the R_f values and to Dr. Keith Freeman for the infrared spectra.

Experimental[13]

Geranyl Chloride.—This preparation was carried out as described by Ruzicka[8] using phosphorus pentachloride and either hexane or ligroin (60–70°) as a diluent. From 90 g. (0.6 mole) of geraniol, 62 g. (60%) of the chloride was obtained, b.p. 93–104° (15 mm.). The thionyl chloride method of Barnard and Bateman[14] was found to be less satisfactory.

Carbonyl-Labeled Ethyl Acetoacetate.—A mixture of 2.87 g. of magnesium, 100 ml. of absolute ethanol, 20 ml. of dry xylene and 2 ml. of carbon tetrachloride was refluxed for 12 hours and then concentrated to dryness under reduced pressure on a steam-bath. Benzene was added twice and removed *in vacuo* to ensure the absence of any alcohol.[15] The residue was heated at 100° under reduced pressure for three hours, cooled, 40 ml. of anhydrous ether added and the mixture stirred vigorously to break up the solid. Ethyl *t*-butyl malonate (22.4 g.) then was added dropwise with stirring and the mixture refluxed until complete solution was obtained. Carboxyl-labeled acetyl chloride, prepared from 10.8 g. of sodium acetate containing 9.9 mc. of C^{14} by distillation from benzoyl chloride, was dissolved in 25 ml. of dry ether and the solution was added dropwise with stirring to the magnesium derivative of the malonic ester. After refluxing for 30 minutes, the reaction mixture was cooled, diluted with water and acidified with dilute sulfuric acid. The aqueous phase was separated and extracted with ether and combined with the above ether. The solvents were distilled, the residue dissolved in 100 ml. of benzene, a small amount of the solvent distilled, 0.75 g. of *p*-toluenesulfonic acid added and the solution refluxed for 90 minutes. The cooled benzene solution was extracted with saturated sodium bicarbonate, saturated sodium chloride and the benzene removed through an 18″ column. The residue was distilled, b.p. 180°, yield 12.2 g. (71.3% based upon sodium acetate).

Geranylacetone.—The carbonyl-labeled ethyl acetoacetate (11.53 g.) was diluted with 11.0 g. of non-radioactive ester and the mixture added dropwise with stirring to a cooled solution of 3.46 g. of sodium in 100 ml. of absolute ethanol. After 15 minutes, 26.4 g. of freshly distilled geranyl chloride was added slowly and the resulting mixture heated under reflux for 25 hours. The solution was diluted with 500 ml. of water, extracted with ether and the ether distilled.

The crude product was dissolved in a solution containing 8 g. of sodium hydroxide, 350 ml. of ethanol and 230 ml. of water and refluxed for 48 hours. The reaction was then diluted with 500 ml. of water, extracted twice with 250-ml. portions of ether, the ethereal solution washed with water until neutral, then with saturated sodium chloride solution and dried over sodium sulfate. The product was distilled, b.p. 115° (1 mm.), yield 15 g. (52.5%).

Labeled "Squalene."—A mixture of 15.0 g. of geranylacetone, 10 g. of tetramethylene bromide, 2.3 g. of magnesium and a crystal of iodine was heated on a steam-bath for 30 minutes under an atmosphere of nitrogen. The mixture was then diluted with 45 ml. of dry ether and refluxed for 45 minutes by which time most of the magnesium had dissolved. Another crystal of iodine was added and the solution refluxed overnight. The reaction was decomposed with water and dilute hydrochloric acid, the ethereal layer separated and dried.

The ether was distilled, 30 ml. of dry benzene and 15 ml. of phosphorus tribromide were added and the solution heated on a steam-bath for 12 hours. The cooled mixture was poured into dilute hydrochloric acid and ice-water, the layers separated and the aqueous layer re-extracted with ether. The combined extracts were washed with dilute alkali, water and saturated sodium chloride solution. The solvents were distilled, the residue dissolved in 60 ml. of collidine and heated under reflux for 3 hours. After dilution with aqueous hydrochloric acid, the mixture was extracted four times with ether, the ethereal solution processed in the usual manner and the product distilled, b.p. 210–212° (1.5 mm.), yield 3.1 g. (19.7%).

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(13) All boiling points are uncorrected.

(14) D. Barnard and L. Bateman, *J. Chem. Soc.*, 926 (1950).

(15) B. Riegel and W. M. Lilienfeld, THIS JOURNAL, **67**, 1273 (1945).

The Infrared Spectra of the Isomeric 2-Decalols and their Acetates. The Effects of Stereochemical Configuration

BY WILLIAM G. DAUBEN, EARL HOERGER AND N. K. FREEMAN

RECEIVED MAY 12, 1952

To date, various methods have been employed in the decalols to assign the configuration of the hydroxyl group and the nearest ring juncture hydrogen atom. Originally, Hückel[1] allocated such configurations on the basis of the von Auwer–Skita rule and many of these assignments have been confirmed by the application of the stereospecific elimination reactions[2] in the 1-decalol series and the utilization of conformational analysis[3] in the *trans*-decalols. There is no direct method which is applicable to the *cis*-2-decalols.[4] Last year, Jones, Humphries, Herling and Dobriner[5] reported that in the sterols, a study of the 1200–1260 cm.$^{-1}$ region of the infrared spectrum could aid in the determination of the stereochemical relationship between the C_3-hydroxyl group and the C_5-hydrogen atom. They found that when the acetoxyl group at C_3 and the hydrogen at C_5 were *trans* to each other, only a single strong band occurred in this region. When such a relationship was *cis*, two or three strong bands were observed. Absorption at these frequencies is characteristic of the acetate group in general and these workers suggested that the multiple bands could be due to an equilibrium mixture of unstable rotational isomers. If such were the case, this type of analysis should be applicable to the corresponding acetates of the 2-decalols. These esters have been prepared and their spectra are shown in Fig. 1. Each spectrum was obtained several times with varying operating conditions to verify the spectral details.

The stereochemical configuration assigned to the four 2-decalols at the present time is shown below.[6] If these assigned configurations are correct and if this spectral analysis is applicable, it would be expected that the acetates of I and III should show a single strong band whereas the acetates of II and IV should exhibit a multiple band structure. An examination of the curves shows that the spectrum of the acetates of *cis*-105° decalol (I) does have a single symmetrical band in this region but it was

(1) W. Hückel, *Ann.*, **441**, 1 (1925); **451**, 109 (1926); **533**, 1 (1938); W. Hückel and C. Kuhn, *Ber.*, **70**, 2479 (1937).

(2) W. Hückel, W. Tappe and G. Legutke, *Ann.*, **543**, 191 (1940); D. H. R. Barton, *J. Chem. Soc.*, 2175 (1949).

(3) D. H. R. Barton, *Experientia*, **6**, 316 (1950).

(4) W. G. Dauben and E. Hoerger (THIS JOURNAL, **73**, 1504 (1951)) have employed an indirect method in which they assign the configuration of a *cis*-decahydro-2-naphthoic acid on the basis of the *cis*-hydrogenation concept of Linstead. The acids obtained were then related to the decalols by the use of stereospecific reactions.

(5) R. N. Jones, P. Humphries, F. Herling and K. Dobriner, *ibid.*, **73**, 3215 (1951).

(6) The positions of the hydrogen atoms are represented in the formulas by black dots, a dot indicating that a hydrogen atom is above the plane of the molecule.

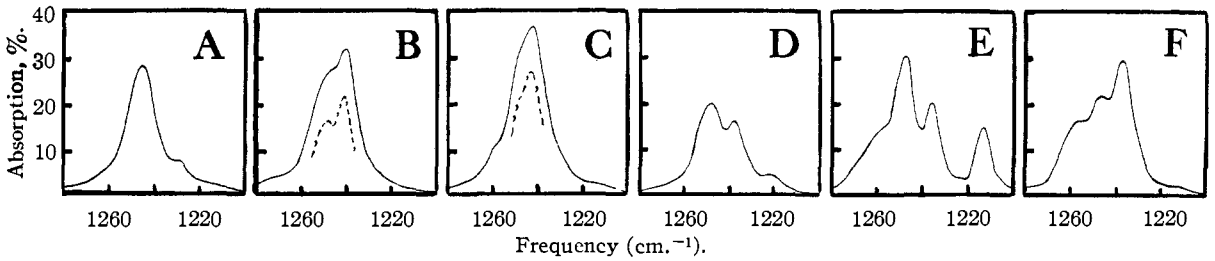
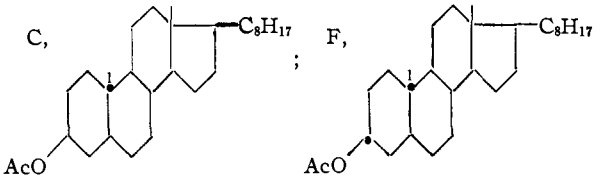
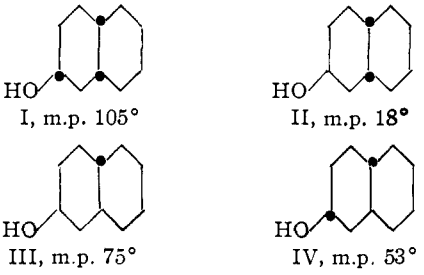


Fig. 1.—Characteristic acetate bands of stereoisomeric 2-decalyl acetates (CS_2 solution) (dotted lines indicate high resolution): acetates of A, cmpd. I; B, cmpd. III; D, cmpd. II; E, cmpd. IV;



found that, under high resolution, the ester of *trans*-75° decalol (III) is split into two bands. The acetates of *cis*-18° (II) and *trans*-53° (IV) decalols do have clear multiplicity. For comparison, the



acetates of cholestanol and epicholestanol were prepared and their spectra are also given in Fig. 1. As reported by Jones and his collaborators,[5] it was found that epicholestanyl acetate (a *cis* relationship) showed a multiplicity of bands but cholestanyl acetate (a *trans* compound) displayed a single band which was unsymmetrical. Such a band shape suggests that it might be a doublet when run under high resolution but it was found that under the running conditions where the band of the acetate of II split, the cholestanyl ester did not. Thus, in those structures in which the acetoxyl group and the ring juncture hydrogen atom have been allocated a *cis* relationship, a clear and definite multiplicity has been found whereas in the *trans* structures a splitting occurred in one isomer. In general, the relationship established by Jones, *et al.*, appears to hold quite well in this series of simpler compounds.

Another interesting correlation involving the C_3-hydroxyl group and the C_5-hydrogen atom of a sterol has recently been observed in the 1000–1100 cm.$^{-1}$ (9–10 μ) region by Rosenkrantz, Milhorat and Farber.[7] They found that compounds having the hydroxyl group *cis* to the ring juncture hydrogen atom, *i.e.*, coprostanol and epicholestanol, had bands at 1041 and 1004 cm.$^{-1}$ (9.61 and 9.96 μ) and 1038 and 1004 cm.$^{-1}$ (9.63 and 9.96 μ), respectively, while compounds with a *trans* relationship, *i.e.*, epicoprostanol and cholestanol, had bands at 1062 and 1040 cm.$^{-1}$ (9.42 and 9.62 μ) and 1075 and 1041 cm.$^{-1}$ (9.3 and 9.61 μ), respectively. Thus a shift of band pairs from 1075–1042 cm.$^{-1}$ (9.3–9.6 μ) to 1042–1000 cm.$^{-1}$ (9.6–10.0 μ) region occurs when the steric relationship changes from *trans* to *cis*. For comparison, the infrared spectra in this region for the 2-decalols are shown in Fig. 2. Assuming the assigned configurations (*vide supra*), decalols I and III should belong to the 1075–1042 cm.$^{-1}$ (9.3–9.6 μ) group and compounds II and IV to the 1042–1000 cm.$^{-1}$ (9.6–10.0 μ) group. It is seen that such a general shift of bands does occur but the difference is not as clearly defined as in the ester work described above. Nevertheless, such a generalization may be of aid, as a first approximation, in suggesting stereochemical configurations in this bicyclic series. It is not certain from this work whether such effects in the infrared discussed above bear any relationship to the C_5-hydrogen atom as suggested by the authors of the sterol papers[5,7] and used in the discussion of the decalol results or whether it is a result of an over-all steric nature of the molecule imposed by the ring juncture configurations or substitutions.

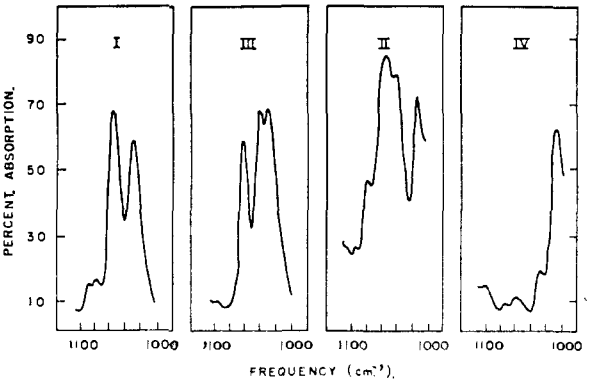


Fig. 2.—1000–1100 cm.$^{-1}$ region absorption of stereoisomeric 2-decalols (CS_2 solution).

The decalols employed in this study were prepared and purified in the most part in the standard fashion reported by Hückel.[8] The preparation of

(7) H. Rosenkrantz, A. T. Milhorat and M. Farber, *J. Biol. Chem.*, **195**, 509 (1952).

(8) W. Hückel, R. Danneel, A. Grosz and H. Naab, *Ann.*, **502**, 99 (1933), and earlier references given in this paper.

the *trans*-75°-decalol was attempted by the method of Baker and Schuetz[9] who reported that when 2-naphthol was hydrogenated at room temperature and high pressure over platinum oxide in acetic acid, the crude product obtained was essentially the pure *trans*-75°-decalol. When this work was repeated, it was found that such was not the case but the *cis*-105° isomer was the main product. Thus starting with 550 g. of 2-naphthol, the hydrogenation product was first separated into neutral and acidic components and the acidic *ar*-tetralol amounted to at least 14%. The neutral fraction was crystallized from hexane to remove the large majority of the *cis*-105°-decalol and this isomer was obtained in 36% yield. The mother liquor residues were distilled in vacuum and yielded 28% mixed decalins, 20% of mixed decalols which consisted mostly of the *cis*-18° isomer and a small amount (0.1%) of the *trans*-53° alcohol. Although no pure *trans*-75° material was isolated it cannot be stated that none is present, but if so, it is a very minor reaction product. When this hydrogenation was run on a smaller scale, the amount of hydrogenolysis was less and the crude product was a solid. It would thus appear that the conclusion of Baker and Schuetz[9] that their crude reaction product was pure *trans*-75°-decalol is erroneous and was due to the fact that their mixture was not purified.

Experimental

Hydrogenation of 2-Naphthol.—A total of 550 g. of 2-naphthol was hydrogenated at high pressure and room temperature using platinum oxide catalyst. For example, in one of the runs, 150 g. of 2-naphthol, 160 ml. of ether, 160 ml. of glacial acetic acid and 3.0 g. of platinum oxide were placed in a glass lined hydrogenation bomb and shaken at room temperature under an initial pressure of 3200 p.s.i. After 15 hours, 6.5 mole equivalents had been absorbed and the shaking was stopped. The runs were combined at this stage.

After removal of the catalyst by filtration, the catalyst was washed with ether and the washings combined with the filtrate. The ether–acetic acid solution was then made alkaline by the cautious addition of concentrated sodium hydroxide solution. Ether was added from time to time to replace that lost by evaporation during the neutralization. The ether layer was separated from the aqueous alkaline layer containing the *ar*-tetralol, washed with water and saturated sodium chloride solution. After drying, the ether was evaporated and the residue dissolved in the minimum quantity of hexane. Several crops of crystals, all melting from 100–104°, were collected and then combined and recrystallized from hexane, yield 210 g. of *cis*-105°-decalol, m.p. 104.0–104.5°.

All hexane mother liquors were evaporated and the residues combined and distilled through a 35-plate tantalum wire-packed column[10] at a reflux ratio of 10 to 1. The following fractions were collected: (1) decalin, 148 g., b.p. 81–84° (20 mm.); (2) *trans*-53°-decalol (impure), 1.5 g., b.p. 125–131° (20 mm.); (3) mixed decalols, 120 g., b.p. 131–138 (20 mm.); (4) *ar*-2-tetralol (impure), 20 g., b.p. 155–158° (20 mm.).

From fraction 2, m.p. 44–46°, 0.4 g. of pure *trans*-53°-decalol, m.p. 53.4–54.7°, was obtained by repeated recrystallization from pentane. Portions of fraction 3, liquid at room temperature, were converted to half phthalates[1] and yielded mainly the solid half phthalate of *cis*-18°-decalol, m.p. 145–148° (lit.[1] 153°). Fraction 4, m.p. 36–38°, was recrystallized from hexane and after one crystallization melts at 51–52°. Further crystallizations yielded material melting 61–62°; this result is in agreement with the known dimorphic character of *ar*-2-tetralol whose two forms melt 53–54° and 62°.[11] Apparently the tetralol was not completely extracted from ether by the alkali in the first step in the separation.

Preparation of Acetates.—The decalyl acetates were prepared by the method of Leroux.[12] The properties reported by Hückel[8] are in agreement with those found in the present research except we were unable to obtain the acetate of *cis*-105°-decalol as a solid; Hückel reports m.p. 32°. The boiling points of the esters of the decalols are as follows with the literature value given in parentheses: I, 136° (19 mm.) (122° (9 mm.)); II, 135° (15 mm.) (not reported[13]); III, 132° (20 mm.) (110° (9 mm.)) and IV, 133° (18 mm.) (118° (9 mm.)).

Infrared Spectra.—The spectra of the decalyl acetates and steroidal acetates were determined with a Model 21 Perkin–Elmer infrared spectrophotometer equipped with a NaCl prism. The carbon disulfide solutions were studied in a KBr cell of 0.1 mm. thickness with no comparison cell in the reference beam. The frequency measurements are estimated to have an uncertainty of less than ±2 cm.$^{-1}$ and the slit width used in the high resolution studies was 5 cm.$^{-1}$. The exact maxima for the acetates are as follows: I, 1244 cm.$^{-1}$; II, 1248, 1238 cm.$^{-1}$; III, 1248, 1240 cm.$^{-1}$; IV, 1247, 1235, 1213 cm.$^{-1}$. The value for cholestanyl acetate is 1243 cm.$^{-1}$ and for epicholestanyl acetate are 1257, 1247, 1237 cm.$^{-1}$. The spectra of the decalols were determined n carbon disulfide solution at a concentration of 10 g. per liter and at a cell thickness of 0.9 mm. on a Baird infrared spectrophotometer equipped with a NaCl prism. The exact maxima for the decalols are as follows: I, 1057, 1029 cm.$^{-1}$; II, 1050, 1012 cm.$^{-1}$; III, 1062, 1022 cm.$^{-1}$; IV, 1007 cm.$^{-1}$.

Acknowledgment.—The authors wish to express their appreciation to Professor George C. Pimentel for his kind coöperation during the progress of this work.

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(10) F. W. Mitchell and J. M. O'Gorman, *Anal. Chem.*, **20**, 315 (1948).

(11) R. T. Arnold, H. Klug, J. Sprung and H. Zaugg, THIS JOURNAL, **63**, 1161 (1941).

(12) H. Leroux, *Compt. rend.*, **140**, 590 (1905).

(13) *Anal.* Calcd. for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 72.98; H, 10.93.

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Effect of Xanthylation on the Recovery of DNP-Amins Acids from Acid Protein Hydrolysates[1]

BY SHERMAN R. DICKMAN AND R. OWEN ASPLUND

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Thompson[2] observed the destruction of DNP-amino acids after acid hydrolysis in the presence of tryptophan or the protein lysozyme which contains 10.6% tryptophan.[3] The acid stability of dixanthyltryptophan[4] prompted us to determine recoveries of N^5-DNP-L-lysine and of di-DNP-L-lysine from DNP-lysozyme and xanthyl-DNP-lysozyme. As shown in Table I recovery of N^5-DNP-L-lysine was 56% of theoretical from DNP-lysozyme and 91% from xanthyl-DNP-lysozyme after the substituted protein was refluxed for twenty-four hours in 6 *N* HCl. Similarly, recovery of di-DNP-L-lysine was 78% of the theoretical from DNP-lysozyme and 97% from xanthyl-DNP-lysozyme. The recovery of approximately one mole

(1) This work supported in part by a research grant from Armour and Co.

(2) A. Thompson, *Nature*, **168**, 390 (1951).

(3) J. C. Lewis, N. S. Snell, D. J. Hirschmann and H. Fraenkel-Conrat, *J. Biol. Chem.*, **186**, 23 (1950).

(4) W. L. Westcott and S. R. Dickman, unpublished.

of di-DNP-L-lysine and 5 moles of N^{ϵ}-DNP-L-lysine per mole of lysozyme confirms the previous analyses of Green and Schroeder[5] and of Lewis, *et al.*[3]

TABLE I

RECOVERY OF N^{ϵ}-DNP-L-LYSINE AND DI-DNP-L-LYSINE FROM DNP-LYSOZYME AND XANTHYL-DNP-LYSOZYME

Sample	Quantity analyzed,[a] μM	N^{ϵ}-DNP-L-lysine recov.[b] μM	%	Di-DNP-L-lysine recov.[b] μM	%
DNP-Lysozyme	1.20	3.37	56.0	0.94	78.0
Xanthyl-DNP-lysozyme	1.34	6.10	91.0	1.31	97.5

[a] Calculated from determination of primary amide groups.[6,7] [b] Calculated from absorbancy at 3460 Å. in glacial acetic acid.

The increased recovery of the DNP-lysines after xanthylation is probably due to the formation of dixanthyltryptophan in the intact protein. This is also indicated by the formation of the characteristic purple color of dixanthyltryptophan in these solutions. Data which indicate that dixanthyltryptophan itself is non-destructive of DNP-alanine under protein hydrolysis conditions is included in Table II. A 56% recovery of DNP-DL-alanine was obtained in the presence of tryptophan. This was increased to a recovery of 82% in the presence of dixanthyltryptophan and 85% in the presence of xanthyllysozyme and in the control. These results suggest that xanthylation of other proteins after reaction with DNFB will result in higher recoveries of DNP-amino acids in acid hydrolysates of proteins.

TABLE II

EFFECT OF ADDED COMPOUNDS ON THE RECOVERY OF DNP-DL-ALANINE FROM ACID SOLUTIONS

Compound[a]	Mg.	Recovery, %
Control	..	85
Tryptophan	10	56
Dixanthyltryptophan	30	82
Xanthyllysozyme	100	85

[a] These quantities provide approximately 10 moles of tryptophan per mole of DNP-DL-alanine.

Experimental

DNP-Lysozyme was prepared by the method described by Sanger[7] for DNP-insulin. Lysozyme (100 mg.) was treated with DNFB (400 mg.) in bicarbonate buffer and 85 mg. of DNP-lysozyme was isolated.

Xanthyl-DNP-lysozyme was prepared by dissolving DNP-lysozyme (100 mg.) and xanthydrol (112 mg.) in 10 ml. of 90% acetic acid. At the end of one hour at room temperature the product was precipitated with ether and washed three times with ether at the centrifuge. The xanthyl-DNP-lysozyme (65 mg.) was dried over calcium chloride and paraffin.

Isolation and determination of N^{ϵ}-DNP-L-lysine and di-DNP-L-lysine from DNP-lysozyme and xanthyl-DNP-lysozyme were carried out according to Porter.[8] Synthesis of the two DNP-lysines which were used as standards was also accomplished by the method of Porter. Absorbancy measurements of the DNP-lysines were made with a Beckman DU spectrophotometer at 3460Å.

Protein concentrations were determined by primary amide group analyses. The protein solutions were autoclaved for one hour in 2 *N* H_2SO_4 at 20 lb. pressure, after which the ammonia was determined as described by Porter.[8]

DNP-DL-alanine was synthesized by the method of Porter.[8] For the stability study DNP-DL-alanine (1.0 mg.) was refluxed twenty-four hours in 12 *N* HCl in the presence of tryptophan (10 mg.), dixanthyltryptophan (30 mg.) and xanthyllysozyme (100 mg.). The DNP-DL-alanine in the solution was chromatographed over silica gel according to Porter[8] and determined photometrically at 4000 Å.

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(6) H. Fraenkel-Conrat, M. Cooper and H. Olcott, *ibid.*, **67**, 314 (1945).

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Amebacidal Agents. II. 5-Acyl- and 5-Alkyl-7-dialkylaminomethyl-8-quinolinols

BY WILLIAM H. EDGERTON AND J. H. BURCKHALTER

RECEIVED JUNE 17, 1952

Interesting amebacidal activity has been reported in a group of Mannich base derivatives of halogenated quinolinols.[1] A similar series of alkylated quinolinols was synthesized following the initial observation of activity. The intermediate 5-acyl-8-quinolinols were prepared by means of the Friedel–Crafts reaction using 8-quinolinol.[2] Reduction of these ketones to the 5-alkyl-8-quinolinols was accomplished by catalytic hydrogenation with 5% palladium-on-charcoal.[2] This reaction was extended with great difficulty to the preparation of several long-chain acylated quinolinols. Reduction of the long-chain acylated quinolines was confirmed by the disappearance of the characteristic infrared absorption band at 5.96 μ.[3]

When the Mannich reaction with 8-hydroxy-5-quinolyl methyl ketone,[2] was attempted, using two molar equivalents of amine and paraformaldehyde only one basic side chain was introduced. Infrared data strongly suggest that the piperidyl methyl group entered the aromatic nucleus at position 7 rather than the α-position of the acetyl substituent.[4] Compound VI, Table I, and 5-chloro-7-(1′-piperidylmethyl)-8-quinolinol dihydrochloride[5] possess similar infrared absorption patterns with bands at 11.6, 12.10, 12.42, 12.75 μ, and 11.66, 12.24, 12.54, 12.75 μ, respectively. Both spectra differ greatly in this region from the spectra of several 5-substituted 8-quinolinols.

The amebacidal activity[6] of these compounds was observed to decrease with increasing molecular weight.

Experimental

8-Hydroxy-5-quinolyl Octyl Ketone (X).—Anhydrous aluminum chloride (120 g.) was added in small portions with cooling to a mixture of 70.5 g. (0.40 mole) of pelargonyl chloride and 45.0 g. (0.31 mole) of 8-quinolinol in 200 g. of nitrobenzene. The mixture was heated at 75° for 16 hours.

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(2) K. Rosenmund and G. Karst, *Arch. Pharm.*, **279**, 154 (1941).

(3) Infrared data were determined and interpreted by Mr. Bruce Scott and Dr. John Vandenbelt of the Physical Chemistry section of these laboratories.

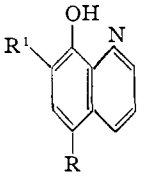
(4) This fact is contrary to the behavior of *p*-hydroxyacetophenone in the Mannich reaction as reported by E. B. Knott, *J. Chem. Soc.*, 1190 (1947).

(5) Unpublished work.

(6) Amebacidal activity data were determined by Dr. Paul Thompson and staff of these laboratories.

TABLE I

5-ACYL- AND 5-ALKYL-8-QUINOLINOLS



Compound No.	R	R¹	M.p.,[a] °C.	Yield, %	Formula	Analyses,[b] % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
I	Methyl[c]	Diethylaminomethyl	174	70	$C_{15}H_{20}N_2O\cdot HBr$	55.38	55.67	6.31	6.31
II	Methyl	4-Phenyl-1-piperazylmethyl	156	91	$C_{21}H_{23}N_3O$	75.65	75.96	6.95	7.30
III	Methyl	1-Piperidylmethyl[d]	268	97	$C_{16}H_{20}N_2O\cdot 2HBr$	45.95	46.24	5.34	5.35
IV	Methyl	4-Morpholinylmethyl	99	73	$C_{15}H_{18}N_2O_2$	69.74	69.76	7.02	7.30
V	Methyl	Ethyl-β-hydroxyethylaminomethyl	200	56	$C_{15}H_{20}N_2O_2\cdot 2HCl$	54.06	54.34	6.66	6.93
VI	Acetyl	1-Piperidylmethyl	208	67	$C_{17}H_{20}N_2O_2$	71.80[e]	71.72	7.09	7.36
VII	Ethyl	1-Piperidylmethyl	242	95	$C_{17}H_{22}N_2O\cdot HBr$	58.12	58.17	6.60	6.65
VIII	Benzoyl	1-Piperidylmethyl	251	81	$C_{22}H_{22}N_2O_2\cdot 2HBr$	51.98	52.24	4.76	5.11
IX	Benzyl	1-Piperidylmethyl	275	56	$C_{22}H_{24}N_2O\cdot 2HBr$	53.45	53.09	5.30	5.50
X	Pelargonyl		67	17[f]	$C_{18}H_{28}NO_2$	75.76	75.92	8.12	8.09
XI	Nonyl		217	16	$C_{18}H_{25}NO\cdot HBr$	61.31	61.27	7.44	7.57
XII	Palmitoyl		223	11	$C_{25}H_{37}NO_2\cdot HBr$	64.64	65.07	8.25	8.33
XIII	Palmitoyl	1-Piperidylmethyl	167	54	$C_{31}H_{48}N_2O_2\cdot HBr$	66.30	67.09	8.79	9.06
XIV	Hexadecyl[g]		63	63					

[a] Melting points are not corrected. Salts melt with decomposition. [b] Analyses are by Mr. Charles Childs and staff of these laboratories. [c] 5-Methyl-8-quinolinol was prepared by the method of E. Noelting and E. Trautmann, *Ber.*, **23**, 3666 (1890). [d] 1-Phenylpiperazine was supplied by Dr. Robert F. Parcell of these laboratories. [e] Calcd.: N, 9.85. Found: N, 10.04. [f] Yield based on hydrochloride. [g] Although an analytical sample could not be obtained, the characteristic infrared absorption band of the ketone moiety is missing.

After 20 hours at room temperature, the dark mixture was decomposed carefully with a slurry of dilute hydrochloric acid and ice. The nitrobenzene was steam distilled. The thick residue was neutralized with strong alkali until faintly acid to *p*H paper. The filtered reaction mass was extracted with several portions of acetone. The acetone solution was saturated with hydrogen bromide to yield 19 g. (17%) of yellow solid, m.p. 229–231° (dec.).

For analysis, a sample was converted to the free base by neutralizing an aqueous suspension with alkali extracting the dried solid with ether and recrystallizing the light brown crystals several times from ethanol; m.p. 66–67°.

The similar pentadecyl ketone (XII) was prepared in like manner. The ketones were reduced catalytically by the method of K. Rosenmund and G. Karst.[3]

5-Acyl- and 5-Alkyl-7-dialkylaminomethyl-8-quinolinols.—A previously heated solution of molar equivalents of amine and paraformaldehyde in ethanol was added to a solution of the quinolinol in ethanol. After a brief reflux period (1–2 hours), the solution was either concentrated and cooled to separate the product or diluted with dry ether and acidified with dry hydrogen bromide gas to separate the salt. The solid was then purified by several recrystallizations from ethanol or isopropyl alcohol.

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Additional Evidence on the Enzymatic Transformation of Histidine into Glutamic Acid

BY J. P. FOURNIER AND L. P. BOUTHILLIER

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By the use of heavy nitrogen as a tracer element, Tabor and his collaborators[1] demonstrated conclusively that the γ-nitrogen of histidine appears in the amino group of the glutamic acid resulting from the enzymatic degradation of the former. They have also presented direct evidence that the initial step in the breakdown of histidine is its deamination to the formation of urocanic acid. Their findings are thus in agreement with the theory formulated by Sera and his co-workers,[2] Takeuchi[3] and Oyamada,[4] whereby histidine would be biologically degraded to urocanic acid, formylisoglutamine, isoglutamine and glutamic acid.

We wish to report here some experimental data which provide additional support to the above theory. Freshly prepared liver homogenates were incubated in presence of carboxyl-C^{14}-labeled DL-histidine. Two-dimensional paper partition chromatograms (solvent mixtures: water-saturated-phenol + HCN + 0.3% NH_3 and water-saturated *n*-BuOH + glacial AcOH) of the original incubation mixtures, as compared to incubation blanks without histidine, revealed upon treatment with ninhydrin the marked intensification of only one spot, that corresponding to glutamic acid. The latter was further identified by the mixed spot technique. The biologically formed glutamic acid was then isolated with carrier, and recrystallized several times to constant radioactivity in the form of its calcium salt. Samples of the regenerated glutamic acid were decarboxylated (α-COOH) by treatment with ninhydrin and the activity of the evolved carbon dioxide was measured. The results appear in Table I. Since our data indicate that only a small fraction of the total activity contained in the glutamic acid was present in the α-carboxyl group of the molecule, it seems reasonable to assume that the radioactivity was concentrated almost entirely in the γ-carboxyl carbon. The conclusion is reached that the α- and γ-carboxyl carbons of the

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(3) M. Takeuchi, *J. Biochem. (Japan)*, **34**, 1 (1941).

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glutamic acid originate, respectively, from the δ and carboxyl carbons of its precursor histidine. Thus our results are consistent with the proposed pathway[2-4] for histidine metabolism and confirm the findings of Tabor, *et al.*[1]

TABLE I

Experiment No.	Specific activity of glutamic acid, counts per min. per mM.	Specific activity of ninhydrin-liberated CO_2 (α-COOH), counts per min. per mM.	C^{14} in α-COOH carbon of glutamic acid, %
1A	4100	170	4.2
1B	4100	188	4.6
2A	5220	125	2.4
2B	5220	133	2.6

Experimental

Radioactive Histidine.—DL-Histidine dihydrochloride labeled with C^{14} on the carboxyl carbon position was synthesized.[5] Its activity was measured with the use of a thin mica window tube and corresponded to approximately 1100 counts per minute per mg.

Incubation of Liver Homogenates in Presence of Labeled Histidine.—Cell-free homogenates of rat liver were prepared.[6] Into each of 50-ml. conical flasks were added 25 mg. of DL-histidine ($C^{14}OOH$)·2HCl, 1 ml. of 0.22 *N* NaOH to neutralize the hydrochloric acidity, 5-ml. aliquots of fresh homogenate and finally 10 mg. of normal L-glutamic acid as trapping agent, in the case of experiments 2A and 2B. The flasks were stoppered with cotton plugs and then agitated for 6 hours in a 38° water-bath.

Isolation and Purification of Glutamic Acid.—At the end of the incubation period, the contents of each flask were mixed with 10 volumes of absolute alcohol and heated to boiling for 10 minutes. The coagulated protein was separated by centrifugation and washed twice with alcohol. The clear alcohol solutions and washings of each preparation were evaporated to about 1 ml. and the volume brought to 10 ml. with distilled water. Into each solution was added as carrier 300 mg. of L-glutamic acid. Glutamic acid was precipitated as the calcium salt, recrystallized three times in water and alcohol, and regenerated according to the method of Foreman.[7] The aqueous solutions were each concentrated to about 4 ml. to which was added 10 ml. of absolute alcohol. Glutamic acid was allowed to crystallize slowly in an ice-box. Quantities of the purified radioactive amino acid as large as 150 mg. were recovered.

Decarboxylation of Glutamic Acid and Radioactivity Measurements.—Fifty-mg. portions of isotopic glutamic acid were decarboxylated by means of ninhydrin[8] and the evolved carbon dioxide was collected as barium carbonate. The radioactivity of the glutamic acid and the barium carbonate (40-mg. samples each) was measured with a thin mica window Geiger counter, corrected for background and self-absorption.[9] The final values were expressed as counts per minute per millimole.

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Solubility of Diborane- and Boron-containing Lithium Salts[1]

BY J. R. ELLIOTT, W. L. ROTH, G. F. ROEDEL AND E. M. BOLDEBUCK

RECEIVED FEBRUARY 14, 1952

As part of a program for studying the preparation of diborane from lithium hydride and boron trihalides in ether type solvents, it became necessary for us to determine the approximate solubility of diborane and several boron-containing lithium salts in the two solvents, diethyl ether and tetrahydrofuran.

The solubility of diborane gas was calculated from measurements of the pressure of the vapor in equilibrium with a solution of diborane at various temperatures. The temperature–pressure data listed in Tables I and II were interpreted by assuming perfect gas laws and estimating the vapor pressure of the solvent on the basis of Raoult's law. The equilibrium partial pressures of solute were obtained by difference, using successive approximations for the lowering of the vapor pressure of the solvent by the solute. Calculations are summarized in Tables III and IV in terms of the equilibria

TABLE I

EQUILIBRIUM PRESSURES FOR DIBORANE IN DIETHYL ETHER

Weight diethyl ether, 20.24 g.; volume of cylinder, 79.3 cc.

Series A 0.395 g. diborane		Series B 0.617 g. diborane		Series C 1.032 g. diborane	
Temp., °C.	Obsd. press., p.s.i. abs.	Temp., °C.	Obsd. press., p.s.i. abs.	Temp., °C.	Obsd. press., p.s.i. abs.
0.5	21.7	0.6	28.7	0.8	54.7
11.3	27.7	12.0	41.2	13.0	60.7
27.2	37.7	24.5	51.2	25.5	74.7
40.3	49.2	40.0	67.7	40.0	94.7
58.3	69.7	60.0	95.7	50.0	111.7
27.0	38.2				

TABLE II

EQUILIBRIUM PRESSURES FOR DIBORANE IN TETRAHYDROFURAN

Wt. diborane, g.	0.540	1.008	1.721	0.993	1.704	2.172
Wt. tetrahydrofuran, g.	25.01	25.01	25.01	24.18	24.18	24.18
Vol. of cylinder, cc.	79.3	79.3	79.3	76.3	76.3	76.3
T, °C.	Observed pressure, p.s.i. abs.					
7	2.9	3.2	4.9	2.9	5.9	13.2
20	3.9	5.6	9.8	5.4	12.2	26.7
30	5.9	9.1	16.7	9.3	21.7	42.7
40	8.3	15.2	27.7	14.2	32.7	66.7
50	...	21.5	42.2	...	49.7	93.7

$$B_2H_6(g) = B_2H_6 \text{ (in ether solution)} \qquad K_1 = S/P \quad (1)$$

$$^1/_2B_2H_6(g) = [BH_3] \text{ (in tetrahydrofuran solution)} \qquad K_1 = S/P^{1/2} \quad (2)$$

where P is the equilibrium pressure of diborane in atmospheres and S is the solubility expressed as moles diborane in 100 g. of solvent.

(1) This work was done on U. S. Army Ordnance Contract No. TUI-2000.

TABLE III

SOLUBILITY OF DIBORANE IN DIETHYL ETHER

T°, K	Initial B_2H_6, moles/ 100 g. solvent	0.706	0.110	0.184	K_1,[a] average
273	Total press., atm.	1.47	1.90	3.70	
	B_2H_6 press.	1.24	1.68	3.49	
	K_1	0.055	0.064	0.051	0.057
283	Total press., atm.	1.82	2.16	4.02	
	B_2H_6 press.	1.46	1.81	3.68	
	K_1	0.047	0.059	0.049	.052
293	Total press., atm.	2.22	3.22	4.64	
	B_2H_6 press.	1.67	2.68	4.13	
	K_1	0.041	0.040	0.043	.041
303	Total press., atm.	2.70	3.85	5.48	
	B_2H_6 press.	1.89	3.06	4.73	
	K_1	0.036	0.035	0.038	.036
313	Total press., atm.	3.33	4.63	6.48	
	B_2H_6 press.	2.17	3.50	5.40	
	K_1	0.032	0.031	0.033	.032
323	Total press., atm.	4.07	5.52	7.60	
	B_2H_6 press.	2.48	3.96	6.11	
	K_1	0.028	0.027	0.029	.028

[a] $K_1 = S/P$ (moles B_2H_6/100 g. ether—atm.).

This suggests that diborane is present in tetrahydrofuran solution as the complex $C_4H_8O:BH_3$. Heats of solution of −2800 cal./mole in ether and −4900 cal./mole in tetrahydrofuran were obtained from the change in equilibrium constants with temperature. These values should be given only qualitative significance.

The unusual solvent properties of tetrahydrofuran on boron-containing salts are shown in Table V. Solubility of the salts was roughly determined by evaporation of solvent from saturated solutions.

Experimental

Determination of Diborane Solubility.—A tared stainless steel cylinder, equipped with a pressure gage, was filled to approximately one-third capacity with dry solvent and was degassed by repeated freezing and evacuation. The cylinder was reweighed and connected by flexible metal tubing to a steel storage tank containing diborane of purity greater than 99%. Connecting lines were evacuated and small portions of diborane were admitted to the cylinder until the desired equilibrium pressure registered on the gage. The cylinder was again weighed, then submerged in a water-bath of known temperature until an equilibrium pressure was established. After a series of pressure–temperature values had been obtained, the cylinder was placed in a bell jar and dried under vacuum until constant weight had been reached.

TABLE IV

SOLUBILITY OF DIBORANE IN TETRAHYDROFURAN

T°, K	Initial B_2H_6 moles/100 g. solvent	0.0779	0.148	0.145	0.248	0.255	0.324	K_2[a] average
280	Total press., atm.		0.198	0.218	0.333	0.401	0.899	
	B_2H_6 press.		.113	.133	.250	.325	.828	
	K_2		.44	.40	.49	.44	.35	0.42
293	Total press., atm.	0.266	0.368	0.381	0.667	0.830	1.819	
	B_2H_6 press.	.100	.215	.227	.530	.694	1.691	
	K_2	.25	.32	.30	.33	.30	0.24	.29
303	Total press., atm.	0.402	0.619	0.633	1.137	1.477	2.910	
	B_2H_6 press.	.147	.388	.398	0.931	1.272	2.716	
	K_2	.20	.23	.23	0.25	0.22	0.18	.22
313	Total press., atm.	0.566	0.967	1.033	1.885	2.230	4.545	
	B_2H_6 press.	.196	.626	0.691	1.579	1.925	4.255	
	K_2	.18	.18	0.17	0.19	0.18	0.14	.17
323	Total press., atm.			1.461	2.874	3.386	6.380	
	B_2H_6 press.			0.967	2.429	2.942	5.967	
	K_2			0.14	0.15	0.14	0.12	.14

[a] $K_2 = S/P^{1/2}$ (moles B_2H_6/100 g. tetrahydrofuran—atm.$^{1/2}$).

The solubility of diborane in diethyl ether is slightly greater than predicted by Raoult's law but is proportional to pressure. In tetrahydrofuran the solubility of diborane is much greater than perfect solution predictions, and solubility increases as the square root of diborane pressure.

TABLE V

COMPARISON OF SOLVENT PROPERTIES OF DIETHYL ETHER AND TETRAHYDROFURAN AT 25°

	Solubility in ether, g. solute/100 g. solvent	Solubility in tetrahydrofuran, g. solute/100 g. solvent
B_2H_6	1.1[a]	8.1[a]
$LiBF_4$	1.9	71
$LiBH_4$	3[2]	28
LiF	0.05	0.6

[a] Calcd. from Tables III and IV. Diborane at 1 atm., 20°.

(2) H. I. Schlesinger, *et al.*, Final Report, Navy Contracts No. N173 S-9058 and N173 S-9820.

A second portion of diborane was then introduced and the above procedure repeated.

Solutions of diborane in ether showed no change in pressure after several days storage. In two weeks, a pressure increase from 2 to 14 lb. and from 28 to 118 lb. had occurred in the two diborane–tetrahydrofuran cylinders.

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Separation of Mixtures with Triethylamine–Sulfur Trioxide

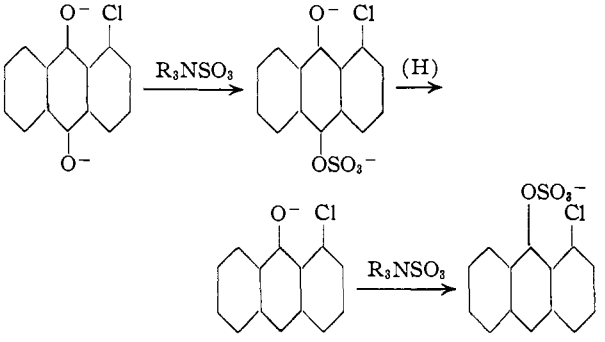
BY WILLIAM B. HARDY AND MARIO SCALERA

RECEIVED MAY 20, 1952

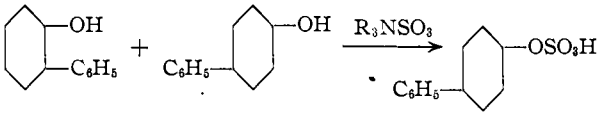
In an earlier paper[1] we have reported that the action of triethylamine–sulfur trioxide on anthrahydroquinones leads to the formation of anthranol sulfuric esters in addition to the expected disulfuric

(1) M. Scalera, W. B. Hardy, E. M. Hardy and A. W. Joyce, THIS JOURNAL, **73**, 3094 (1951).

esters. While this side reaction occurs with anthrahydroquinone itself, it was found to be greatly enhanced by the presence of α-substituents in the anthraquinone molecule. The postulation that steric effects accounted for the enhancement of the side reaction by the α-substituent was borne out by the nature of the reduction products. For example, in the esterification of 1-chloroanthraquinone, 1-chloro-9-anthranolsulfuric ester was isolated as the principal reduction product. This is the expected product if the α-substituent hinders the esterification, as can be seen by examination of the equations



In view of these facts, we considered it of interest to determine if this postulated steric effect on the esterification rate would be observable in simple compounds. In order to avoid the tedious measurements which would be involved in the determination of reaction rates, we resorted to the simple expedient of carrying out competitive esterifications on mixtures. Application of the esterification reaction to an equal molecular mixture of *o*- and *p*-phenylphenol in aqueous alkaline medium led to the formation of the sulfuric ester of *p*-phenylphenol in high yield, as

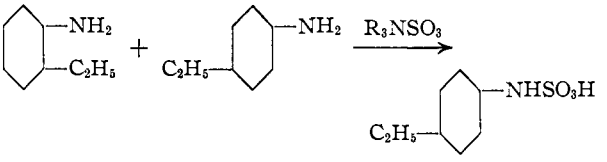


The regenerated material from this ester was of exceedingly high purity. In an independent experiment it was shown that *o*-phenylphenol was esterified in high yield under the same conditions as used for esterification of the mixture, thus demonstrating that the exclusive formation of para isomer from the mixture was simply the result of its greater esterification rate.

Application of the esterification procedure to a mixture of 8-benzamido-1-naphthol and 5-benzamido-1-naphthol in pyridine solution led to esterification of the 1,5-isomer as would be expected based on steric effects. However, in aqueous medium the 1,8-isomer only was esterified. Independent experiments showed that the failure of the reaction to take the expected course was probably due to the low solubility of the 5-benzamido-1-naphthol in the organic phase of the aqueous reaction mixture. Indeed, the 1,5-isomer was not esterified at all under the conditions of aqueous esterification.

The remarkably sharp separation of the components of the *o*- and *p*-phenylphenol mixture made it of interest to examine the possible suitability of triethylamine–sulfur trioxide as a reagent for the separation of other isomeric compounds or compounds having active hydrogen atoms.

When a mixture of *o*- and *p*-ethylaniline was treated with the sulfating agent in chloroform, a clean-cut separation was obtained with the para isomer being converted to the sulfamic acid in a high state of purity.



The separation of 1-propanol and 2-propanol by means of triethylamine–sulfur trioxide represents a case where two compounds may be separated due to the difference in degree of dissociation of the hydrogen–oxygen bond. Heating a mixture of these two alcohols with the esterification reagent resulted in a good yield of the sulfuric ester of *n*-propanol identified as its benzylisothiouronium salt. That this was a case of selective action on the 1-propanol is demonstrated by an experiment in which 2-propanol was heated with triethylamine–sulfur trioxide under the same conditions and the ester of 2-propanol was readily obtained.

These results were obtained in connection with a broad research program on the esterification of leuco vat dyes by trialkylamine–sulfur trioxide compounds, and sufficient time was not available to explore further this interesting method of separation. However, in addition to being applicable to the separation of isomeric compounds containing amino or hydroxy groups, it is felt that this procedure could be used in many cases where the hydrogen atoms of two compounds show differing reaction rates toward triethylamine–sulfur trioxide.

Experimental

Intermediates.—With the exception of triethylamine–SO_3[2] and the benzamidonaphthols, the intermediates used were commonly available materials. 1-Benzamido-8-naphthol was prepared from peri acid by alkali fusion followed by benzoylation with benzoic anhydride; m.p. 187–189°.[3]

1-Benzamido-5-naphthol, a new compound, was prepared by the above procedure starting with Eastman Kodak Co. purified 1-amino-5-naphthol hydrochloride. The yield of gray-white solid was 45%. It sintered at 261° and melted at 270–273°.

Anal. Calcd. for $C_{17}H_{13}O_2N$: C, 77.5; H, 4.90; N, 5.30. Found: C, 77.7; H, 4.84; N, 5.94.

Separation of Phenols. Aqueous Process.—Samples weighing 8.5 g. (0.05 mole) each of *o*-phenylphenol and *p*-phenylphenol were dissolved at 70° in a solution consisting of 4.4 g. (0.11 mole) of sodium hydroxide in 58 cc. of water. Nine and two-tenths grams (0.11 mole) of sodium bicarbonate and 13.8 g. (0.075 mole) triethylamine–SO_3 were added. The mixture was stirred for 3.5 hours at 45–50°. After cooling, the mixture was extracted with ether. The two lower layers were diluted to 125 cc. with water and 30 cc. of 5 *N* sodium hydroxide was added. Addition of sodium chloride to the solution precipitated the sulfuric ester of *p*-phenylphenol in 81% yield, as shown by hydrolysis in acid solution to pure *p*-phenylphenol; m.p. 163–164°. The high purity of this product is demonstrated by the fact that a mixture comprised of 10% *o*-phenylphenol and 90% *p*-phenylphenol softened at 80° and melted at 112–157°.

(2) H. Z. Lecher and W. B. Hardy, THIS JOURNAL, **70**, 3789 (1948).
(3) F. Fichter and R. Gageur, *Ber.*, **39**, 3331 (1906).

Working up the filtrates and ether extract yielded 8.2 g. of crude ortho isomer melting at 52–87°.

Separation of Naphthols. Aqueous Process.—A mixture consisting of 2.6 g. (0.01 mole) each of 8-benzamido-1-naphthol and 5-benzamido-1-naphthol was dissolved in 10 cc. of water by addition of 4.2 cc. of 5 *N* sodium hydroxide. Addition of 1.7 g. (0.02 mole) of sodium bicarbonate precipitated the naphthols. Then 2.8 g. (0.015 mole) of triethylamine–SO_3 was added. After stirring for six hours at 30°, 10 cc. of 5 *N* sodium hydroxide was added and the triethylamine was extracted with ether. Acidification with 20% acetic acid precipitated 2.6 g. of product identified as being principally 5-benzamido-1-naphthol.

From the filtrate the sulfuric ester of 8-benzamido-1-naphthol was isolated in 81% yield.

Separation of Naphthols. Anhydrous Process.—A mixture consisting of 1.3 g. (0.005 mole) each of 5-benzamido-1-naphthol and 8-benzamido-1-naphthol was placed in 15 cc. of dry pyridine and 1 g. (0.005 mole) of triethylamine–SO_3 was added. The clear brown solution was allowed to stand for 24 hours at room temperature. Ten cc. of water and 5 cc. of 5 *N* sodium hydroxide were added and the organic bases were extracted with ether. The aqueous layer was neutralized with 80% acetic acid and the upper layer was decanted from the oil and clarified. A 50-cc. portion was taken from the total volume of 115 cc. and boiled with hydrochloric acid. The dried product resulting from this hydrolysis weighed 0.3 g. and melted at 233–242°. Thus, the principal product isolated is 5-benzamido-1-naphthol formed in about 53% yield.

Separation of Anilines.—A mixture consisting of 12.1 g. (0.1 mole) each of *o*-ethylaniline and *p*-ethylaniline was placed in 100 cc. of chloroform in a flask fitted with mechanical stirrer and 20.2 g. (0.11 mole) of triethylamine–SO_3 was added. While stirring, the temperature was allowed to rise gradually from 15 to 25° during a five-hour period. The white solid was filtered off at 7° and washed with hexane. It weighed 19.4 g., 64.2% yield, m.p. 101–103°. The identity of this material as the para isomer is shown by the fact that no depression in melting point occurs when it is mixed with an authentic sample of the para isomer. Furthermore, the ortho isomer yields an oil under these conditions.

Separation of Alcohols.—A mixture of 30 g. (0.5 mole) each of 2-propanol and 1-propanol was treated in 125 cc. of chloroform with 97 g. (0.525 mole) of triethylamine–SO_3. The clear solution was allowed to stand at room temperature for two and one-half days. The solvent was then evaporated under reduced pressure so that the liquid temperature did not exceed 40°. Addition of 200 cc. of hexane caused a layer separation and the lower layer weighing 177 g. was separated and cooled. Since crystallization could not be induced, a 3.5-g. (0.01 mole real) aliquot was added to 10 cc. of water containing 2.2 g. of benzylisothiouronium chloride. The vacuum-dried product obtained weighed 2.4 g., a 77.2% yield of the sulfuric ester of 1-propanol as the benzylisothiouronium salt; sintering point 113°, m.p. 115–116°.

Anal. Calcd. for $C_{11}H_{17}N_2O_4S_2$: C, 43.2; H, 5.6; S, 20.9. Found: C, 43.2; H, 5.8; S, 20.6.

***o*-Phenylphenol Sulfuric Ester.**—A 17-g. (0.1 mole) sample of *o*-phenylphenol was dissolved to a clear solution in 90 cc. of water by addition of 20 cc. of 5 *N* sodium hydroxide. Then 8.4 g. (0.1 mole) of sodium bicarbonate, 5.3 g. (0.05 mole) of sodium carbonate and 28 g. (0.15 mole) of triethylamine–SO_3 were added. The mixture was stirred for three hours at 45–50° to give a two-layer system. The cooled reaction mixture was extracted with ether. The two remaining lower layers were neutralized with dilute hydrochloric acid and again extracted with ether. The aqueous layer was salted to 15% concentration with potassium chloride at 50°, and the white solid was filtered off at 10° and washed with 15% potassium chloride–2% potassium hydroxide solution. The wet cake weighed 68.5 g. One-fourth of this was clarified from 75 cc. of water and resalted. The dry product weighed 7.6 g., an 83% yield based on the carbon content.

Anal. Calcd. for $C_{12}H_9KO_4S$: C, 51.4; H, 3.1; S, 11.0; C/S, 12.0. Found: C, 38.5; H, 2.93; S, 8.62; C/S, 11.9.

8-Benzamido-1-naphthol Sulfuric Ester.—A 2.6-g. portion (0.01 mole) of 8-benzamido-1-naphthol was treated with triethylamine–SO_3 in aqueous carbonate solution as described in the preparation of the ester of *p*-phenylphenol. The product weighed 4.3 g., a yield of 72%.

Under these same conditions 1-benzamido-5-naphthol was recovered unchanged.

Anal. Calcd. for $C_{17}H_{12}KO_5NS$: C, 53.4; H, 3.19; N, 3.68; S, 8.40; C/S, 17.0; N/S, 1.00. Found: C, 42.2; H, 3.34; N, 2.93; S, 6.57; C/S, 17.0; N/S, 1.03.

***p*-Ethylaniline Sulfamic Acid.**—Six grams (0.049 mole) of *p*-ethylaniline and 9.5 g. (5% excess) of triethylamine–SO_3 were dissolved in 50 cc. of chloroform. After warming at 60° for 15 minutes, the solution was cooled to 10° and the product was filtered off and washed with hexane. The crude dry product weighed 16.0 g. and melted at 75–80°. An 8.0-g. sample recrystallized from 50 cc. of chloroform gave 6.6 g. of white solid melting at 99–102°, an 89% yield as the triethylamine salt of *p*-ethylanilinesulfamic acid.

Anal. Calcd. for $C_{14}H_{26}N_2O_3S$: C, 55.6; H, 8.6; N, 9.28; S, 10.6. Found: C, 55.7; H, 8.48; N, 9.29; S, 10.8.

Under the same conditions, *o*-ethylaniline failed to yield a solid derivative.

2-Propanol Sulfuric Ester.—Six grams (0.1 mole) of 2-propanol was heated with 18.1 g. (0.1 mole) of triethylamine–SO_3 at a bath temperature of 125° for two hours. Since the viscous reaction mixture could not be crystallized, 4.5 g. (0.019 mole) of the mixture was dissolved in 20 cc. of water and the product was precipitated by addition of 4.0 g. (0.02 mole) of benzylisothiouronium chloride in 16 cc. of water. After recrystallization from water, 1.4 g. of dry product sintering at 141°, m.p. 142–144°, was obtained, a yield of 24%.

Anal. Calcd. for $C_{11}H_{17}N_2O_4S_2$: C, 43.2; H, 5.6; N, 9.2; S, 20.9. Found: C, 43.3; H, 5.0; N, 9.8; S, 20.7.

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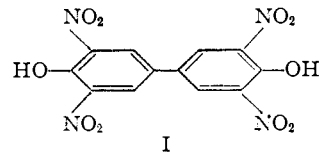
The Dissociation of 3,3′,5,5′-Tetranitro-4,4′-dihydroxydiphenyl in Methanol[1]

BY HAROLD HART AND WILLIAM J. DETROIT

RECEIVED MAY 12, 1952

The effect of nitro groups ortho or para to the hydroxyl function of phenols on the acidity of the latter is well known. It was of interest to determine the acidity of a dihydric phenol in which two such arrangements were present in the same molecule, but isolated from each other. Accordingly, the dissociation constant of 3,3′,5,5′-tetranitro-4,4′-dihydroxydiphenyl (I) was measured.



I

The absorption spectrum of I was determined in methanol, in methanol containing hydrogen chloride and in methanol containing sodium methoxide. Several of the curves so obtained are given in Fig. 1. The maximum at 355 mμ is taken to represent the undissociated species. A solution 1.87×10^{-4} *M* in I and 1.85×10^{-4} *M* in hydrogen chloride increased the extinction coefficient from 5920 (in neutral methanol) to 6560, but a further increase (tenfold) in the hydrogen chloride concentration had a negligible effect. Curve 1, therefore, represents I in the undissociated form. Addition of in-

(1) Taken in part from the Master of Science thesis of W. J. D., March, 1952.

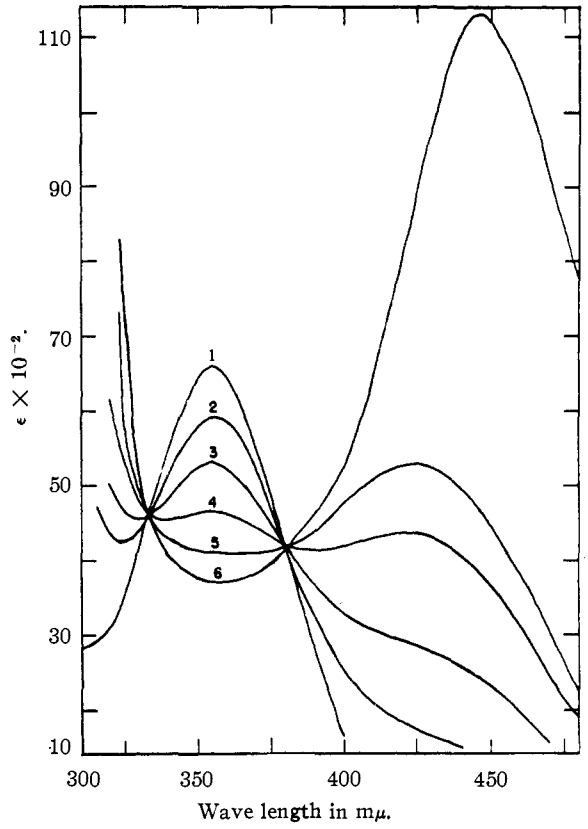


Fig. 1.—Spectrum of 3,3′,5,5′-tetranitro-4,4′-dihydroxydiphenyl (I) (approximately 2×10^{-4} *M* in I) in methanol of varying acidity: curve 1, 1.85×10^{-4} *M* and 1.85×10^{-3} *M* in hydrogen chloride; curve 2, in neutral methanol; curve 3, 3.9×10^{-5} *M*; curve 4, 7.8×10^{-5} *M*; curve 5, 1.04×10^{-4} *M*; and curve 6, 1.3×10^{-4} *M* in sodium methoxide.

creasing quantities of sodium methoxide decreased the extinction at 355 mμ linearly, as shown in Fig. 2. Curve 6, of Fig. 1, the last curve which continued to pass through the isobestic points, was taken to represent complete disappearance of the undissociated form of I. As methoxide concentration was increased, another maximum appeared, shifting gradually from 422 to 477 mμ and becoming more intense. This probably represents the monovalent anion. When further methoxide was added, the curve no longer passed through the isobestic points. This probably represents loss of the second proton and conversion to the divalent anion. This second dissociation, unfortunately, could not be measured spectrophotometrically, due to crystallization from the alcohol–sodium methoxide solution of red crystals, probably the sodium salt.

The first dissociation constant of I in methanol was evaluated from the spectra, using data at several different wave lengths between the isobestic points, in the usual manner. It was found to be $1.27 \pm 0.18 \times 10^{-6}$ (pK 4.90 ± 0.06, room temperature). The pK of 2,6-dinitrophenol[2] in water at 18° is 3.58. Schwarzenbach and Rudin[3] have shown that the measured acidity may decrease by

(2) D. C. Martin and J. A. V. Butler, *J. Chem. Soc.*, 1366 (1939).

(3) G. Schwarzenbach and E. Rudin, *Helv. Chim. Acta*, **22**, 360 (1939).

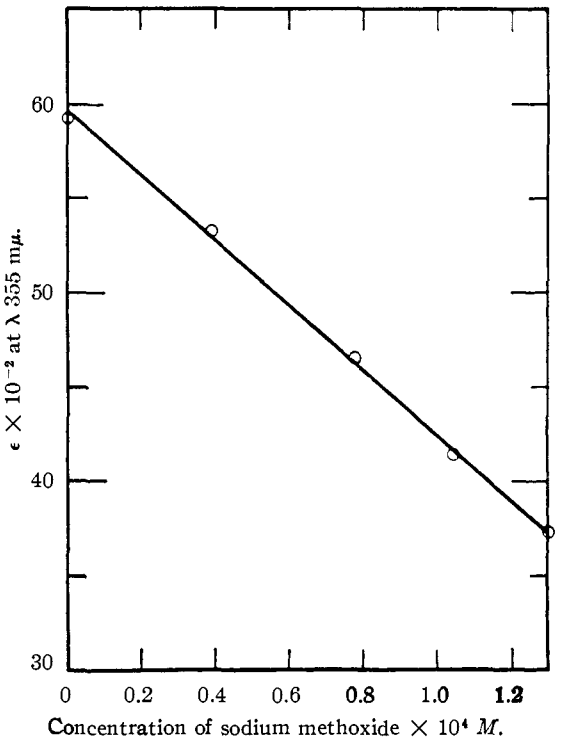


Fig. 2.—Linear dependence of the extinction coefficient of I at 355 mμ on the concentration of sodium methoxide in methanol.

as much as 2.5 pK units in going from water to 95% ethanol for *o*- and *p*-nitrophenol. The dissociation constant we have determined for I in methanol is, therefore, a reasonable one.

Experimental

Materials.—3,3′,5,5′-Tetranitro-4,4′-dihydroxydiphenyl was prepared from benzidine in 70% yield by the procedure of Borsche and Scholten.[4] Absolute methanol was the solvent for the spectra. When acidic or basic methanol solutions were required, anhydrous hydrogen chloride or sodium methylate, respectively, were dissolved in absolute methanol. The solutions were standardized in the usual manner.

Spectra.—A Beckman model DU spectrophotometer, with 1-cm. quartz cells, was used for determination of the spectra.

(4) W. Borsche and B. G. B. Scholten, *Ber.*, **50**, 508 (1917).

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Studies in the Diphenoquinone Series[1]

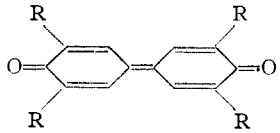
BY WILLIAM J. DETROIT AND HAROLD HART

RECEIVED JUNE 4, 1952

The reaction of dienes proceeds well with *p*- and *o*-quinones, naphthoquinones, and other cyclenones.[2] Because of the nature of the products which might be obtained, we became interested in studying the possible reaction of diphenoquinone (I) and related compounds with dienes. The only previously reported attempt at the condensation of

(1) Taken from the thesis presented for the Master of Science degree by W.J.D., March, 1952.

(2) L. W. Butz and A. W. Rytina, Chapter in R. Adams, "Organic Reactions," Volume 5, John Wiley and Sons, Inc., New York, N Y., 1949, p 136.



(R = H); II (R = CH_3); III (R = t-C_4H_9); IV (R = Cl)

I with a diene was that of Nara Boon-Long,[3] who reported the formation of ill-characterized and possibly polymeric products when a solution of I in benzene was heated with 2,3-dimethyl-1,3-butadiene in a sealed tube at 100° for 24 hours. The rather vigorous conditions and lack of control experiments prompted us to reinvestigate the reaction.

The first of our difficulties was encountered in the preparation of the parent compound, I. It had first been synthesized by Willstätter and Kalb[4] who oxidized an ether solution of 4,4′-diphenol by shaking with a suspension of lead dioxide at room temperature for 24 hours. Subsequent workers[3,5,6] also employed this procedure[7] but noted that the method was inconsistent, and did not always result in the desired product. In our hands, using commercially manufactured lead dioxide, the method was a complete failure. The state of subdivision or the recrystallization solvent for the 4,4′-diphenol, factors which were claimed to be of importance,[5] had little effect. It was found, however, that if the lead dioxide was freshly prepared from lead tetraacetate in a highly active form, according to the recent procedure of Kuhn and Hammer,[8] and the reaction time for the oxidation was decreased from 24 hours to about 30 minutes or less, a reasonable yield (55%) of the red crystalline modification of I was *consistently* obtained.

No exothermic reaction occurred between I and cyclopentadiene in alcohol, benzene, or chloroform solvents, nor could any well-defined adduct be obtained by refluxing. Blank experiments showed that I is readily polymerized by refluxing in the above solvents, but that II can be recovered quantitatively, even when cyclopentadiene is present.

The absorption spectra of I and of several substituted diphenoquinones were determined, and are summarized in Table I. Only the spectrum of I[5] and a portion of the spectrum of III[9] have been previously reported.

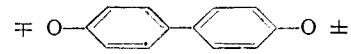
TABLE I

MAXIMA IN THE VISIBLE AND ULTRAVIOLET ABSORPTION SPECTRA OF SOME DIPHENOQUINONES

Compound	λ[c]	ε	λ	ε	λ	ε	λ	ε
I[a]	395	62,600	261	2990	252	3130	...	...
II[a]	414	67,600	...	...	...	...	...	...
III[a]	420	70,800	269	4920	260	5480	251	4740
II[b]	421	73,200	...	...	...	...	...	...
III[b]	427	66,000	271	4240	262	4800	253	4320
IV[b]	435	71,800	283	3470	273	4520	261	5390

[a] In ethyl alcohol. [b] In chloroform. [c] All wave lengths are in mμ.

The principal maximum in the visible is probably due to contributions, in the first excited state, from resonance structures of the type



Substituents in the 3,3′,5,5′-positions apparently have only a slight effect on these principal contributing forms. The shift of 19 mμ (from 395 to 414 mμ) when a hydrogen atom is replaced by a methyl group may be interpreted in terms of hyperconjugation involving the methyl groups, and this shift is only slightly different (to 420 mμ) for the *t*-butyl group. Pianka, *et al.*,[10] have interpreted the similar bathochromic shift on going from the 2,4-dinitrophenylhydrazone of formaldehyde to those of acetaldehyde and higher aldehydes[11] in a similar manner, and point out the possible generality of bathochromic and hypsochromic shifts on alkyl substitution. The main feature of the spectra of the diphenoquinones, however, is their similarity, and the relative independence of the nature of the substituent.

Experimental

Diphenoquinone (I).—To 5 g. of 4,4′-dihydroxydiphenyl[12] dissolved in 720 ml. of ether there was added 25 g. of activated[8] lead dioxide. The mixture was shaken mechanically for about 30 minutes. After filtration, the lead dioxide residue containing I was extracted by refluxing for 15 minutes once with 1 l. and twice with 500 ml. of benzene. Cooling the combined extracts gave 1.69 g. of red crystalline I. Concentration of the mother liquors gave an additional 0.58 g. Additional product (0.40 g.) was precipitated from the mother liquors with ligroin, the gold crystalline modification of I being obtained. Recrystallization of the red crystals from benzene gave the gold form. The total yield was 2.67 g. (53.9%). The reaction time could be varied from 15 to 45 minutes without an appreciable effect on the yield.

Anal.[13] Calcd. for $C_{12}H_8O_2$: C, 78.25; H, 4.38. Found: red form, C, 78.55; H, 4.39; gold form, C, 78.42; H, 4.60.

Spectra.—Chloroform was purified by the method of Fieser,[14] and absolute alcohol was dried by distillation from calcium oxide. The spectra were determined with a Beckman model DU quartz spectrophotometer, using 1-cm. matched quartz cells. It should be noted that solutions of I in alcohol are unstable, and the spectrum must be determined rapidly. In chloroform I decomposes too rapidly for the determination of its spectrum. The same holds for alcoholic solutions of IV. Solutions of II and III in both solvents are stable.

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(4) R. Willstätter and L. Kalb, *Ber.*, **38**, 1232 (1905).

(5) N. A. Valyashko and M. M. Shcherbak, *J. Gen. Chem.* (*U.S.S.R.*), **8**, 1597 (1938); *C. A.*, **33**, 4589 (1939).

(6) L. F. Fieser, THIS JOURNAL, **52**, 4915 (1930).

(7) After developing the successful procedure described below, we noted that L. F. Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co., New York, N. Y., 2nd Ed., 1941, p. 439, mentions the use of lead tetraacetate to oxidize diphenol to I. We could not find the details of this procedure in the literature, and after four unsuccessful attempts, gave this method up.

(8) R. Kuhn and I. Hammer, *Ber.*, **83**, 413 (1950).

(9) H. Hart and F. A. Cassis, THIS JOURNAL, **73**, 3179 (1951).

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(11) E. A. Braude and E. R. H. Jones, *J. Chem. Soc.*, 499 (1945).

(12) R. Hirsch, *Ber.*, **22**, 335 (1889).

(13) Clark Microanalytical Laboratories, Urbana, Illinois.

(14) L. F. Fieser, ref. 7, p. 365.

Phenolphthalol

BY MAX H. HUBACHER

RECEIVED APRIL 19, 1952

By reduction of phenolphthalin (4′,4″-dihydroxytriphenylmethane-2-carboxylic acid) with sodium

amalgam, Baeyer[1] obtained a product melting at 190°, which he called phenolphthalol. He reported that this compound is oxidized to phenolphthalein by potassium ferricyanide. He also described a red, water-insoluble condensation product formed by treatment of phenolphthalol with concentrated sulfuric acid.

By reduction of phenolphthalin with lithium aluminum hydride, in this Laboratory, a compound which melted at 201° was obtained. This substance neither produced Baeyer's red product, nor did it yield phenolphthalein on oxidation. This phenolphthalol, 2-(4′,4″-dihydroxybenzhydryl)-benzyl alcohol (I), gave a mono- as well as a triacetyl derivative, as would be expected from its formula.

Experimental

Phenolphthalol (I).—A three-necked flask fitted with a rubber-sleeved stirrer, an inlet tube for nitrogen, and a glass tube holding a 25 × 85 mm. glass thimble topped by a reflux condenser, was charged with 500 ml. of absol. ether and 3.0 g. of $LiAlH_4$. Into the thimble was placed 6.40 g. (0.02 mole) of phenolphthalin (m.p. 233–236°). After two hours of refluxing, the latter had dissolved. Stirring was continued for 16 hours at 36°. Then a mixture of 50 ml. of water and 35 ml. of concd. hydrochloric acid was carefully added and the ether layer extracted with 2 *N* sodium carbonate. Phenolphthalin (0.81–0.97 g.) was recovered from the extract. After evaporation of the ether, the solid was recrystallized from either water (1 g. in 750 ml.) or from 20% ethanol (1 g. in 110 ml.). The yield was 4.65–4.96 g. (76–81%); m.p. 201–202°.

The pure I, colorless needles, melts at 201.5–201.9° cor. It can be sublimed at 180° and 8 microns pressure.[2] It is very soluble in acetone or ethanol, soluble in ether, and insoluble in chloroform or benzene. Its solution in dilute alkali is colorless; a 0.001 molar solution in concd. sulfuric acid is of moderate orange color.

Anal. Calcd. for $C_{20}H_{18}O_3$: C, 78.42; H, 5.92; mol. wt., 306. Found: C, 78.59; H, 6.25; mol. wt., 292.[3]

When a solution of phenolphthalein in dilute acetic acid was treated with sodium amalgam according to Baeyer's procedure,[1] a crude product which melted at about 190° was obtained in very low yield. After several crystallizations from water it melted at 198–199° and proved to be identical with I.

Monoacetyl Derivative of I.—A mixture of 1.0 g. of I and 10 ml. of acetic acid was refluxed for one hour. The crude product was treated with 50 ml. of hot benzene and then filtered; the insoluble portion was I. Yellow crystals separated from the cooled filtrate. After further crystallizations from either benzene or chloroform, the pure monoacetate was obtained in the form of colorless crystals, m.p. 171.5–173.6° cor. It is soluble in dilute sodium hydroxide.

Anal. Calcd. for $C_{22}H_{20}O_4$: C, 75.84; H, 5.78; CH_3CO–, 12.3; mol. wt., 348. Found: C, 75.68; H, 5.75; CH_3CO–, 12.2; mol. wt., 329.[3]

Triacetyl Derivative of I.—A mixture of 1.0 g. of I, 2 ml. of acetic anhydride and a trace of sulfuric acid was heated for 30 minutes at 100°. The crude material was crystallized from 5 ml. of ethanol (1.29 g., 91%). The pure compound, obtained from methanol (1 g. in 3 ml.) or from ethanol (1 g. in 4 ml.) forms colorless crystals which melted at 104.8–105.6° cor.; it is insoluble in dilute alkali.

Anal. Calcd. for $C_{26}H_{24}O_6$: C, 72.21; H, 5.59; mol. wt., 432. Found: C, 71.88; H, 5.76; mol. wt., 410.[3]

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(1) A. Baeyer, *Ann.*, **202**, 87 (1880).
(2) M. H. Hubacher, *Ind. Eng. Chem., Anal. Ed.*, **15**, 448 (1943).
(3) Signer method, as described by E. P. Clark, *ibid.*, **13**, 820 (1941).

The Synthesis of Nitrogen-containing Ketones. II. Ketones Derived from 2-Picoline, Quinaldine and 2,6-Lutidine

BY NEWTON N. GOLDBERG AND ROBERT LEVINE

RECEIVED MAY 21, 1952

In connection with an extensive program which is in progress in this Laboratory on the synthesis of potential chelating agents[1–5] containing heterocyclic nuclei, we have been interested in developing general methods for the synthesis of heterocyclic ketones. To date progress has been made in the thiophene, furan and 2-picoline series.[6–10]

The present report is concerned with further acylations of 2-picoline and the extension of the method recently described[10] to the condensation of quinaldine and 2,6-lutidine with a number of esters. Of the three ketones described in this paper which were obtained by acylating 2-picoline, 2-pyridyl 2-picolyl ketone was previously prepared by Wibaut and de Jong[11] in 13% yield by the interaction of 2-lithiopicolyl with benzonitrile and hydrolyzing the resulting ketimine. Five of the quinaldyl ketones, prepared in our study, have also been synthesized earlier. The methods employed by the earlier workers involved the interaction of the sodium or potassium derivative of quinaldine (prepared from the tar base and either sodium or potassium amide) with the appropriate esters. Thus, the methyl, ethyl and isopropyl ketones were prepared in 17–36% yields by Weiss and Hauser[12]; while the phenyl and 2-furyl ketones have been reported by Bergstrom and Moffat[13] in yields of 60–65% and 28%, respectively. Apparently only one acylated derivative of 2,6-lutidine has been reported. Thus, de Jong and Wibaut[14] have prepared 2-methyl-6-phenacylpyridine in 30% yield by the ketimine synthesis.

The method employed in our syntheses may be summarized by the following general equations where CH_3R represents 2-picoline, quinaldine or 2,6-lutidine.

$$C_6H_5Li + CH_3R \longrightarrow C_6H_6 + RCH_2L$$

$$RCH_2Li + R'CO_2R'' \longrightarrow R''OLi + RCH_2COR'$$

$$RCH_2COR' + RCH_2Li \longrightarrow (RCHCOR')Li \text{ and } R'C(OH)(CH_2R)_2$$

Our results are summarized in Table I. It may be seen that good to high yields of condensation products were obtained in all cases. While the present acylations of 2-picoline and quinaldine gave only ketonic products, the acylation of 2,6-

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(3) J. K. Sneed and R. Levine, *ibid.*, **72**, 5219 (1950).
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(5) L. B. Barkley and R. Levine, *ibid.*, **73**, 4625 (1951).
(6) J. V. Heid and R. Levine, *J. Org. Chem.*, **13**, 409 (1948).
(7) R. Levine, J. V. Heid and M. W. Farrar, THIS JOURNAL, **71** 1207 (1949).
(8) M. W. Farrar and R. Levine, *ibid.*, **72**, 3695 (1950).
(9) M. W. Farrar and R. Levine, *ibid.*, **72**, 4433 (1950).
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(12) M. J. Weiss and C. R. Hauser, THIS JOURNAL, **71**, 2023 (1949).
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(14) A. P. de Jong and J. P. Wibaut, *Rec. trav. chim.*, **70**, 962 (1951).

TABLE I

SYNTHESIS OF PYRIDYL AND QUINOLYL KETONES OF THE TYPE RCH_2COR'

R	R'	Acylating ester methyl	Yield,[a] %	M.p. or b.p., °C. (mm.)	Analyses,[b] % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found	Picrate	M.p.,[c] °C.	Analyses,[b] % Nitrogen Calcd.	Nitrogen Found
2-Pyridyl	2-Pyridyl	Picolinate	55.0[d]	149–150 (1.2)[e] M. 86–87[f]					14.14	14.23	Di	154–155[g,s]	17.07	16.77
2-Pyridyl	3-Pyridyl	Nicotinate	50.3	158.5–160.0 (1.3) M. 69–70[f]					14.14	14.37	Di	187.3–187.8[g,q]	17.07	16.76
2-Pyridyl	4-Pyridyl	Isonicotinate	75.7	M. 114.7–115.2[f]					14.14	14.25	Di	200.5–201.0[g,r]	17.07	17.14
2-Quinolyl	Methyl	Acetate	87.6	145–147 (2.5)[h] M. 76–77[i]							Mono	182–183[g,q]	13.52	13.26
2-Quinolyl	Ethyl	Propionate	94.0	142–143 (1.4)[h]							Mono	181–182[g,h,q]		
2-Quinolyl	Isopropyl	Isobutyrate[j]	89.2	152–154 (2.0)[h]					6.57	6.49	Mono	145–146[g,q]	12.67	12.50
2-Quinolyl	Phenyl	Benzoate	85.5	M. 115–116[h,k]							Mono	172–173[g,q]	11.76	11.79
2-Quinolyl	2-Furyl	2-Furoate	68.6	185–190 (1.2)[k] M. 103.0–103.3[f]					5.91	5.91	Mono	172–173[g,q]	12.01	12.19
2-Quinolyl	2-Thienyl	2-Thenoate	75.5	220–223 (2.2) M. 125.5–126.5[f]					5.53	5.76	Mono	159.5–160.0[g,r]	11.61	11.42
2-Quinolyl	2-Pyridyl	Picolinate	58.4	M. 152.5–154[f]					11.29	11.46	Di	171.5–172.0[g,r]	15.86	15.66
2-Quinolyl	3-Pyridyl	Nicotinate	53.2	M. 121–122[f]					11.29	11.17	Di	215.0–215.5[g,r]	15.86	15.83
2-Quinolyl	4-Pyridyl	Isonicotinate	77.1	M. 147.3–147.8[f]					11.29	11.20	Di	218.5–219.5[g,s]	15.86	15.92
6-Methyl-2-pyridyl	Methyl	Acetate	41.6[l,m]	105–106 (9.9)	72.45	72.43	7.43	7.24	9.39	9.61	Mono	137.7–138.3[r]	14.81	15.08
6-Methyl-2-pyridyl	Ethyl	Propionate	46.0[n]	114–115 (9.5)	73.59	73.43	8.03	7.88	8.58	8.66	Mono	121.5–122.2[r]	14.28	14.19
6-Methyl-2-pyridyl	*n*-Propyl	*n*-Butyrate[j]	55.6[o]	126–127 (10.3)	74.54	74.66	8.53	8.58	7.90	8.14	Mono	124.4–124.9[r]	13.79	13.85
6-Methyl-2-pyridyl	Isopropyl	Isobutyrate[j]	61.9[p]	119.5–120.5 (9.5)	74.54	74.68	8.53	8.67	7.90	8.00	Mono	124.0–124.5[r]	13.79	13.65
6-Methyl-2-pyridyl	Phenyl	Benzoate	94.5	150–151 (1.7) M. 77.3–77.7[f]	79.59	79.65	6.20	6.38	6.63	6.51	Mono	180–181[g,q]	12.72	12.75
6-Methyl-2-pyridyl	2-Furyl	2-Furoate	78.6	136–137 (1.4)	71.62	71.67	5.51	5.46	6.96	6.97	Mono	160.5–161.5[g,q]	13.02	13.11
6-Methyl-2-pyridyl	2-Thienyl	2-Thenoate	82.9	156–157 (1.6)	66.33	66.55	5.10	5.40	6.45	6.28	Mono	173–174[g,q]	12.55	12.57
6-Methyl-2-pyridyl	2-Pyridyl	Picolinate	66.4	156–157 (1.2) M. 48–49					13.20	13.22	Di	218.5–219.5[g,r]	16.71	16.84
6-Methyl-2-pyridyl	3-Pyridyl	Nicotinate	62.3	160–161 (1.2)					13.20	13.06	Di	198.2–198.8[g,r]	16.71	16.91
6-Methyl-2-pyridyl	4-Pyridyl	Isonicotinate	90.5	M. 111.0–111.7[f]					13.20	13.21	Di	200.0–200.5[g,s]	16.71	16.82

[a] All yields based on molar quantity of ester. [b] All analyses were performed by Mr. George Stragand of the Microanalytical Laboratory of the University of Pittsburgh. [c] Recrystallized from 95% ethanol. [d] This ketone and all those derived from 2-picoline give a blue-green color test with alcoholic iron(III) chloride solution. [e] See ref. 11. [f] Recrystallized from 60–70° petroleum ether. [g] Melts with decomposition. [h] See ref. 12. [i] Recrystallized from 60–70° petroleum ether cooled in a Dry Ice–acetone mixture. [j] Ethyl ester. [k] See ref. 13. [l] This ketone and all those derived from 2,6-lutidine give a weak red color test with alcoholic iron(III) chloride solution. [m] There was also obtained 35.3% of methyl bis-(2,6-lutidyl)-carbinol, b.p. 152–153° (1.3 mm.). *Anal.* Calcd. for $C_{16}H_{20}ON_2$: C, 74.96; H, 7.86; N, 10.93. Found: C, 75.11; H, 7.62; N, 11.01. Dipicrate recrystallized from 95% ethanol; m.p. 206.5–207.5° (dec.). *Anal.* Calcd. for $C_{28}H_{26}O_{15}N_8$: N, 15.86. Found: N, 15.42. [n] There was also obtained 31.8% of ethyl bis-(2,6-lutidyl)-carbinol, b.p. 164–165° (1.7 mm.). *Anal.* Calcd. for $C_{17}H_{22}ON_2$: C, 75.52; H, 8.20; N, 10.36. Found: C, 75.54; H, 8.14; N, 10.25. Dipicrate recrystallized from 95% ethanol; m.p. 190–190.7° (dec.). *Anal.* Calcd. for $C_{29}H_{28}O_{15}N_8$: N, 15.38. Found: N, 15.56. [o] There was also obtained 27.3% of *n*-propyl bis-(2,6-lutidyl)-carbinol, b.p. 150–152° (0.9 mm.). *Anal.* Calcd. for $C_{18}H_{24}ON_2$: C, 76.02; H, 8.51; N, 9.85. Found: C, 76.33; H, 8.71; N, 9.59. Dipicrate recrystallized from 95% ethanol; m.p. 185.8–186.6° (dec.). *Anal.* Calcd. for $C_{30}H_{30}O_{15}N_8$: N, 15.09. Found: N, 15.21. [p] There was also obtained 23.8% of isopropyl bis-(2,6-lutidyl)-carbinol, b.p. 154–155° (1.0 mm.). *Anal.* Calcd. for $C_{18}H_{24}ON_2$: C, 76.02; H, 8.51; N, 9.85. Found: C, 76.15; H, 8.58; N, 9.79. Dipicrate recrystallized from 95% ethanol; m.p. 180.8–181.4° (dec.). *Anal.* Calcd. for $C_{30}H_{30}O_{15}N_8$: N, 15.09. Found: N, 15.18. [q] Picrate colored yellow. [r] Picrate colored orange. [s] Picrate colored red.

lutidine with aliphatic esters gave rise to both ketones and carbinols as had been observed earlier[10] when 2-picoline was acylated with aliphatic esters. It should be noted that while those ketones derived from 2-picoline and 2,6-lutidine appeared to give copper salts when treated with copper(II) acetate solution, the salts could not be obtained in crystalline form. Furthermore, the ketones derived from quinaldine did not exhibit a visible reaction when treated similarly.[15]

Experimental

Starting Materials.—The tar bases and the methyl esters were obtained from commercial sources with the exception of the methyl pyridinecarboxylates which were prepared by the method of Levine and Sneed.[16]

Operating Procedure for Conducting Condensations.—The syntheses were carried out by the interaction of the lithium derivatives of the tar bases with the appropriate esters as described earlier.[10]

Acknowledgment.—The authors gratefully acknowledge the support of the U. S. Atomic Energy Commission during the course of the investigation.

(15) The reaction between divalent cations and these ketones is being studied by Dr. W. C. Fernelius and his co-workers at the Pennsylvania State College. Their results will be reported at a later date.

(16) R. Levine and J. K. Sneed, THIS JOURNAL, **73**, 5614 (1951).

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An Agent from *E. Coli* Causing Hemorrhage and Regression of an Experimental Mouse Tumor. II. The Component Monosaccharides[1]

BY MIYOSHI IKAWA, J. B. KOEPFLI, S. G. MUDD AND CARL NIEMANN[2]

RECEIVED MAY 19, 1952

It has been shown previously[3] that the agent, isolated from cultures of *E. coli*, which produces a hemorrhagic response in and causes the regression of the experimental mouse sarcoma 180 is a complex polysaccharide which contains both a peptide and a phospholipide component. An acid hydrolysate of the above polysaccharide was found to possess a reducing power of 52–55 equivalent % glucose and a hexosamine content of 15–17 equivalent % glucosamine.

Ultraviolet absorption spectra of solutions of the experimental mouse tumor hemorrhagic agent in 79% sulfuric acid[4,5] are given in Fig. 1. The lack of any appreciable absorption at 25° is indicative of the absence of ketoses and nucleic acids. The character of the spectrum of the heated solution suggests the probable absence of 6-desoxyaldehexoses (no maximum in the 327 mμ region), aldopentoses (low extinction value at 300 mμ), aldohexuronic acids (low extinction values at 220 and 294 mμ), and mannose (no maximum in the 250 mμ region). Paper chromatography, with phenol and collidine as solvents,[6] of an acid hydrolysate of the hemorrhagic agent gave evidence of the presence of glucosamine and of either or both glucose and galactose. Of the qualitative carbohydrate tests applied directly to the agent, the Scherer test for inositol[7] was negative, the mucic acid test for galactose, or galacturonic acid, positive, and the Morgan–Elson test for apparent N-acetylhexosamine,[8] negative. The phenylhydrazone test for mannose, performed on a hydrolysate of the agent, was negative. The presence of hexosamine has been commented upon previously.[3] By drastic hydrolysis of the hemorrhagic agent D-glucosamine was isolated and identified as the hydrochloride and the N-carbobenzoxy derivative. With milder conditions of hydrolysis D-glucose and D-galactose were isolated and identified as the diethyl mercaptals,[9] the substituted benzimidazoles[10] and the picrates thereof.[10] The properties of the above derivatives are summarized in Table I.

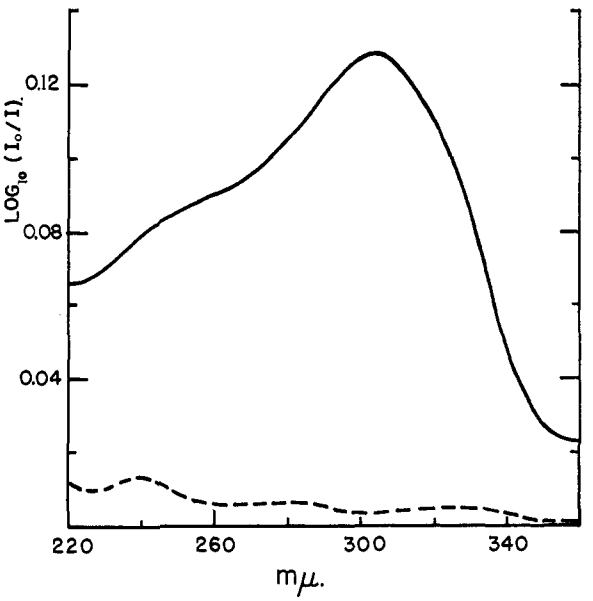

Fig. 1.—Ultraviolet absorption spectra of solutions of the mouse tumor hemorrhagic agent from *E. coli* in 79% sulfuric acid; solid line, after 15 min. at 100°; dotted line, after 2 hours at 25°.

The observation that the component monosaccharides of the experimental mouse tumor hemorrhagic agent from *E. coli* are D-glucosamine, D-glucose and D-galactose serves to differentiate this substance from the corresponding agent obtained from *B. prodigiosus* which was reported to contain hexosamine, a methylpentose, and presumably an aldehexose.[11]

Experimental

Hemorrhagic Agent.—All experiments were conducted on the ethanol-fractionated material designated in our previous communication[3] as fraction B_1.

(1) Supported from 1938 to 1943 by grants from the Argonaut Foundation and from 1948 onwards by grants from the National Cancer Institute of the U. S. Public Health Service.

(2) To whom inquiries regarding this article should be sent.

(3) M. Ikawa, J. B. Koepfli, S. G. Mudd and C. Niemann, *J. Nat. Cancer Inst.*, **13**, 157 (1952).

(4) M. Ikawa and C. Niemann, *J. Biol. Chem.*, **180**, 923 (1949).

(5) M. Ikawa and C. Niemann, *Arch. Biochem. Biophys.*, **31**, 62 (1951).

(6) S. M. Partridge, *Biochem. J.*, **42**, 238 (1948).

(7) J. Scherer, *Ann.*, **81**, 375 (1852).

(8) W. T. J. Morgan and L. A. Elson, *Biochem. J.*, **28**, 988 (1934).

(9) M. L. Wolfrom and J. V. Karabinos, THIS JOURNAL, **67**, 500 (1945).

(10) S. Moore and K. P. Link, *J. Biol. Chem.*, **133**, 297, 303 (1940).

(11) J. L. Hartwell, M. J. Shear, J. R. Adams, Jr., and A. Perrault, *J. Nat. Cancer Inst.*, **4**, 107 (1943).

TABLE I

PROPERTIES OF THE CARBOHYDRATE DERIVATIVES OBTAINED FROM THE MOUSE TUMOR HEMORRHAGIC AGENT FROM *E. coli*.

Sugar	Derivative	Melting point, °C. Obsd.[a]	Lit.	Mixed[b]	$[\alpha]_D$ Obsd.[c]	Lit.
D-Glucosamine	Hydrochloride[d]	.....	.....	.....	+73[e]	+72.5[e]
	N-Carbobenzoxy	213–214[f]	214[f]	214–215[f]		
D-Glucose	Diethylmercaptal	128.5–130	127–128	128–130		
	Benzimidazole	211–212[f]	215[f]	210–211[f]	+10[g]	+ 8.7[h]
	Benzimidazole picrate	203[f]	203[f]			
D-Galactose	Diethylmercaptal	143.5–145	140–142	144–145		
	Benzimidazole	242[f]	245[f]	241[f]	+42[g]	+45.1[h]
	Benzimidazole picrate	214–215[f]	217[f]			
	Mucic acid	217–220[f]	222	218–220[f]		

[a] All melting points are corrected. [b] Mixed melting point with an authentic sample. [c] At 25°. [d] N, calcd. 6.5, found 6.4. [e] Final value in water. [f] With decomposition. [g] In 1.0 *N* hydrochloric acid. [h] In 1.0 *N* hydrochloric acid at 20°, *cf.* N. K. Richtmyer and C. S. Hudson, THIS JOURNAL, 64, 1612 (1942).

Ultraviolet Absorption Spectra in 79% Sulfuric Acid.—One ml. of a solution of fraction B_1 in water (100 γ/ml.) was added to 9 ml. of 84% sulfuric acid as previously described[4,5] and the ultraviolet absorption spectra determined after 2 hours at 25° or 15 min. at 100°.

Paper Chromatography.—A small sample of fraction B_1 was hydrolyzed with 1 *N* sulfuric acid for 1.5 hours, the hydrolysate neutralized with barium hydroxide, the barium sulfate removed, and the clear solution evaporated to dryness *in vacuo*. The residue was redissolved in water and the procedure of Partridge[6] followed.

Isolation of Mucic Acid.—Fraction B_1 (365 mg.) was heated with 5 ml. of nitric acid (sp. gr. 1.15) on a steam-bath until the mixture was transformed into a thick yellow sirup. The sirup was triturated with 0.3 ml. of water, extracted with ether to remove fatty material, and allowed to stand overnight. The solid that had formed was collected, and washed successively with a small amount of water and ethanol. The crude mucic acid so obtained was dissolved in a small amount of dilute sodium hydroxide, the solution filtered, and acidified with dilute nitric acid to give 7.7 mg. of mucic acid, *cf.* Table I.

Isolation of D-Glucosamine Hydrochloride.—A sample of 169 mg. of fraction B_1 was heated, under refluxing conditions, with 25 ml. of 5 *N* hydrochloric acid for 4 hours. The cooled solution was filtered, extracted with chloroform, and concentrated to dryness *in vacuo*. The resulting crystalline solid was washed with ethanol until no further colored substances were extracted. The solid was then dissolved in water, the insoluble material removed, and the solution again evaporated to dryness. The resultant colorless crystalline solid was washed with ethanol and dried to give 20.7 mg. of D-glucosamine hydrochloride, *cf.* Table I.

Isolation of N-Carbobenzoxy-D-glucosamine.—To 1.61 g. of carbohydrate mixture obtained as described in the isolation of the mercaptal derivatives (see below) was added 25 ml. of 5 *N* hydrochloric acid and the solution heated, under refluxing conditions, for 4 hours. The black insoluble material which had formed was removed and the filtrate evaporated *in vacuo* to dryness. A crystalline residue was obtained which was washed with absolute ethanol giving 245 mg. of solid. This material was treated with carbobenzoxy chloride according to Chargaff and Bovarnick[12] to give, after two recrystallizations from 30% aqueous methanol, 98 mg. of N-carbobenzoxy-D-glucosamine, *cf.* Table I.

Isolation of Diethylmercaptal Derivatives.—To a solution of 558 mg. of fraction B_1 in 100 ml. of water was added 3 ml. of concd. sulfuric acid and the solution heated under refluxing conditions for one hour. The hydrolysate was cooled, extracted with chloroform, the aqueous phase neutralized with barium hydroxide, the barium sulfate removed, and the filtrate evaporated to dryness *in vacuo* at 40°. This residue was dissolved in one ml. of concd. hydrochloric acid and mercaptalated with ethyl mercaptan according to Wolfrom and Karabinos.[9] However no crystalline material was obtained until after acetylation and deacetylation.[9] The crystalline material so obtained was fractionally recrystallized from acetone to give the diethylmercaptals of D-glucose and D-galactose, *cf.* Table I.

(12) E. Chargaff and M. Bovarnick, *J. Biol. Chem.*, **118**, 421 (1937).

Isolation of Substituted Benzimidazole Derivatives.—Fraction B_1, 2.2 g., was hydrolyzed as described in the preceding section to give 1.28 g. of a mixture of monosaccharides. This mixture was oxidized with potassium hypoiodite in methanol as directed by Moore and Link[10] to give 0.38 g. of a potassium aldonate fraction and 1.29 g. of a barium aldonate fraction. The former fraction was converted into the corresponding benzimidazoles[10] and, when no crystalline material was obtained directly from the reaction mixture, the benzimidazoles were precipitated and purified as the copper salts.[10] From these latter salts a small amount of D-galactobenzimidazole was obtained. The barium aldonate fraction also gave no crystalline benzimidazoles directly, but after purification through the copper salts and fractional crystallization from water and ethanol there was isolated 32 mg. of the less soluble D-galactobenzimidazole and 38 mg. of the more soluble D-glucobenzimidazole. Upon further recrystallization from water and aqueous ethanol 25 mg. of each of the above products were obtained in a relatively pure state, *cf.* Table I. For further confirmation these latter benzimidazoles were converted into the corresponding picrates, *cf.* Table I.

CONTRIBUTION NO. 1693 FROM THE
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4β-Acetoxy-Δ⁵-cholestene-3β,7α-diol

BY ROBERT W. JAILER,[1] DAVID K. FUKUSHIMA AND SEYMOUR LIEBERMAN[2]

RECEIVED JUNE 5, 1952

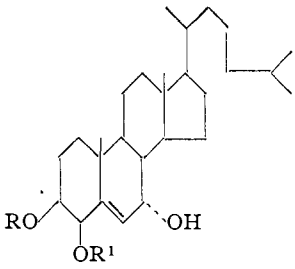
In a recent paper[3] the isolation of Δ⁵-cholestene-3β,4β,7α-triol monoacetate (Ia or Ib) from the reaction of cholesterol acetate and N-bromosuccinimide followed by chromatography was reported. The acetate group was tentatively assigned to C-3 since the starting material was cholesterol acetate. However, it was recognized[3] that acetyl migration during chromatography was possible and the product may have been the isomeric 4β-acetoxy-Δ⁵-cholestene-3β,7α-diol (Ib). Evidence that acetyl migration had indeed occurred is now presented.

It has previously been shown[3] that of the two free hydroxyl groups in I, only that on C-7 is oxidized by chromic acid or N-bromosuccinimide to yield

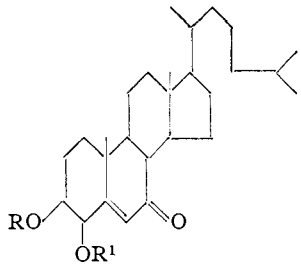
(1) Abstracted from the thesis of R. W. Jailer presented in partial fulfillment for the degree of Master of Science in Chemistry at New York University.

(2) Departments of Biochemistry and of Obstetrics and Gynecology, College of Physicians and Surgeons, Columbia University, New York, N. Y.

(3) S. Lieberman and D. K. Fukushima, THIS JOURNAL, **72**, 5211 (1950).



Ia, R = CH_3CO, R^1 = H
b, R = H, R^1 = CH_3CO



IIa, R = CH_3CO, R^1 = H
b, R = H, R^1 = CH_3CO
c, R = CH_3CO, R^1 = C_6H_5CO
d, R = C_6H_5CO, R^1 = CH_3CO

IIa or IIb. Benzoylation of the unoxidized hydroxyl group in IIa or IIb resulted in the acetoxybenzoxy-unsaturated-7-ketone (IIc or IId). This compound could not be obtained in crystalline form even after purification by chromatography and vacuum sublimation. All attempts at crystallization resulted in a gel which gave an amorphous white powder on drying. Formation of gels in this series of compounds has been found to occur frequently.[4] 3β,4β-Dihydroxy-Δ⁵-cholesten-7-one acetate benzoate thus obtained melted at 194–197°, $[\alpha]^{23}D$ −58.3° (chloroform), $\epsilon_{233m\mu}$ 23,000. In order to prove the structure of this compound, both isomers, IIc and IId were prepared by unequivocal methods.

Chromic acid oxidation of the known 3β-acetoxy-4β-benzoxy-Δ⁵-cholestene[5] yielded 3β-acetoxy-4β-benzoxy-Δ⁵-cholesten-7-one (IIc) which in contrast to the amorphous product described above readily crystallized, m.p. 163–164°, $[\alpha]^{23}D$ −58.1° (chloroform), $\epsilon_{233\ m\mu}$ 24,400. Its m.p., crystalline form and especially its characteristic infrared spectrum in the region of 1185–875 cm.$^{-1}$ [6] definitely established its non-identity with the amorphous ketone obtained from the triol monoacetate I.

Similar oxidation of 3β-benzoxy-4β-acetoxy-Δ⁵-cholestene[5] gave 3β-benzoxy-4β-acetoxy-Δ⁵-cholesten-7-one (IId) which could not be obtained crystalline. The product on drying gave an amorphous powder,[7] m.p. 185–188°, $[\alpha]^{23}D$ −57.1° (chloroform), $\epsilon_{233m\mu}$ 23,000.

These physical constants together with the infrared spectrum (1185–875 cm.$^{-1}$), identical in every respect with that of the product obtained from I, proved that the latter was the 3β-benzoxy-4β-acetoxy derivative (IId). It is evident from these results that the reaction of cholesterol acetate with N-bromosuccinimide followed by chromatography gave rise to the 4-acetoxy derivative Ib rather than Ia as previously formulated.

Experimental[8]

Benzoylation of 7-Keto-Δ⁵-cholestene-3β,4β-diol Monoacetate (IIb).—One hundred and eighty-six mg. of 7-keto-Δ⁵-cholestene-3β,4β-diol monoacetate (IIb) was benzoylated overnight at room temperature with pyridine and benzoyl chloride. The benzoylated product was chromatographed on alumina and the petroleum ether eluates gave 139 mg. of amorphous material. Attempts to crystallize the product from a number of solvents always led to the formation of a gel. Sublimation in a high vacuum yielded a hard glassy material and attempts at crystallization of this product also failed. The acetate-benzoate was finally purified by allowing a concentrated methanol solution to gel, filtering with vacuum and washing the gel with cold methanol. This procedure was repeated three times to give an amorphous powder of IId, m.p. 194–197° with previous sintering at 190°, $[\alpha]^{23}D$ −58.3 ± 1° (chloroform), $\epsilon_{233m\mu}$ 23,000 (ethanol).

Anal. Calcd. for $C_{36}H_{50}O_5$: C, 76.83; H, 8.96. Found: C, 76.10; H, 8.69.

3β-Acetoxy-4β-benzoxy-Δ⁵-cholesten-7-one (IIc).—To 600 mg. of 3β-acetoxy-4β-benzoxy-Δ⁵-cholestene[5] in 12 cc. of glacial acetic acid was added portionwise, a solution of 0.48 g. of chromic oxide, 0.4 cc. of water and 1.8 cc. of glacial acetic acid over a period of 2 hours. The oxidation mixture was maintained at 60° during this time and for an additional 2 hours. The excess chromic oxide was destroyed with ethanol and the solvent removed *in vacuo*. The residue was taken up in ether and washed with dilute hydrochloric acid, sodium carbonate solution and water. The ether solution was dried and the solvent evaporated to give 267 mg. of crystalline product. This material was chromatographed on silica gel and the petroleum ether–ether (4:1) eluates gave 188 mg. of crystalline 3β-acetoxy-4β-benzoxy-Δ⁵-cholesten-7-one (IIc). Recrystallizations from methanol and acetone gave IIc, m.p. 163–164°, $[\alpha]^{23}D$ −58.1 ± 1° (chloroform), $\epsilon_{233\ m\mu}$ 24,400 (ethanol).

Anal. Calcd. for $C_{36}H_{50}O_5$: C, 76.83; H, 8.96. Found: C, 77.09; H, 8.72.

The infrared spectrum in the region 1185–875 cm.$^{-1}$ was different from that of its isomer 3β-benzoxy-4β-acetoxy-Δ⁵-cholesten-7-one (IId) and the product obtained by the benzoylation of 7-keto-Δ⁵-cholestene-3β,4β-diol monoacetate.

3β-Benzoxy-4β-acetoxy-Δ⁵-cholesten-7-one (IId).—A suspension of 190 mg. of 3β-benzoxy-4β-acetoxy-Δ⁵-cholestene[5] in 4 cc. of glacial acetic acid was oxidized in the same manner as above with 1.1 cc. of a solution containing 0.48 mg. of chromic oxide, 0.4 cc. of water and 1.8 cc. of glacial acetic acid. Upon chromatographic separation on silica gel, the petroleum ether–ether eluates gave 87 mg. of amorphous material. All attempts at crystallization were unsuccessful.[7] The oxidation product was purified by allowing a concentrated solution in methanol to gel, filtering with vacuum and washing the amorphous material with cold methanol. This process was repeated three times to give an amorphous powder of 3β-benzoxy-4β-acetoxy-Δ⁵-cholesten-7-one (IId), m.p. 185–188° with previous sintering at 179.5°, $[\alpha]^{23}D$ −57.1 ± 1° (chloroform), $\epsilon_{233m\mu}$ 23,000 (ethanol), Petrow and Starling[4] reported m.p. 217–218°, $[\alpha]D$ −59.4° (chloroform).

Anal. Calcd. for $C_{36}H_{50}O_5$: C, 76.83; H, 8.96. Found: C, 76.85; H, 8.92.

The infrared spectrum in the region 1185–875 cm.$^{-1}$ was identical in every respect to the benzoylation product of 7-keto-Δ⁵-cholestene-3β,4β-diol monoacetate.

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(4) V. A. Petrow and W. W. Starling, *J. Chem. Soc.*, 749 (1946).

(5) V. A. Petrow, O. Rosenheim and W. W. Starling, *ibid.*, 135 (1943).

(6) We wish to express our gratitude to the late Dr. K. Dobriner and to Mrs. P. Humphries for their help in determining and interpreting the infrared spectra.

(7) Petrow and Starling[4] have reported the preparation of this compound in crystalline form, m.p. 217–218°, $[\alpha]D$ −59.4° (chloroform). However, attempts to crystallize IId by their methods were unsuccessful.

(8) All melting points are corrected.

The Heat of Fusion of Lithium

BY SCOTT B. KILNER

RECEIVED MAY 12, 1952

The heat of fusion of lithium has been variously reported as 0.15,[1] 0.23,[2] 0.76[3] and 1.1[4] kcal./gram

(1) J. Sherman, *Chem. Revs.*, **11**, 93 (1932).

(2) A. Thum, Dissertation, Zurich, 1906.

(3) F. R. Bichowsky and F. D. Rossini, "The Thermochemistry of the Chemical Substances," Reinhold Publishing Corp., New York, N. Y., 1936.

(4) K. K. Kelley, U. S. Bur. Mines, Bull., No. 393, 166 p. (1936).

atom. We have determined the heat of fusion calorimetrically and find it to be 0.69 ± 0.07 kcal./gram atom. The value agrees, within the rather large uncertainty of our measurements, with that of Bichowsky and Rossini,[3] which was calculated from the (calorimetric) entropies of fusion of the other alkali metals. Kelley's value[4] of 1.1 kcal./gram atom was calculated from freezing point–composition data for several binary alloys; his calculations for sodium gave values in agreement with those obtained calorimetrically, whereas for potassium the calorimetric value was less than the alloy value by approximately the same factor that we find for lithium. The melting point, which has been reported as 179 and 186°,[3] was found to be 179 ± 1°.

The heat of fusion was calculated from the heat content *vs.* temperature curve of an ampoule of $^3/_4$-in. o.d. stainless steel tubing containing slightly more than 13 g. of lithium. The lithium (99.5%) was handled in an atmosphere of argon, and the ampoule closed by heliarc welding. The heat content of the ampoule was measured by an adaptation of the method of mixtures for temperatures between 164 and 191°. The calorimeter was calibrated with pure copper for the same range of temperatures. Values for the heat capacity of copper were taken from the National Bureau of Standards compilation.[5]

(5) F. D. Rossini, D. D. Wagman, W. H. Evans, E. J. Blau and S. Levine, "Selected Values of Chemical Thermodynamic Properties," U. S. National Bureau of Standards, Washington, D. C., 1947.

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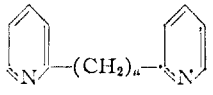
The Synthesis of 2,2′- and 4,4′-Polymethylenebipyridines

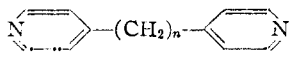
BY L. M. JAMPOLSKY, M. BAUM, S. KAISER, L. H. STERNBACH AND M. W. GOLDBERG

RECEIVED MAY 16, 1952

The present paper describes the preparation of several new 2,2′- and 4,4′-polymethylenebipyridines of the general structures I and II. They were required as intermediates for the synthesis of the corresponding polymethylene-bipyridinium compounds,[1] some of which were found to have interesting curare-like properties.[2]



I



II

Of the compounds of formula I, only the 2,2′-trimethylenebipyridine (I, n = 3) was known. It was obtained by Michael addition of 2-picoline to 2-vinylpyridine.[3] We have now prepared the corresponding pentamethylene (I, n = 5), hexamethylene (I, n = 6), heptamethylene (I, n = 7) and octamethylene (I, n = 8) homologs by treating 2-picolyllithium with the appropriate polymethylene dibromide. All four compounds were high boiling oils and gave crystalline dimethobromides.

The only known member of the 4,4′-polymethylenebipyridine series (II) was the dimethylene compound (II, n = 2). It was obtained by heating 4-picoline with sulfur.[4] We used the same method for its preparation, and synthesized the missing members of this series from the monomethylene to the octamethylene compound by a variety of other reactions. The monomethylene compound (II, n = 1) was made by treating 4-chloropyridine with 4-picolylpotassium in liquid ammonia. The trimethylene compound (II, n = 3) was prepared by condensing 4-picoline with 4-vinylpyridine in the presence of potassium (sodium was unsuitable for this purpose), and the tetramethylene compound (II, n = 4) was obtained by condensing 3-(4-pyridyl)-1-bromopropane with 4-picolylpotassium in liquid ammonia. We also attempted to prepare the tetramethylene compound by reacting ethylene dibromide with 4-picolylpotassium in liquid ammonia. However, the only product obtained in this case was the known 4,4′-dimethylenebipyridine (25% yield). The unexpected course of this reaction can best be explained by assuming a simultaneous formation of ethylene from the ethylene dibromide. Similar, but not completely analogous reactions are known, for example, the formation of bromobenzene, ethylene and lithium bromide from phenyllithium and ethylene dibromide.[5]

The 4,4′-pentamethylenebipyridine (II, n = 5) and the corresponding hexamethylene (II, n = 6), heptamethylene (II, n = 7) and octamethylene (II, n = 8) compounds were all prepared by reacting 4-picolylpotassium in liquid ammonia with the appropriate polymethylene dibromide. The lower members of the 4,4′-polymethylenebipyridine series crystallize readily. The hexamethylene compound was isolated in form of its crystalline dimethobromide and the hepta- and octamethylene homologs in form of their crystalline dihydrobromides.

Experimental[6]

2,2′-Polymethylenebipyridines.—The compounds of this series were prepared by treating 2-picolyllithium in ether with the appropriate polymethylene dibromide. The 2,2′-pentamethylenebipyridine was obtained in 40% yield using trimethylene dibromide, the 2,2′-hexamethylenebipyridine in 62% yield using tetramethylene dibromide, the 2,2′-heptamethylenebipyridine in 46% yield using pentamethylene dibromide, and the 2,2′-octamethylenebipyridine in 41% yield using hexamethylene dibromide. All data on these new compounds and their derivatives are summarized in Table I. The reaction conditions were identical in all cases, and we describe, therefore, in detail only the preparation of the **2,2′-hexamethylenebipyridine**: To a stirred solution of phenyllithium, prepared from 31 g. (4.4 g. atoms) of lithium and 345 g. (2.2 moles) of bromobenzene in 1 liter of absolute ether, was added 186 g. (2 moles) of dry 2-picoline. This was followed by the dropwise addition of 152 g. (0.7 mole) of tetramethylene dibromide. The reaction mixture was refluxed for 2 hours. Ice and about 275 ml. of concentrated hydrochloric acid were then added and the aqueous phase separated. It was made strongly alkaline by the addition of 50% potassium hydroxide solution and extracted with ether. The ether extract was concentrated and the residue fractionated in high vacuum. The main fraction, b.p. 160–165° (0.5 mm.), gave a crystalline **dimethobromide**

(1) To be reported in subsequent papers.

(2) See L. O. Randall, *Ann. N. Y. Acad. Sci.*, **54**, 460 (1951), and *J. Pharmacol. Exptl. Therap.*, **105**, 7 (1952).

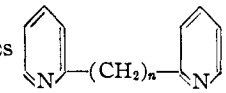
(3) N. J. Leonard and J. H. Boyer, THIS JOURNAL, **72**, 4818 (1950).

(4) H. I. Thayer and B. B. Corson, *ibid.*, **70**, 2330 (1948).

(5) G. Wittig and G. Harborth, *Ber.*, **77**, 306 (1944).

(6) All melting points are corrected.

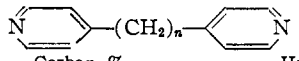
TABLE I

2,2′-POLYMETHYLENEBIPYRIDINES AND DERIVATIVES 

n	Type[a]	M.p., °C.	B.p. °C.	Mm.	$n^{t}D$	t, °C.	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
5	B		153–154	1	1.5478	25	$C_{15}H_{18}N_2$	79.60	79.49	8.02	7.85
5	MB	199–203					$C_{17}H_{24}N_2Br_2$	49.05	49.34	5.81	5.37
6	B		160–165	0.5	1.5408	25	$C_{16}H_{20}N_2$	79.95	80.12	8.39	8.24
6	MB	225–228					$C_{18}H_{26}N_2Br_2$	50.25	49.62	6.09	5.68
7	B		166–168	.8	1.5379	24	$C_{17}H_{22}N_2$	80.27	80.41	8.72	8.51
7	MB[b]	202–204					$C_{19}H_{28}N_2Br_2.{}^1/_2H_2O$	50.34	50.16	6.45	6.30
8	B		177	.6	1.5339	26	$C_{18}H_{24}N_2$	80.55	79.99	9.01	9.10
8	MB[c]	200–201					$C_{20}H_{30}N_2Br_2.H_2O$	50.43	50.65	6.77	6.37

[a] B, base; MB, di-(methyl bromide). [b] Hemihydrate. [c] Monohydrate.

TABLE II

4,4′-POLYMETHYLENEBIPYRIDINES AND DERIVATIVES 

n	Type[a]	M.p., °C.	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
1	B	138–140	$C_{11}H_{10}N_2$	77.62	77.74	5.91	5.86
2	MB	285–292[b]	$C_{14}H_{18}N_2Br_2$	44.94	45.24	4.85	4.95
2	PB	251–253[b]	$C_{18}H_{28}N_2Br_2$	50.25	50.18	6.09	5.78
2	BB[c]	198–200[b]	$C_{20}H_{30}N_2Br_2.{}^1/_2H_2O$	51.41	51.32	6.67	6.65
2	NB	271–280[b]	$C_{26}H_{24}O_4N_4Br_2$	50.66	50.45	3.92	4.02
3	B	57–60	$C_{13}H_{14}N_2$	78.75	78.95	7.12	7.01
3	MB	212–221[b]	$C_{15}H_{20}N_2Br_2$	46.41	46.33	5.19	5.11
4	B	111–115	$C_{14}H_{16}N_2$	79.21	79.37	7.60	7.76
4	NB	218–227[b]	$C_{28}H_{28}O_4N_4Br_2$	52.19	52.07	4.38	4.54
5	B	56–58	$C_{15}H_{18}N_2$	79.60	79.52	8.02	8.20
6	MB[d]	206–209[b]	$C_{18}H_{26}N_2Br_2\cdot H_2O$	48.23	48.62	6.29	6.13
7	HB	209–211[b]	$C_{17}H_{22}N_2\cdot 2HBr$	49.05	48.87	5.81	5.83
8	HB	284–290[b]	$C_{18}H_{24}N_2\cdot 2HBr$	50.26	50.60	6.09	6.30

[a] B, base; HB, dihydrobromide; MB, di-(methyl bromide); PB, di-(propyl bromide); BB, di-(butyl bromide); NB, bis-(*p*-nitrobenzyl bromide). [b] With decomposition. [c] Hemihydrate. [d] Monohydrate.

when treated with an excess of methyl bromide in acetone. It was recrystallized from methanol–acetone; m.p. 225–228°.

4,4′-Polymethylenebipyridines.—All data on the new compounds of this series are summarized in Table II. The preparation was carried out as follows:

4,4′-Methylenebipyridine.—To one liter of liquid ammonia containing 8.5 g. of potassium amide was added, with stirring at −80°, 14 g. of 4-picoline. After the mixture had stirred for 15 minutes at −80°, an ether solution containing 12.3 g. of 4-chloropyridine was added and the stirring continued at the same temperature for three additional hours. A small amount of ammonium chloride was then added and the ammonia allowed to evaporate. The residue so obtained was dissolved in water and extracted with benzene. The benzene was evaporated *in vacuo* at 100° and the residue crystallized from acetone–ether. The recrystallized material melted at 138–140°. The yield was 35%.

4,4′-Trimethylenebipyridine.—Eighty-four grams of 4-vinylpyridine and 372 g. of dry 4-picoline were added to 80 ml. of benzene containing 20 mg. of hydroquinone. While stirring, 1 g. of potassium was added and the temperature raised to 105°. After 45 minutes, the reaction mixture was cooled, the potassium destroyed with ethanol and the benzene solution extracted with water and with a saturated aqueous sodium bisulfite solution. The benzene solution was then dried and evaporated *in vacuo*. The oily residue was crystallized from acetone. The recrystallized material melted at 57–60°. The yield was 44%.

4,4′-Tetramethylenebipyridine.—Seventy-two grams of 3-(4-pyridyl)-1-methoxypropane[7] was refluxed with 700 ml. of 48% hydrobromic acid for four hours and the reaction mixture evaporated to dryness *in vacuo*. The residue, consisting of a mass of hygroscopic needles of 3-(4-pyridyl)-1-bromopropane hydrobromide, was directly converted into the unstable free base by dissolving it in ice-water, adding solid potassium carbonate and extracting with ether. The ether solution was dried, and an aliquot equivalent to 40 g. of 3-(4-pyridyl)-1-bromopropane hydrobromide was cooled to about −80°. This was slowly added to a stirred liquid ammonia suspension of 4-picolylpotassium, prepared by the addition of 20 g. of 4-picoline to 2 liters of liquid ammonia containing 12 g. of potassium amide. The reaction mixture was stirred for about three hours at about −30° and then the ammonia was allowed to evaporate. The residue so obtained was dissolved in water and extracted with ether. The crystalline residue obtained by evaporation of the dried ether extract was recrystallized from methanol and from acetone. The pure product melted at 111–115°. The yield was 20%.

4,4′-Pentamethylenebipyridine.—To 2 liters of liquid ammonia containing about 28 g. of potassium amide (prepared in this and all other experiments by dissolving potassium metal in liquid ammonia in the presence of an iron catalyst) was added, with stirring at −80°, 47 g. of 4-picoline. After the mixture had stirred for 10 minutes at this temperature, a solution of 51 g. of trimethylene dibromide in 250 ml. of ether was slowly added.[8] The reaction mixture was stirred for 3 additional hours at −80°, and then 10 g. of ammonium chloride was added. The ammonia was allowed to evaporate, the residue was taken up in water and extracted with ether. The dried ether extract was evaporated to dryness, and the crystalline residue so obtained was recrystallized from benzene–petroleum ether; m.p. 56–58°. The yield was 64%.

4,4′-Hexa-, Hepta- and Octamethylenebipyridine.—These three compounds were made from 4-picolinepotassium and the appropriate polymethylene dibromide using the procedure for the pentamethylene homolog. Tetramethylene dibromide gave a 65% yield of 4,4′-hexamethylenebipyridine, pentamethylene dibromide a 36% yield of the heptamethylene homolog, and hexamethylene dibromide a 15%

(7) T. R. Norton, R. A. Seibert, A. A. Benson and F. W. Bergstrom, THIS JOURNAL, **68**, 1572 (1946).

(8) The reaction can become violent if the trimethylene dibromide is added too quickly.

yield of the octamethylene compound. The hydrobromides of the two last mentioned compounds were prepared from the crude reaction products and recrystallized from aqueous acetone.

The bis-pyridinium compounds listed in Table II were prepared by heating a mixture of the polymethylenebipyridine with the appropriate alkyl or aralkyl bromide in acetone or benzene. They were recrystallized from methanol–acetone.

Acknowledgment.—We wish to express our thanks to Dr. Al Steyermark and his staff for the microanalyses.

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The Preparation of Nickel(II) Thiocyanate Complex Compounds with Picolines and the Determination of their Heats of Formation[1]

BY ALBERT V. LOGAN AND DON W. CARLE[2]

RECEIVED MAY 26, 1952

Work reported in an earlier paper[3] discussed the effect of negative groups upon the heat of formation of nickel(II) and cobalt(II) pyridinated compounds. We have now prepared a series of complexes in which the same metal salt has been combined with methyl substituted pyridines in an effort to determine the effect of the character of the base upon the heat of formation of the complexes. The heats of reaction of the simple salt, the amine and the complex with 2 *N* HCl were determined and the heat of formation of the complex calculated according to the equation

$$\Delta H_f = L_s + L_a - L_c$$

Preparation of Compounds

Nickel(II) Di-2-methylpyridine Thiocyanate.—17.48 g. (0.1 mole) of nickel thiocyanate was added to 300 ml. of α-picoline (b.p. 128.4–130°). The mixture was maintained at 125 to 130° for four hours under a reflux condenser. The salt changed to a red color immediately on contact with the hot α-picoline. The salt was completely dissolved after four hours heating producing a green solution. The solution was transferred to a large evaporating dish and low heating continued until a viscous mass was obtained. Rapid cooling produced a solid. The solid was pulverized and excess base removed in an air stream while the solid was continually stirred. The product, a brick red solid, was passed through a 60-mesh screen, air-dried for one-half hour. The compound may be kept indefinitely in a sealed container but will decompose almost quantitatively if left in the air overnight. The nickel content of this compound and others described later was determined by silver cyanide titration. *Anal.* Calcd. for $Ni(SCN)_2 \cdot 2C_6H_7N$: Ni, 16.25. Found: Ni, 16.07.

Nickel(II) Tetra-3-methylpyridine Thiocyanate.—The β-picoline available was the practical grade. Purification was effected by the method of Riethof.[4] The fraction distilling at 143–144° was collected for use in preparation of the complex compounds: 18.3 g. (0.077 mole) of $NiCl_2 \cdot 6H_2O$ was dissolved in 2 l. of H_2O, 33 ml. of β-picoline was added, a deep blue solution was formed. A solution of 15 g. (0.1544 mole) of KSCN in 200 ml. of H_2O was added slowly with constant stirring. A light blue microcrystalline precipitate formed immediately. The precipitate was obtained as a hard cake by use of a suction filter. The cake was pulverized and dried in air for four hours, then passed through a 60-mesh screen and placed in a desiccator over solid KOH for 2 days. The yield was nearly quantitative. The compound is stable in air for several days; at elevated temperatures it is readily converted to $Ni(SCN)_2$ and β-picoline. *Anal.* Calcd. for $Ni(SCN)_2 \cdot 4C_6H_7N$: Ni, 10.73. Found: Ni, 10.73.

Nickel(II) Tetra-4-methylpyridine Thiocyanate.—This compound was prepared in a manner identical to that described for the β-picoline complex. The color and characteristics of the compound are the same. *Anal.* Calcd. for $Ni(SCN)_2 \cdot 4C_6H_7N$: Ni, 10.73. Found: Ni, 10.77.

Attempts were made to prepare the above compounds by chloroform extraction as had been previously employed in the preparation of a number of pyridinated compounds. The compounds obtained by this method indicated some entrapment of chloroform in the crystals of the complex. The slow evaporation of a chloroform solution, obtained by the extraction of an aqueous suspension of the β-picoline compound, produced large blue transparent crystals. These crystals contained 8.7% nickel. Each preparation by this method produced the same product. Test for water in the crystals was negative. To check for the presence of chloroform, a pure sample of $Ni(SCN)_2 \cdot 4BC_6H_7N$ prepared by precipitation from water, was dissolved in chloroform and the solution was evaporated. The large blue crystals obtained were crushed, then dried in air for an hour. Analysis showed 7.60% nickel. No attempt was made at the time to investigate the subject further since we were interested in the compound containing 4 molecules of the amine.

Determination of Heats of Reaction.—The method and the calorimeter employed in determining the heats of reaction of the $Ni(SCN)_2$, the bases and the complexes with 2 *N* HCl were similar to those employed by Logan, Bush and Rogers in this Laboratory.[3] The values obtained and the heats of formation calculated from them are recorded in Table I.

Results and Discussion

TABLE I

Substance	Heat of solution cal./mole at 25°[a]	Heat of formation cal./mole at 25°
β-Picoline	−9200 (±50)	
γ-Picoline	−9450 (±90)	
Pyridine[b]	−7860 (±25)	
$Ni(CNS)_2$	1140 (±10)	
$Ni(CNS)_2 \cdot 4\beta$-Pic	2340 (±60)	−36,000
$Ni(CNS)_2 \cdot 4\gamma$-Pic	1450 (±40)	−38,110
$Ni(CNS)_2 \cdot 4Py$[b]	7860 (±100)	−38,300

[a] Averages obtained from 3 to 5 determinations on each compound. [b] Reported in an earlier article (ref. 3).

The heats of formation of cobalt(II) (37,700 cal./mole) and nickel(II) (38,300 cal./mole) tetrapyridine thiocyanates and the cobalt(II) (22,300 cal./mole) and nickel(II) (18,500 cal./mole) hexapiperidine cyanates reported earlier, indicate that the negative groups play a more important role in the heat of formation of the complex compounds than do the metals. The fact that a stable tetra-α-picoline could not be obtained limited this study of the effect of bases on the heat of formation to the β- and γ-picolines. It is assumed that the proximity of the methyl group to the nitrogen atom in the amine prevented the formation of the tetra-α-picoline compound.

The relative basic strengths of pyridine, β-picoline and γ-picoline are evidenced by their heats of reaction with 2 *N* HCl recorded in Table I. By comparing the values calculated for the heats of formation of the complexes produced by the reaction of nickel thiocyanate with the three bases, Table I, it may be concluded that the heat of form-

(1) Published with the approval of the Monograph Publishing Committee, Oregon State College, as Research Paper No. 206, School of Science, Department of Chemistry.

(2) This article is based on a thesis submitted by Don W. Carle in partial fulfillment of the requirements for the degree of Master of Science at Oregon State College, June, 1952.

(3) A. V. Logan, O. C. Bush and C. S. Rogers, THIS JOURNAL, **74**, 4194 (1952).

(4) G. Riethof, S. G. Richards, S. A. Savitt and D. F. Othmer, *Ind. Eng. Chem., Anal. Ed.*, **18**, 458 (1946).

ation of the nickel thiocyanate complex is practically independent of the amine used in its formation.

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Tetramethyldisiloxane-1,3-diol

BY GLENNARD R. LUCAS AND ROBERT W. MARTIN

RECEIVED FEBRUARY 29, 1952

A number of diorganosilane diols and tetraorganodisiloxane-1,3-diols have been prepared where one or more of the organic groups are larger than methyl.[1-4] However silane diols containing only methyl groups are very susceptible to condensation and have not been reported. We have now found that tetramethyldisiloxane-1,3-diol (I), the dimer of dimethylsilanediol, can be obtained in 60% yield by adding dimethyldichlorosilane to excess cold water maintained near neutrality by simultaneously adding ammonia. The compound is a snow-white crystalline solid, m.p. 67–68°, which may be stored, when pure, at room temperature without decomposition. The compound dissolves in water, but crystallizes from a cold aqueous solution upon the addition of salt.

The structure of the compound was shown by elemental analysis and determination of molecular weight and active hydrogens. On heating alone or in an inert solvent a mole of water is eliminated per mole of disiloxanediol with the formation of dimethylpolysiloxanes. Refluxing the compound with *n*-butanol and an acidic catalyst resulted in rapid dehydration and slow alcoholysis to form dimethyldibutoxysilane.

Experimental

Preparation of Tetramethyldisiloxane-1,3-diol.—Fifteen liters of water was placed in a flask equipped with a high speed stirrer and surrounded by an alcohol–Dry Ice cooling bath. Brom thymol blue and phenolphthalein indicators were added and the water was cooled to 2°. Ten moles of dimethyldichlorosilane was slowly added from a dropping funnel with rapid stirring. The dimethyldichlorosilane hydrolyzed almost instantly and the hydrogen chloride generated was neutralized with gaseous ammonia bled in from a cylinder through a glass tube which dips well below the surface of the water. The addition of the chlorosilane and ammonia was adjusted so that color of solution was in the blue range, *p*H 6.5–8.5. The addition of the silane required 48 minutes during which time the reaction temperature was kept at 0 to 2° and bath temperature at −30 to −40°. Five thousand grams of salt was added, and the reaction mixture was allowed to stand 24 hours at 10°. The crystalline mass which separated was filtered and taken up in two liters of boiling hexane. Upon cooling the hexane solution to 10° 494 g. of tetramethyldisiloxane-1,3-diol separated as snow-white needles. A sample for analysis was recrystallized from hexane, m.p. 67–68°.

Anal. Calcd. for $C_4H_{14}O_3Si_2$: C, 28.91; H, 8.49; Si, 33.78; mol. wt., 166.27; hydroxyl, 20.4. Found: C, 28.9, 29.2; H, 8.3, 8.5; Si, 33.61 (average of 12 determinations); mol. wt., 176 (in phenol), 171 (in camphor), 170 (in dioxane); hydroxyl (Zerewitinoff), 20.2.

Condensation of (I).—Refluxing of 16.6 g., 0.10 mole, of (I) in 100 ml. of dry benzene containing 1 g. of *p*-toluenesulfonic acid in a flask equipped with a Birdwell–Sterling water trap resulted in the formation in 20 minutes of a maximum 1.8 ml. of water. This is the theoretical amount required for complete dehydration to form dimethylpolysiloxanes.

Alcoholysis of (I).—Fifty-hour refluxing of 16.6 g., 0.10 mole, of (I) in a dry solution of 0.5 g. of *p*-toluenesulfonic acid in 100 ml. of *n*-butanol and 25 ml. of benzene resulted in the separation of 4.8 ml. of water of which 1.8 ml., 0.10 mole, separated in the first few minutes. No water was formed by refluxing the reactants in the absence of (I). Independent experiments showed that the rapid elimination of 0.1 mole of water was largely due to self-condensation of (I) and that the slow elimination of water that followed was due to the alcoholysis of the condensation products. Complete alcoholysis of 0.1 mole of (I) to dimethyldibutoxysilane would yield 5.4 ml. of water as compared to 4.8 ml. obtained. A larger run, in which the reaction mixture was neutralized and distilled, resulted in the isolation of dimethyldibutoxysilane (b.p. 190–200°; Si found 13.7 and 13.4, theory 13.73) together with a probable mixture of the latter with 1,3-dibutoxytetramethyldisiloxane,[5] b.p. 200–216°; Si found 17.7 and 17.6, theory 20.15.

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(5) R. O. Sauer, THIS JOURNAL, **68**, 138 (1946).

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X-Ray Studies of Rare Earth Oxide Systems. II. The Oxide Systems Ce^{IV}–Sm^{III}, Ce^{IV}–Gd^{III}, Ce^{IV}–Y^{III}, Pr^{IV}–Y^{III} and Pr^{III}–Y^{III}

BY J. D. MCCULLOUGH AND J. D. BRITTON

RECEIVED MAY 19, 1952

Solid solutions of the trivalent rare earth oxides La_2O_3, Ce_2O_3, Pr_2O_3, Nd_2O_3 and Sm_2O_3 in the tetravalent rare earth oxides CeO_2 and PrO_2 have been studied by a number of investigators.[1-10] Although the separate studies have involved the use of X-ray powder photographs, density determinations and measurement of electric conductivities, complete studies of all of these systems have not as yet been reported. All of the systems studied show a homogeneous region with the fluorite structure from the pure tetravalent oxide to about 60 atom per cent. of the trivalent oxide. The deficiency of oxygen caused by substitution of M^{III} for M^{IV} in the fluorite structure leads to random vacancies in the anion lattice. This contention is supported by the relative intensities of the X-ray diffraction lines[1,9] and by the correlation of density measurements with the lattice constants.[1,7]

The present communication reports an extension of the X-ray studies to some trivalent rare earth ions of smaller radius. Yttrium has been included because of its great similarity to the rare earth elements of higher atomic number and because of its

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(2) U. Croatto, *Ricerca Sci.*, **12**, 830 (1942).

(3) U. Croatto and A. Mayer, *Gazz. chim. ital.*, **73**, 199 (1943).

(4) U. Croatto, *ibid.*, **73**, 257 (1943).

(5) U. Croatto, *ibid.*, **74**, 20 (1944).

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TABLE I

LATTICE CONSTANTS FOR AIR-IGNITED SOLID SOLUTIONS OF TRIVALENT RARE EARTH OXIDES IN CERIC OXIDE

Values in parentheses are one-half the true lattice constants for the "C" form

Ce^{IV}-Sm^{III}		Ce^{IV}-Gd^{III}		Ce^{IV}-Y^{III}	
Atomic % Sm	Lattice constant, Å.	Atomic % Gd	Lattice constant, Å.	Atomic % Y	Lattice constant, Å.
0	5.411 ± 0.001	0	5.411 ± 0.001	0	5.411 ± 0.001
10.0	5.423 ± .001	9.92	5.415 ± .002	9.99	5.411 ± .002
20.0	5.433 ± .002	23.1	5.423 ± .003	25.0	5.405 ± .002
34.9	5.441 ± .002	42.8	5.432 ± .003	39.9	5.395 ± .002
49.9	5.453 ± .002	67.0	(5.428 ± .003)	60.0	(5.374 ± .003)
64.8	5.462 ± .003	83.1	(5.420 ± .003)	75.0	(5.355 ± .003)
80.0	(5.466 ± .001)			90.0	(5.324 ± .002)
90.0	(5.466 ± .002)				
100	(5.461)[a]	100	(5.407 ± .002)	100	(5.304 ± .001)

[a] Value given by Iandelli,[13] corrected to true ångstrom units and divided by 2.

use in the studies of the oxidation of praseodymium carried out by Prandtl and Rieder[11] and by Marsh.[12]

Experimental

Materials.—The starting materials used were $(NH_4)_2Ce(NO_3)_6$ (99.99%), Pr_6O_{11} (99.8%), Sm_2O_3 (99%), Gd_2O_3 (98%) and Y_2O_3 (99%). The cerium compound was a product of the G. F. Smith Chemical Co., Columbus, Ohio, and the oxides were products of the Research Chemicals Inc., Burbank, California.

Procedure.—Stock solutions of the rare earths were prepared by dissolving weighed samples of the starting materials and diluting to the desired volume. The cerium compound was dissolved in water. The oxides were ignited 2–3 hours at 850–900° before weighing and dissolved in nitric acid. Except as noted later, the general procedure was the same as that described in the earlier work.[9]

Hydrogen Reduction.—Reduction of the praseodymium–yttrium solid solutions was accomplished by heating the samples for 4 hours at 800° in a stream of pure, dry hydrogen gas. Although this treatment converts pure Pr_2O_3 to the "A" hexagonal form, the presence of only 5% Y_2O_3 stabilizes the "C" cubic form. The preparation of pure Pr_2O_3 in the "C" form may be accomplished by reducing Pr_6O_{11} in a platinum boat in a quartz tube. The heating should be done cautiously with a bunsen flame just long enough to complete the reduction which is indicated by the strong yellow color of the "C" form. Heating for too long a period or to too high a temperature causes transition to the gray-green "A" form.[13]

Air Ignition.—After decomposing the precipitated hydroxides at lower temperatures, all samples were ignited in air for approximately 5 hours at 1100–1200°. Small nickel boats were found to be satisfactory containers for the samples in the high-temperature furnace.

Oxidation of Praseodymium.—A simpler and more reliable method for the oxidation of Pr^{III} to Pr^{IV} was developed. This makes use of a heavy-wall pure silver tube ($^1/_4$" o.d., $^1/_8$" i.d. by 8" long) closed at one end and silver soldered into a standard fitting at the other. Several samples contained in small quartz tubes may be oxidized at the same time The system is first flushed free of air by alternate evacuation and admission of oxygen from a cylinder and finally subjected to the full pressure of the cylinder at approximately 2000 p.s.i. (135 atmospheres). The silver tube is then heated to 650° for 4 hours. The tube may be quenched, or cooled slowly, as desired. The oxygen pressure should not be released, however, until the tube has cooled since otherwise PrO_2 might decompose. The newer method has the advantage of being faster, of permitting the oxidation of several samples at once and of oxidizing Pr_2O_3 when in the "A" form. The latter caused some trouble in the method previously employed.

X-Ray Diffraction.—Powder diffraction photographs of all samples were prepared after grinding in an agate mortar. Filtered copper radiation was used in a Norelco Powder Camera having a nominal radius of 5.73 cm. All lattice constants were determined by extrapolation of measurements in the back-reflection region, referred to the wave lengths CuK_{α_1} = 1.5405 Å. and CuK_{α_2} = 1.5443 Å.

(11) W. Prandtl and G. Rieder, *Z. anorg. Chem.*, **238**, 225 (1938).
(12) J. K. Marsh, *J. Chem. Soc.*, 5 (1946).
(13) Aldo Iandelli, *Gazz. chim. ital.*, **77**, 312 (1947).

Results and Discussion

The experimental results are given in Tables I and II. In order to simplify comparison of results, the lattice constants for all solid solutions in the "C" form have been divided by two in order to put them on the same scale as the fluorite phase lattice constants. Values resulting from this treatment are in general shown in parentheses in the tables but the dividing line between the fluorite and "C" forms is quite arbitrary.

TABLE II

LATTICE CONSTANTS FOR SOLID SOLUTIONS IN THE PRASEODYMIUM OXIDE–YTTRIUM OXIDE SYSTEMS

Values in parentheses are one-half the true lattice constants for the "C" form

Atomic % Y	Reduced in hydrogen Pr^{III}-Y^{III}	Ignited in air Pr^{IV}-Pr^{III}-Y^{III}	Heated in oxygen Pr^{IV}-Y^{III}
0	(5.570 ± 0.002)	5.468 ± 0.001	5.394 ± 0.002
5.0	(5.561 ± .003)	5.463 ± .002	
10.0	(5.545 ± .015)	5.465 ± .010	
14.9			5.398 ± .003
19.9	(5.527 ± .006)	5.448 ± .006	
30.0			5.398 ± .004
35.0	(5.480 ± .001)	5.423 ± .005	
50.0	(5.437 ± .004)	(5.395 ± .002)	(5.385 ± .005)
65.0	(5.397 ± .003)	(5.367 ± .002)	
70.0			(5.355 ± .005)
80.0	(5.358 ± .005)	(5.344 ± .003)	
85.1			(5.330 ± .003)
87.5	(5.355 ± .002)	(5.344 ± .002)	
90.0	(5.329 ± .001)	(5.327 ± .001)	
100	(5.304 ± .001)	(5.304 ± .001)	(5.304 ± .001)

One of the interesting features of the present study is the gradual and continuous change from the face-centered cubic fluorite structure shown by pure CeO_2 and PrO_2 to the "C" type body-centered cubic structure shown by the trivalent rare earth oxides. This is shown best in the systems Ce^{IV}–Y^{III} and Pr^{IV}–Y^{III}. On the diffraction photographs of samples in these systems, lines characteristic of the "C" structure appear when as little as 15 atomic per cent. of yttrium is present and gradually increase in relative intensity with increasing yttrium content. This effect is shown with decreasing tendency in going to the systems Ce^{IV}–Gd^{III} and Ce^{IV}–Sm^{III} and was not in evidence in the systems Ce^{IV}–Nd^{III} and Ce^{IV}–Pr^{III}. This indicates that ordering of the vacant anion sites re-

quired by the "C" structure is favored by the trivalent ions of smaller radius. The continuous transition from the fluorite structure to the "C" type M_2O_3 structure is possible because of the close similarities of the two structures.[14]

Although the previous studies indicated rather definite upper solubility limits of around 60–70 atomic per cent. of the trivalent oxides in the tetravalent oxides, only the Ce^{IV}–Gd^{III} system shows an indication of a limit in the present work. Due to tendencies toward supersaturation in this case, however, it is possible to explore the entire range of solid solutions and it is difficult to determine just where the solubility limit is.

Another point of interest is the inability of praseodymium to be oxidized beyond the tetravalent state in the Pr–Y system. This is worth noting because it was their work on this system which Prandtl and Rieder[11] offered as proof of the ability of praseodymium to be oxidized to Pr^V. This claim was later refuted by Marsh[12] and by one of the present authors.[9] The rigorous oxidizing conditions used in the present work leave little doubt about the extreme reluctance of praseodymium to be oxidized beyond the tetravalent state. It was Prandtl and Rieder's belief that the presence of Y_2O_3 should promote the oxidation of praseodymium to the pentavalent state by forming the compound $YPrO_4$. However, the present study indicated a definite increase in the difficulty of oxidizing praseodymium with increasing yttrium content.

(14) L. Pauling and M. D. Shappell, *Z. Krist.*, **75**, 138 (1930).

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1,3,5,7,9-Decapentaene and 1,3,5,7,9,11,13-tetradecaheptaene

BY ALEXANDER D. MEBANE

RECEIVED APRIL 21, 1952

In the series of unsubstituted linear polyenes, $H(CH{=}CH)_nH$, the first four members are known. By application of the sodamide–liquid ammonia coupling of allylic halides[1] to pentadienyl and heptatrienyl halides, what are undoubtedly the $n = 5$ and $n = 7$ members of the series have now been prepared. Decapentaene was obtained in 5% yield as cream-colored crystals melting at *ca.* 145°; tetradecaheptaene, in minute yield, only as an impure concentrate.

The ultraviolet absorption spectra (Fig. 1) continue the series defined by those of butadiene, hexatriene[2] and octatetraene.[3] The absorption maxima of the five compounds fall on a smooth curve.[4] The "fine structure" shows a consistent increase as the series is ascended, until in decapentaene and tetradecaheptaene the longest wave length absorption peak has become the most intense one, and the spectrum is clearly approaching, as a limit, a series of equally-spaced discrete absorption "lines" of diminishing intensity. It may be recalled that the absorption spectra of the α,ω-diphenylpolyenes undergo a similar evolution as the series is ascended.[5] The separation between the individual absorption peaks, which in both series ranges from about 1350 to 1550 cm.$^{-1}$, is customarily identified with the stretching frequency of the double bond.

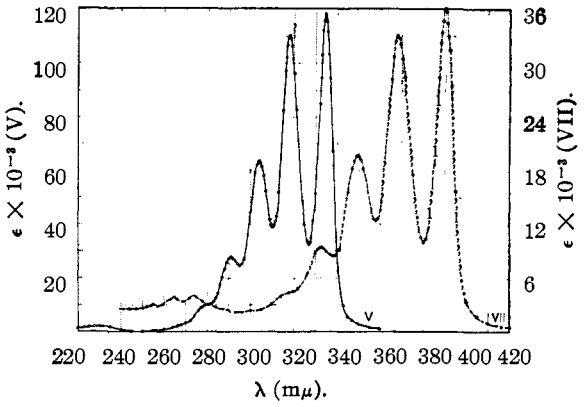

Fig. 1.—Ultraviolet absorption spectra, in "isoöctane," of: V, crystalline all-*trans*-decapentaene; VII, tetradecaheptaene concentrate.

The infrared spectrum of decapentaene (Fig. 2) closely resembles those of hexatriene[2] and octatetraene,[3] except in the extreme lowness of the 7.1-μ peak and the differing appearance of the 6.1–6.6-μ system.[6] The entire absence of the infrared *cis*-peak (14.0 ± 0.5 μ) shows that the all-*trans* stereoisomer was the one isolated in crystalline form. This conclusion was confirmed by the results of catalytic iodine treatment.

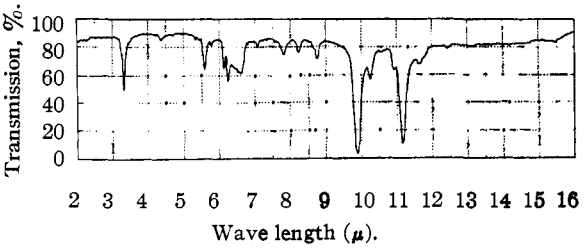

Fig. 2.—Infrared spectrum of all-*trans*-decapentaene (1.7% solutions, 0.2-mm. cell).

In the chromatographic forerun of decapentaene, a *cis*-isomer or isomers (not obtained in solid condition) appeared to be present.

The tetradecaheptaene was obviously not sterically homogeneous, since the absorption maxima at the beginning and end of the chromatographic fraction differed by more than 2 mμ. However, the highest λ_{max} obtained probably corresponds

(1) M. S. Kharasch and E. Sternfeld, THIS JOURNAL, **61**, 2318 (1939); M. S. Kharasch, W. Nudenberg and E. K. Fields, *ibid.*, **66**, 1276 (1944); D. R. Howton, *J. Org. Chem.*, **14**, 1 (1949).

(2) G. F. Woods and L. H. Schwartzman, THIS JOURNAL, **70**, 3394 (1948); D. R. Howton, ref. 1.

(3) G. F. Woods and L. H. Schwartzman, *ibid.*, **71**, 1396 (1949).

(4) Empirical equations for this curve will be discussed in a subsequent communication.

(5) K. W. Hausser, R. Kuhn and A. Smakula, *Z. physik. Chem.*, **29B**, 384 (1935). In this series the first peak is just reaching equality with the second by $n = 7$, the highest member studied. (The $n = 8$, $n = 11$ and $n = 15$ members of the series have been reported by Kuhn and his co-workers, but their absorption curves have apparently not been published.)

(6) Since the solutions measured had been in transit at ordinary temperatures for about 24 hours, it is probable that some polymer was present at the time the spectrum was taken.

to the all-*trans* isomer, since iodine equilibration gave an intermediate spectrum.

Neither compound gives any appreciable color with antimony trichloride in chloroform; it appears therefore that the Carr–Price reaction requires the participation of alkyl substituents.

Experimental

2,4-Pentadien-1-ol.—Vinylacrylic acid[7] (50 g.) was reduced with 18.7 g. of lithium aluminum hydride. The reaction and work-up were carried out as described below for methyl heptatrienoate, except that the temperature of reduction was −25°. The dried ethereal extracts were fractionated through a 20-cm. vacuum-jacketed Vigreux column. The fraction coming over at 70–72.5° (31 mm.) weighed 14.9 g. (35% yield), $n^{22}D$ 1.4808, λ_{max} 223.7 mμ (alc.), ε 23,700.[8] This pentadienol was impure, analyzing 1.4% low in carbon; but the impurity (possibly water) was removed in the next step.

5-Chloro-1,3-pentadiene.—Crude pentadienol (12.6 g., 0.15 mole) was shaken for a few minutes with 100 ml. of cold, concentrated hydrochloric acid, and the mixture was extracted with petroleum ether. The extract was washed with hydrochloric acid, dried over anhydrous magnesium sulfate, and fractionated as above, in the presence of a little hydroquinone. The only significant fraction (6.1 g., 40% yield) came over at 65–67° (130 mm.), $n^{24}D$ 1.4923[9]; d^{24} 0.946, λ_{max} 226.5 mμ (isoöctane), ε 25,300; sharp odor.

Anal. Calcd. for C_5H_7Cl: C, 58.54; H, 6.88; Cl, 34.57; MR_D, 27.9. Found: C, 58.74; H, 6.87; Cl, 34.18; MR_D, 31.5.

1,3,5,7,9-Decapentaene.—Sodamide (2.0 g., 0.05 mole) was added portionwise, over a 10-minute period, to 5.1 g. (0.05 mole) of chloropentadiene dissolved in 10 ml. of ether and 50 ml. of liquid ammonia. After a further 10 minutes, 20 ml. of hexane was added, and the ammonia was evaporated by gentle warming. The reaction mixture was drowned in ice-water, and the ether–hexane extract (50 ml.) dried over anhydrous potassium carbonate and poured onto an adsorption column (4 × 30 cm.) of Alcoa F-20 activated alumina. Development with 10% ether–hexane gave a single zone, white-fluorescent under a G.E. Purple-X bulb, which was eluted with increasing proportions (finally 40%) of ether in hexane. The eluate containing the first eighth of the zone was rejected; the remainder (400 ml.) was concentrated from lukewarm water under partial vacuum in the presence of a trace of hydroquinone, finally admitting nitrogen. The concentrate (oil and pale-yellowish plates) was washed by decantation with a few ml. of cold petroleum ether, again evacuated, and then taken up in 80 ml. of lukewarm 95% ethanol containing a little hydroquinone, and filtered. After 18 hours at −5° under nitrogen, the precipitated crystals (minute flat needles, of irregular form, cream-colored in mass) were filtered off with cold-alcohol rinses and vacuum-dried, finally admitting nitrogen; yield 160 mg. (4.8%). The rather spicy-sweet, allylic odor was strong and persistent.

Anal. Calcd. for $C_{10}H_{12}$: C, 90.85; H, 9.15. Found: C, 90.69; H, 9.19.

The m.p. could not be determined in the usual way, because of rapid polymerization when warmed. When a crystal was slipped under the cover-glass of a preheated Fisher–Johns block, the lowest temperature at which fusion was observed before polymerization supervened was 145 ± 2°.

Antimony trichloride in chloroform gave no color. (In contrast, decatetraene gives a raspberry-red.[10])

The absorption spectrum in 2,2,4-trimethylpentane ("isoöctane") exhibited maxima at 230, 280 (infl.), 290.8, 303.9, 318.0 and 334.3 mμ; $\epsilon_{max}^{334.3}$ 118,000 (Fig. 1). In 95% ethanol, the spectrum was identical in shape, with λ_{max} 335.3 mμ.

The infrared spectrum was determined by Samuel P. Sadtler & Son, Inc., of Philadelphia. A 1.7% solution in carbon tetrachloride was used from 2 to 7.5 μ, a 1.7% solution in carbon disulfide from 7.5 to 16 μ. Since these solutions spent about 24 hours in transit before examination, the curves obtained are probably not entirely representative of the freshly-made solutions.

The isoöctane spectroscopic solution, after five days at room temperature under nitrogen, showed practically no alteration in the ultraviolet absorption curve. Iodine, 15% by weight of the decapentaene, was then added. Eighty minutes later, all of the four main $\lambda\lambda_{max}$ had decreased by 0.3–0.4 mμ, $\epsilon_{max}^{334.0}$ had dropped to 106,000 (although $\epsilon^{290.4}$ remained unchanged), and the *cis*-peak, now at 235 mμ, had nearly tripled in height. These changes are similar to those observed when all-*trans*-phytofluene (a substituted pentaene) is stereo-equilibrated with iodine.[11]

The first eluates from the chromatogram showed (in addition to a major proportion of diene, λ_{max} 226) a three-peaked absorption curve of much less conspicuous fine structure, $\lambda\lambda_{max}$ 303.3–*316.8*–332.6 mμ (isoöctane), the long wave length peak being the lowest of the triplet. An excess of iodine (barely-visible pink tint) was added to this solution. Twenty minutes later, all of the $\lambda\lambda_{max}$ had increased by 0.6–1.0 mμ, and the shape of the spectrum much more nearly resembled that of all-*trans*-decapentaene, the longest wave length peak (now at 333.6 mμ) having risen strikingly while the third peak dropped. Evidently a *cis* form of decapentaene had been present initially.

Decapentaene was also obtainable by sodamide coupling of *bromo*pentadiene.[12] The spectrum of the product was the same as that obtained from the chloride, and the yield was of the same order.

As would be expected, decapentaene is a delicate substance, very prone to polymerize during handling, although it can be kept for long periods at −40° under nitrogen. On prolonged exposure to air, it forms peroxides that puff vigorously on the hot block.

2,4,6-Heptatrien-1-ol.—Methyl 2,4,6-heptatrienoate[13] (50.9 g., 0.365 mole) in 150 ml. of dry ether was added dropwise during one-half hour to a stirred suspension of 10.3 g. (0.27 mole, 50% excess) of commercial lithium aluminum hydride in 200 ml. of dry ether, maintaining the temperature at −45° with a Dry Ice-bath. After a further half-hour stirring, during which the temperature was permitted to reach 10°, the mixture was treated at 0–10° with 20 ml. of ethyl acetate followed by 150 ml. of 20% sulfuric acid. The aqueous phase was separated, diluted with water, and twice ether-extracted; the combined ethereal extracts were bicarbonate-washed, dried over magnesium sulfate, and rapidly distilled at 0.005 mm. through a 30-cm. Vigreux column. Two arbitrary fractions were collected: bulk, 43–"58°" (superheated), $n^{23}D$ 1.5540, m.p. 11–14°, 33.1 g.; tails: "50"–43°, $n^{23}D$ 1.5576, m.p. 14–16°, 1.4 g. Both

(7) E. P. Kohler and F. R. Butler, THIS JOURNAL, **48**, 1041 (1926); H. Burton and C. K. Ingold, *J. Chem. Soc.*, 2028 (1929). In this preparation, it proved to be best to isolate the crude product by a very rapid vacuum distillation (b.p. 82° at 4 mm.); a single crystallization from 1.7 parts of hexane then furnished large, transparent prisms of m.p. 71–73°, in 25% yield.

(8) L. Crombie, S. H. Harper and D. Thompson, *ibid.*, 2906 (1951), obtained by this reaction an 18% yield of pentadienol of $n^{20}D$ 1.4838. By substituting pentadienal for pentadienoic acid as starting material, they obtained a 77% yield of pure *trans*-pentadienol, $n^{20}D$ 1.4890, in good agreement with $n^{26}D$ 1.4857 by Meerwein-Ponndorf reduction of pentadienal (G. F. Woods and H. F. Lederle, THIS JOURNAL, **73**, 2245 (1951)) and $n^{18}D$ 1.4902 by rearrangement of divinylcarbinol (E. R. H. Jones, J. T. McCombie and B. C. L. Weedon, *J. Chem. Soc.*, 84 (1945)). The latter authors found λ_{max} 223 mμ (alc.), ε 25,000; Crombie *et al.* report λ_{max} 226 mμ, ε 25,200.

(9) G. F. Woods and H. F. Lederle (ref. 8) found $n^{25}D$ ranging from 1.4696 to 1.4919 for material of correct boiling point and analysis prepared by means of thionyl chloride. Although this was obtained from *trans*-pentadienol, it appears to have been a *cis-trans* mixture. For material obtained, in 92% yield, by means of phosphorus trichloride, Crombie *et al.* (ref. 8) found "$n^{20}D$ 1.492–1.493," only slightly lower than the $n^{20}D$ 1.494 of the present product, which should be the nearly-pure *trans*-isomer.

(10) R. Kuhn, *Angew. Chem.*, **50**, 705 (1937).

(11) F. J. Petracek and L. Zechmeister, THIS JOURNAL, **74**, 184 (1952).

(12) This was obtained (in only 3% yield) by Ziegler bromination of piperylene: b.p. 65–68° (58 mm.), $n^{24}D$ 1.5308, lachrymatory. *Anal.* Calcd. for C_5H_7Br: Br, 54.36. Found: Br, 52.7.

(13) G. H. Kalb and J. C. Sauer, U. S. Patent 2,540,736 (to E. I. du Pont de Nemours & Co.), 1951. Dr. Kalb very kindly furnished us with a generous sample of this compound, which has λ_{max} 285.5 mμ in *n*-heptane, ε 28,400. Its lithium aluminum hydride reduction had previously been carried out in the du Pont laboratories (personal communication from Dr. Kalb; T. L. Cairns, *et al.*, Abstracts of Papers, 120th Meeting of the A.C.S., 1951, p. 14-M).

fractions were pale greenish-yellow and had a sweet, oily, alcoholic odor; total yield 85.5%.

Anal. Calcd. for $C_7H_{10}O$: C, 76.30; H, 9.15. Found (main fraction): C, 76.40; H, 9.27.

The absorption spectrum of the purer "tail" fraction consisted of a sharp triplet system: $\lambda\lambda_{max}$ 252, 261.2, 271.7 mμ in 95% ethanol, ϵ_{max} 26,500, 34,300, 25,800. No diene was present. The bulk fraction gave a curve of identical shape, but lower ϵ_{max} (30,600).

This preparation was probably sterically heterogeneous (variation in ϵ) and in any case was not the pure *trans-trans* isomer, for which a melting point of 79–80° has been reported.[14]

1-Bromo-2,4,6-heptatriene.—With stirring and cooling, 3.9 ml. (0.041 mole) of phosphorus tribromide was dropped into a mixture of 11 g. (0.1 mole) of heptatrienol with 2.7 ml. (0.035 mole) of dry pyridine. The viscous mixture, intermittently stirred, was kept in a −10° bath for 30 min., at room temperature for 30 min., and in a 45° bath for 15 min.; then poured into 30 ml. of ice and water and thrice extracted with ether–petroleum ether. (Considerable tar remained undissolved.) The water-washed extract, dried over magnesium sulfate, was distilled through a 15-cm. center-rod column, giving a single fraction, b.p. 48–49° (0.8 mm.), $n^{25}D$ 1.5983, d^{25} 1.295, m.p. 2–6.2°. The light-yellow, fragrant, rather lachrymatory liquid weighed 8.2 g. (51% yield). Stored at −70° under nitrogen, it remained unchanged for nearly a year.

Anal. Calcd. for C_7H_9Br: C, 48.58; H, 5.24; Br, 46.18; MR_D, 39.0. Found: C, 49.04; H, 5.19; Br, 46.15, 45.75; MR_D, 45.7.

The absorption spectrum consisted of a smooth peak entirely devoid of fine structure; λ_{max} 272 mμ (isoöctane), ϵ 31,200.

The steric configuration of this bromide would be expected to be the same as that of the starting material, or approximately so.

1,3,5,7,9,11,13-Tetradecaheptaene.—When bromoheptatriene was coupled with sodamide as previously described, the expected heptaene peaks appeared, but only a minute trace of the compound was formed. A better yield (though still well below 1%) was obtained by quickly adding the bromide (2.2 g., in 10 ml. of ether) to a liquid ammonia solution of slightly less than one equivalent of potassamide, prepared *in situ* from potassium. A transient dark-violet color was observed. The final orange extract, in 50% methylene dichloride–hexane, was dried, filtered, and immediately chromatographed on a 3 × 25-cm. alumina column, precooled to 5°, developing with the same solvent. The main, red-fluorescent zone required 750 ml. of solvent for substantially complete elution. It was sterically inhomogeneous, the first λ_{max} (isoöctane) ranging from 388.1 mμ early in the fraction to 390.4 mμ at its end. This eluate was considerably richer in a triene, λ_{max} 264 mμ, than in the desired heptaene. The first two-thirds (A) and the final third (B) were separately vacuum-concentrated to dryness with a trace of hydroquinone; nitrogen was admitted, and 10 ml. of 10% ether–alcohol was added to dissolve the non-heptaene constituents. After 12 hours at −40°, filtration with cold alcohol rinses gave 7.5 mg. (vacuum-dry weight) of minute golden-yellow flakes from (A) and 2 mg. from (B). The material from (B) was dissolved in a little ether (not all was soluble) and diluted with isoöctane. The resulting absorption spectrum (Fig. 1) showed an ϵ_{max} of only 36,000; the compound was therefore still very impure. The 255-265-275 triplet system in this spectrum is no doubt attributable in large measure to persisting triene contamination rather than to the true *cis*-peak.

In isoöctane, the absorption peaks appeared at 332.3, 349.7, 367.9 and 390.0 mμ. In 95% ethanol, the long wave length peak occurred at 391.4 mμ; the shape was identical.

The solid from fraction (A) gave a curve of substantially identical shape, though much higher at 265 mμ, with the $\lambda\lambda_{max}$ occurring at 331.1, 348.4, 366.4 and 388.5 mμ (isooctane). A catalytic amount of iodine was added, and the solution was illuminated with a 100-watt bulb. After 80 minutes, all of the $\lambda\lambda_{max}$ had increased by 1.0 mμ; and although the height of the main absorption peaks had scarcely altered, that of the 265-mμ peak had decreased by 50%. These changes indicate the presence of a *cis* isomer (or isomers) in fraction (A).

Tetradecaheptaene had no detectable odor. The Carr–Price reagent gave a faint greenish-blue, which was stronger in the specimens richer in the triene contaminant. (Tetradecahexaene gives an indigo-blue.[10])

Apparatus.—The spectrophotometer used was a Beckman model DU, whose wave length scale, above 250 mμ, had been calibrated to the nearest 0.05 mμ against a mercury lamp.

Acknowledgment.—For the analyses, I am indebted to Mr. Joseph Grodsky of this Laboratory.

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(14) I. N. Nazarov and L. B. Fisher, *Zhur. Obshchei Khim.*, **20**, 1107 (1950) [*C. A.*, **44**, 9460 (1950)]. These authors prepared heptatrienol by an allylic rearrangement, which by analogy with pentadienol (I. M. Heilbron, *et al.*, reference 8) would undoubtedly furnish a *trans-trans* product.

Diaryloxyalkane Derivatives. Some Miscellaneous Diphenoxypropanes[1]

BY FREEMAN H. MCMILLAN[2]

RECEIVED MAY 15, 1952

As part of a program leading to the preparation of some moderately high molecular weight compounds several new derivatives of 1,3-diphenoxypropane have been prepared.

It has been found that by substituting ethylene glycol for ethanol as the solvent for the reaction between trimethylene bromide and the potassium salt of a phenol and heating to 130° the time required for the reaction is materially shortened. For example, potassium *p*-nitrophenoxide was condensed with trimethylene bromide in ethylene glycol at 130° for one hour giving a 61% yield of *p,p'*-dinitro-1,3-diphenoxypropane[3] whereas the same reaction in refluxing ethanol for three hours gave only a 22% yield. An additional advantage of this procedure is that even the more difficultly soluble potassium salts, *e.g.*, potassium *p*-nitrophenoxide, are more soluble in this solvent than in ethanol. Either the anhydrous potassium salt of the phenol may be used or the theoretical amount of 85% potassium hydroxide may be dissolved in the ethylene glycol with the phenol and the trimethylene bromide.

p,p'-Dinitro-1,3-diphenoxypropane was reduced with Raney nickel in quantitative yield to the corresponding diamine. This in turn was converted to the N,N'-dibenzyl derivative by reduction with Raney nickel in the presence of benzaldehyde. The intermediate Schiff base was also isolated and characterized. Treatment of *p,p'*-diamino-1,3-diphenoxypropane with hydrogen chloride and phosgene in refluxing toluene gave 1,3-diphenoxypropane *p,p'*-diisocyanate.

Two carboxylic acid derivatives of 1,3-diphenoxypropane were prepared. Ethyl *p*-hydroxybenzoate was condensed with trimethylene bromide in a solution of potassium hydroxide in ethylene glycol. The resulting diester was hydrolyzed to 1,3-diphenoxypropane-*p,p'*-dicarboxylic acid

(1) For previous papers *cf.* J. A. King, THIS JOURNAL, **66**, 2076 (1944), and J. A. King and F. H. McMillan, *ibid.*, **67**, 336 (1945).

(2) Warner Institute for Therapeutic Research, 113 West 18th Street, New York 11, N. Y.

(3) J. A. Goodson, *et al.*, *Brit. J. Pharmacol.*, **8**, 62 (1948), report m.p. 132°.

with aqueous sodium hydroxide. *m*-Hydroxyacetophenone similarly gave *m,m'*-diacetyl-1,3-diphenoxypropane which underwent the Willgerodt reaction with sulfur and morpholine[4] giving 1,3-diphenoxypropane-*m,m'*-diacetic acid.

Experimental[5,6]

***p,p'*-Dinitro-1,3-diphenoxypropane.**—A mixture of potassium *p*-nitrophenoxide (35.4 g., 0.20 mole), trimethylene bromide (20.2 g., 0.10 mole) and ethylene glycol (60 ml.) was stirred and heated at 130° for one hour. The cooled mixture was poured into cold water (600 ml.) giving 19.5 g. (61%) of product melting at 122–125°; after two crystallizations from ethanol it melted at 129.5–130.5°.

***p,p'*-Diamino-1,3-diphenoxypropane.**—When the above dinitro compound (120 g., 0.375 mole), dissolved in ethyl acetate (1 liter), was shaken with Raney nickel and hydrogen at 60° and 500 p.s.i., the theoretical amount of hydrogen was taken up in two hours. The residue, after removal of catalyst and solvent, weighed 97 g. (100%) and melted at 102–105°. An analytical sample, after two crystallizations from Skellysolve C, melted at 104.5–105.5°.

Anal. Calcd. for $C_{15}H_{18}N_2O_2$: N, 10.93. Found: N, 10.89 (by titration with acetous perchloric acid).

***p,p'*-Dibenzalamino-1,3-diphenoxypropane.**—*p,p'*-Diamino-1,3-diphenoxypropane (12.9 g., 0.05 mole) and benzaldehyde (10.6 g., 0.10 mole) were mixed and heated until a uniform melt was obtained (internal temperature about 130°). The cooled mixture was crystallized from ethanol giving 17.5 g. (80%) of product melting at 120–125°. An analytical sample, after two more crystallizations from ethanol, melted at 125–126.5°.

Anal. Calcd. for $C_{29}H_{26}N_2O_2$: N, 6.45. Found: N, 6.40 (Kjeldahl).

***p,p'*-Dibenzylamino-1,3-diphenoxypropane.**—The above dibenzal compound was hydrogenated over Raney nickel in ethyl acetate at 60°. After one crystallization from ethanol the diamine was obtained in 70% yield melting at 88–89°. An analytical sample, after an additional crystallization from ethanol, melted at 88.5–89.5°.

Anal. Calcd. for $C_{29}H_{30}N_2O_2$: N, 6.38. Found: N, 6.25 (by acetous perchloric acid titration).

This compound was also obtained in 82% yield melting at 83–87° by direct hydrogenation of a solution of *p,p'*-diamino-1,3-diphenoxypropane and benzaldehyde in ethyl acetate.

1,3-Diphenoxypropane *p,p'*-Diisocyanate.—*p,p'*-Diamino-1,3-diphenoxypropane (25.0 g., 0.10 mole) was suspended in dry toluene (100 ml.). This mixture was heated to reflux with stirring and then saturated with hydrogen chloride. Phosgene was then bubbled into the mixture with continued refluxing and stirring for three hours at which time there was no further evidence of clearing of the mixture. The hot mixture was filtered through Filter-cel and the toluene was removed from the filtrate by distillation *in vacuo*. The residue on cooling crystallized; it weighed 21.7 g. (70%) and melted at 100–105°. An analytical sample, after crystallization from Skellysolve C, melted at 103–105°.

Anal. Calcd. for $C_{17}H_{14}N_2O_4$: N, 9.03. Found: N, 8.71 (micro-Dumas).

***p,p'*-Dicarbethoxy-1,3-diphenoxypropane.**—A mixture of ethyl *p*-hydroxybenzoate (83 g., 0.50 mole), trimethylene bromide (50.5 g., 0.25 mole) and 85% potassium hydroxide (33 g., 0.50 mole) was heated at 130° with stirring for three hours. The cooled mixture was poured into water (1500 ml.) giving a solid which after crystallization from ethanol (500 ml.) weighed 58 g. (63%) and melted at 93–100°. An analytical sample, after two more crystallizations from ethanol, melted at 102–105°.

Anal. Calcd. for $C_{21}H_{24}O_6$: C, 67.74; H, 6.45. Found: C, 67.70; H, 6.39.

1,3-Diphenoxypropane-*p,p'*-dicarboxylic Acid.—The above diester (7.4 g., 0.02 mole) was refluxed with 20% sodium hydroxide solution (175 ml.) for three hours. Chilling gave 6.5 g. (90%) of the disodium salt of 1,3-diphenoxypropane-*p,p'*-dicarboxylic acid. This solid was boiled with ethanol (250 ml.) to remove any unhydrolyzed ester, then taken up in water (30 ml.) and reprecipitated by pouring into ethanol (250 ml.). The product weighed 5.9 g. (82%).

Anal. Calcd. for $C_{17}H_{14}O_6Na_2$: Na, 12.78. Found: Na, 12.90.

This disodium salt was taken up in water (50 ml.) and the solution was acidified by slow addition of dilute hydrochloric acid. The 1,3-diphenoxypropane-*p,p'*-dicarboxylic acid which separated weighed 4.9 g. (77% based on ester used) and melted at 305–309°. The compound is extremely insoluble in water and no suitable recrystallization solvent could be found.

Anal. Calcd. for $C_{17}H_{16}O_6$: neut. equiv., 158. Found: neut. equiv., 163.

***m,m'*-Diacetyl-1,3-diphenoxypropane.**—A mixture of *m*-hydroxyacetophenone (272 g., 2.0 mole), trimethylene bromide (202 g., 1.0 mole) and 85% potassium hydroxide (132 g., 2.0 mole) in ethanol (1.0 liter) was refluxed with stirring for 14 hours. The solid which formed when the cooled mixture was poured into water was so fine it filtered with great difficulty; consequently it was filtered with the aid of Filter-Cel from which it was subsequently removed by extraction with chloroform. The residue, after removal of the chloroform by distillatin *in vacuo*, rapidly crystallized, weighed 221 g. (71%) and melted at 71–80°. An analytical sample, after two crystallizations from ethanol, melted at 91–93°.

Anal. Calcd. for $C_{19}H_{20}O_4$: C, 73.00; H, 6.41. Found: C, 72.97; H, 6.66.

1,3-Diphenoxypropane-*m,m'*-diacetic Acid.—A mixture of *m,m'*-diacetyl-1,3-diphenoxypropane (15.6 g., 0.05 mole), sulfur (8.0 g., 0.25 mole) and morpholine (17.4 g., 0.20 mole) was heated at reflux for one hour. The reaction mixture was taken up in chloroform (250 ml.) and the chloroform solution was washed with dilute hydrochloric acid. The chloroform was removed under vacuum and the residue was hydrolyzed by refluxing with 50% (by weight) sulfuric acid (200 ml.). The crude diacid was removed from the cooled hydrolysis mixture by filtration and after crystallization from water (4 l.) it weighed 4.8 g. (28%) and melted at 168–170°. An analytical sample, after crystallization from methanol, melted at 171–172.5°.

Anal. Calcd. for $C_{19}H_{20}O_6$: C, 66.28; H, 5.81. Found: C, 66.15; H, 5.72.

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(4) E. Schwenk and E. Bloch, THIS JOURNAL, **64**, 3051 (1942); J. A. King and F. H. McMillan, *ibid.*, **68**, 2335 (1946).

(5) Melting points are uncorrected.

(6) Analyses were performed in the analytical laboratories of this Institute under the direction of Mr. Morris E. Auerbach.

Condensations of Cinchoninaldehyde. V.[1] With Phenylacetonitriles

BY ARTHUR P. PHILLIPS

RECEIVED JUNE 11, 1952

Cinchoninaldehyde reacted rapidly with a variety of substituted phenylacetonitriles to produce the α-(substituted phenyl)-β-(4-quinolyl)-acrylonitriles (see Table I).

When an alcohol solution of the reactants was treated with alkali the mixture turned first yellow, then orange, and finally deep red and the colorless product separated, all within less than a minute. The intense color changes may be associated with anionic intermediates.

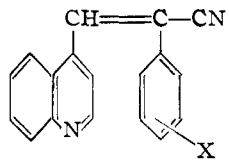
The condensation of the *p*-nitrophenylacetonitrile, expected to be more reactive because of activation by the *p*-nitro, gave a poor yield of IV (Table I) in the usual procedure with alkali catalyst. When a more weakly basic catalyst, such as diethylamine or piperidine, was used the reaction gave good yields of IV. Apparently with the more reactive nitrile the stronger base catalyst is detrimental.

In the condensation with *o*-methoxyphenyl-

(1) Paper IV, THIS JOURNAL, **70**, 452 (1948).

TABLE I

CONDENSATION PRODUCTS FROM CINCHONINALDEHYDE AND PHENYLACETONITRILES



Compound number	X	M.p., °C.[a]	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
I	H	134–135	$C_{18}H_{12}N_2$	84.4	84.4	4.7	4.7
II	4-CH_3	168–169	$C_{19}H_{14}N_2$	84.4	84.5	5.2	5.3
III	4-Cl	165–166	$C_{18}H_{11}ClN_2$	74.3	74.4	3.8	4.0
IV	4-NO_2[b]	199–200	$C_{18}H_{11}N_3O_2$	71.7	71.9	3.7	3.9
V	2-CH_3O[c]	149–150	$C_{19}H_{14}N_2O$	79.7	80.0	4.9	4.9
VI	4-CH_3O	180–181	$C_{19}H_{14}N_2O$	79.7	79.7	4.9	4.9
VII	4-C_2H_5O	155–156	$C_{20}H_{16}N_2O$	80.0	80.0	5.4	5.4
VIII	3-CH_3O-4-C_2H_5O	160–161	$C_{21}H_{18}N_2O_2$	76.3	76.3	5.5	5.7
IX	H[d]	184–185	$C_{18}H_{14}N_2O$	78.8	78.7	5.2	5.2

[a] All melting points are uncorrected. [b] Several variations of the usual conditions were used in this case: (1) the reaction mixture was left 24 hours at 25° (1 cc. of KOH) and gave 20% of IV; (2) the reaction mixture was heated 2 hours at 100° (5 drops of Et_2NH) and gave 60% of IV; (3) the reaction mixture was left 24 hours at 25° (5 drops of piperidine) and gave 95% of IV. [c] No color developed here. The mixture was heated 3 hours at 100° and a second 1 cc. of 20% aqueous KOH was added. The final yield was 70%. [d] This compound is the aldol related to I. The usual reaction mixture, using 5 drops of Et_2NH as the catalyst, was heated 2 hours at 100°; yield of IX was 60%.

acetonitrile to give V (Table I), no color appeared in the solution and the reaction seemed to go more slowly. Both of these deviations might possibly be relatable to the increased steric hindrance of the *o*-methoxy superimposed on the already partially hindered cinchoninaldehyde.

When the condensation with phenylacetonitrile, itself, was carried out as usual but using diethylamine as the catalyst, the unsaturated product I (Table I) was not obtained. Instead the corresponding intermediate aldol IX (Table I) was isolated in good yield. In the case of phenylacetonitrile, which is of lesser reactivity or acidity than its *p*-nitro derivative, the more weakly basic catalyst appears to be inadequate to accomplish the dehydration of the intermediate aldol. The aldol, IX, was also obtained when a dilute suspension of the reactants in water was treated with a little diethylamine.

Experimental

Condensation of Cinchoninaldehyde with Phenylacetonitriles.—In the usual conditions a solution of 0.01 *M* of cinchoninaldehyde and 0.01 *M* of the phenylacetonitrile in 30 cc. of 95% alcohol was treated with 1 cc. of 20% aqueous potassium hydroxide. The reaction mixture underwent several rapid color changes, from yellow to orange to deep red, and in some cases a little heat was evolved. The product precipitated out, usually in less than a minute, as white or pale yellow crystals.

The products were purified by recrystallization from alcohol or from mixtures of benzene with Skellysolve B. Yields ordinarily were 80% or greater. Details for all compounds appear in Table I.

Acknowledgment.—The author is grateful to Mr. S. W. Blackman who supplied the microanalyses.

THE WELLCOME RESEARCH LABORATORIES
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Transformations of Organic Nitrogen Base Iodide and Bromide Salts to Chlorides

BY ARTHUR P. PHILLIPS AND RICHARD BALTZLY

RECEIVED JUNE 25, 1952

In many preparative reactions organic bases are first obtained as iodide or bromide salts, due to the common use of alkyl iodides and bromides which are more available and more reactive toward nucleophilic reagents than the corresponding chlorides. For certain purposes, such as for drugs which are to be taken internally in moderate quantities and in various catalytic hydrogenation procedures, the chlorides are preferred to avoid toxic properties associated with iodides or bromides. When conversion to chlorides is desired this is frequently accomplished by liberation and separation of the base, with subsequent addition of hydrogen chloride. Iodides can also be converted to chlorides by short warming with silver chloride in aqueous or, as found in these laboratories, methanol solution. This latter method is less suitable for conversion of bromides to chlorides, and the former procedure is not applicable to quaternary ammonium salts or to amines which are unstable as the free bases, such as primary α-aminoketones.

In preparing amines from organic bromides and hexamethylenetetramine it was observed that after hydrolysis of the intermediate quaternary salts with ethanolic hydrogen chloride the products were obtained as hydrochlorides containing no appreciable amount of bromide ion. The absence of bromides in the products suggests that bromide might have been lost as ethyl bromide.

This led to the concept of a simple, rapid method for preparing chlorides from bromides and iodides which avoids the use of expensive silver chloride, which eliminates the necessity for liberating the free base, and which no longer requires the time-consuming process of evaporation of large quantities of water, usually used in the silver chloride method, to obtain the dry salt. When a solution of the amine salt, iodide or bromide, either quaternary ammonium or hydrohalide of primary, secondary or tertiary amine, in excess of methanolic hydrogen chloride was evaporated on a steam-bath it was rapidly and completely transformed into the corresponding chloride. The yields were nearly quantitative and reaction was usually complete in less than one-half hour, although heating times

TABLE I

TRANSFORMATIONS OF IODIDE AND BROMIDE SALTS TO CHLORIDES USING METHANOLIC HYDROGEN CHLORIDE

Reactant	Product[a]	M.p., °C.[b]	Chlorine, % Calcd.	Found
1-Methyl-4-(4′-dimethylamino)-stilbazoline hydroiodide[c]	Dihydrochloride	212–213	22.2	22.2
N,N′-Dibenzylpiperazine methiodide[d]	Chloride hydr ochloride	207–210	20.1	20.2
2-Stilbazole methiodide[e]	Chloride	255–256	15.3	15.3
2-Picoline methiodide[f]	Chloride[f]	*ca.* 70,[f] very hygroscopic		
Nicotinic acid methyl ester methiodide[g]	Chloride[g]	100–101		
Homoveratryltrimethylammonium bromide[h]	Chloride[i]	204–205		

[a] Under product is described just the nature of the anionic portions associated with the reactant molecule. [b] All melting points are uncorrected. [c] A. P. Phillips, THIS JOURNAL, 72, 1850 (1950). [d] W. van Rijn, *Nederland. Tijdschr. Pharm.*, 10, 5 (1898); through *Chem. Centr.*, 79, I, 381 (1898). [e] A. P. Phillips, *J. Org. Chem.*, 12, 333 (1947). [f] P. Murrill, THIS JOURNAL, 21, 841, 842 (1899). [g] A. Hantzsch, *Ber.*, 19, 31 (1886). [h] White crystals from alcohol–ether; m.p. 232–233°. *Anal.* Calcd. for $C_{13}H_{22}BrNO_2$: C, 51.3; H, 7.3; N, 4.6. Found: C, 51.3; H, 7.6; N, 4.6. [i] J. S. Buck, R. Baltzly and W. S. Ide, THIS JOURNAL, 60, 1789 (1938).

of between one and two hours were commonly used. The desired chloride is obtained pure simply by crystallization from the methanol solution, either by cooling or by the addition of appropriate precipitating solvents.

The process is believed to go by the scheme

$$R_4N^+I^- + H^+Cl^- + MeOH \rightleftharpoons MeO^+H_2 + I^- \longrightarrow MeI + H_2O + R_4N^+Cl^-$$

This depends upon the greater nucleophilic reactivity of iodide or bromide over that of chloride in combining with the alcohol solvent. Methanol is believed to represent a more favorable reactant than ethanol because of the greater susceptibility of methyl to nucleophilic attack than ethyl and because of the greater volatility of the lower alkyl halides allowing easier removal from the reaction mixture during the evaporation. In several experiments methyl iodide was collected from the evaporating mixture through a distilling condenser. It was identified by combination with dimethylaniline to form phenyltrimethylammonium iodide.

Experimental

Transformations of Iodide and Bromide Salts to Chlorides.—In general a solution of 0.02 mole of iodide or bromide salt in about 30–40 cc. of methanol containing 0.1 to 0.2 mole of hydrogen chloride was allowed to evaporate freely on a steam-bath. After one hour the product was crystallized from the methanol solution by cooling or by the addition of a second solvent such as ethyl acetate, acetone, or ether. The absence of any iodide in the product was determined by treating an aliquot in aqueous hydrochloric acid in the presence of carbon tetrachloride with a few drops of dilute sodium nitrite solution.

The transformation works well for quaternary ammonium iodides or bromides as well as for the hydrogen iodides or bromides of primary, secondary or tertiary amines.

The reaction is very rapid. In cases where the rate of disappearance of iodide was followed, using the test method given above, the test for iodide, strongly positive initially, was very faint after 15 minutes, and was negative after 20 minutes.

In several cases evaporation was accomplished through a distillation condenser collecting methanol and methyl iodide. After addition of an excess of dimethylaniline, evaporation of solvent, and recrystallization, a 50% yield of phenyltrimethylammonium iodide was obtained; melting point 215–216°. This gave a strong test for iodide.

Pertinent details for a number of specific compounds transformed by this procedure are shown in Table I.

THE WELLCOME RESEARCH LABORATORIES
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Anodic Polarography: Catechol[1]

BY CHARLES M. WHEELER, JR., AND RAYMOND P. VIGNEAULT

RECEIVED JUNE 17, 1952

In a recent paper, Doskocil[2] reported polarographic data for the system catechol–*o*-quinone in the *p*H range 6.20 to 7.89. Vlcek[3] and coworkers obtained polarographic data for catechol in the *p*H range 3.70 to 8.32. Each of the investigators uses phosphate buffers which give ill-defined diffusion currents for catechol in the low *p*H ranges. This is due to a sudden reversal of current at the dropping mercury electrode, occurring in phosphate buffer solutions at potentials corresponding to the oxidation potential of catechol in the *p*H range 5 to 6. The sharp discontinuity in the anodic wave prevents one from obtaining a complete polarographic wave for catechol in this *p*H range.

Vlcek considered the discontinuity observed to be the anodic oxidation wave of catechol. The present authors feel that the reversal of current is caused only by the anodic dissolution mercury and the formation of a film of mercurous phosphate at the electrode–solution interface. Work in progress in this Laboratory indicates that the potential at which the discontinuity is observed is dependent upon the concentration of the phosphate buffer.

Müller[4] has calculated the usable potential ranges for solutions containing the $HPO_4^=$ ion and we have found that actual values obtained from polarograms of solutions of phosphate buffers agree in general with his calculations. Polarograms of catechol in acetate buffer solutions obtained by Doskocil[2] and in this research indicate that the discontinuity observed by Vlcek in phosphate buffer solutions is due only to the buffer components, since no reversal of current occurs in acetate buffer solutions and a well-defined oxidation wave for catechol is obtained.

Because of the indefinite waves obtained for catechol due to the peculiar effect of phosphate

(1) Taken in part from the M. S. thesis of R. P. Vigneault.

(2) J. Doskocil, *Collection Czechoslov. Chem. Communs.*, **15**, 599 (1950).

(3) A. K. Vlcek, V. Mansfeld and D. Krkoskova, *Collegium*, No. 874, 245 (1943).

(4) O. H. Müller, "The Polarographic Method of Analysis," 2nd edition, Chemical Education Publishing Co., Easton, Pa., 1951, p. 152.

buffers, it was decided to investigate the anodic behavior of catechol in other buffer systems and in more basic solutions than have been reported.

Table I summarizes the values of $E_{1/2}$ obtained in the *p*H range 4.15 to 12.40. When these data are plotted a satisfactory straight line results, with a slope of −0.058 in close agreement with the theoretical value, −0.059. Extrapolation of the graph gives $E^0 = +0.570$ volt relative S.C.E. in perfect agreement with the value similarly obtained by Doskocil[2] over the shorter *p*H range 6.20 to 7.89. Ball and Chen[5] obtained the value 0.566 for this oxidation–reduction system from static measurements.

TABLE I

HALF-WAVE POTENTIALS OF CATECHOL, CONCENTRATION 1×10^{-3} *M*

Buffer	*p*H	$E_{1/2}$ *vs.* S.C.E.
Acetate	4.15	0.337
Acetate	4.82	.290
Acetate	5.20	.260
Acetate	6.00	.220
Phosphate	7.40	.135
Phosphate	8.05	.102
Glycine	9.10	.030
Glycine	10.77	− .058
Glycine	11.88	− .105
Glycine	12.40	− .160

Values for $E_{d.e.}$ *versus* $\log i/(i_d - i)$ plotted for well-defined catechol waves produced in the three buffers used, give straight lines and "*n*" values as follows: acetate buffer, *p*H 6.00, $n = 1.32$; phosphate buffer, *p*H 7.40, $n = 1.39$; glycine buffer, *p*H 10.77, $n = 1.15$. These values for "*n*" fall considerably below the value $n = 2$, which was assumed for the oxidation of catechol to *o*-quinone. This would indicate that the anodic reaction is not reversible.

In order to ascertain whether catechol obeys the Ilkovic equation, polarograms of varying concentrations of catechol were taken in each of the three buffers at certain selected *p*H values. The data obtained for the three buffer systems with the concentration of catechol and the diffusion current, respectively, are: acetate buffer *p*H 6.01, 5×10^{-4} *M* and 4.42 μa., 1×10^{-3} *M* and 7.9 μa., 2×10^{-3} *M* and 15.32 μa.; phosphate buffer *p*H 8.01, 5×10^{-4} *M* and 3.79 μa., 1×10^{-3} *M* and 7.74 μa., 2×10^{-3} *M* and 15.48 μa.; glycine buffer *p*H 11.9, 5×10^{-4} *M* and 4.52 μa., 1×10^{-3} *M* and 8.3 μa., 2×10^{-3} *M* and 15.48 μa. When these data are plotted a linear relationship between the concentration of catechol and the diffusion current is obtained.

Taking the mean value of i_d as 7.9 microamps., concentration of catechol 1×10^{-3} and *n* as 2, the diffusion coefficient, *D*, for catechol is found to be of the order of 5.0×10^{-6} cm.²/sec. at 25°. Kolthoff and Orleman[6] report the diffusion coefficient for hydroquinone at 25° to be about 7.4×10^{-6} cm.²/sec. Because of similar structure and identical molecular weight, catechol would not be expected to differ greatly from this. However, Doskocil[2] found a somewhat smaller diffusion current for catechol than for hydroquinone at the same concentration, although he does not report the diffusion coefficient for either compound.

In properly chosen buffer systems, well-defined catechol oxidation waves can be obtained over the *p*H range studied. These waves can be successfully employed for quantitative and qualitative determination of catechol.

Experimental

Polarograms were obtained at 25 ± 0.01° using a photographically recording Heyrovsky Polarograph Model XII, E. H. Sargent and Co. The electrolysis vessel was an H-shaped cell with a 4% agar plug, saturated with KNO_3, separating the solution being electrolyzed and the reference electrode, a saturated calomel electrode. Polarograms were obtained for buffer solutions to determine the residual current. The half-wave potentials were calculated directly from the polarograms by the method described in a technical bulletin distributed by E. H. Sargent and Co.[7] with the exception of half-wave potentials obtained in the *p*H range 10.77 to 12.40. In this *p*H range the limiting current of the catechol wave was not sufficiently flat to allow determination of $E_{1/2}$ by the method referred to above, half-wave potentials were calculated in this *p*H range by plotting dI/dE against $E_{d.e.}$. All potential values reported in this paper are referred to the saturated calomel electrode.

Capillary characteristics for the dropping mercury electrode used are $m = 3.81$ mg./sec., $t = 2.25$ sec.; $m^{2/3}t^{1/6} = 2.79$. The height of the mercury reservoir, $h = 64$ cm.

Buffer solutions were prepared from 0.1 *M* stock solutions according to the directions of Britton[8] and Clark,[9] with the exception that all constituents of the buffers containing chloride ion were replaced by the corresponding nitrate compound to eliminate the presence of the chloride ion which produces an interfering wave in the potential range used.

For determination of the *p*H, a Beckman model H meter was used, and National Technical Laboratory buffer (*p*H 7.00 ± 0.02) was used for standardization of the glass electrode.

The catechol was Eastman Kodak Co. white label and melted sharply at 104.5°, literature[10] 105°. 0.1 *M* catechol solutions were prepared daily and all variations in concentrations were made by dilutions of the freshly-prepared stock solution.

(5) E. G. Ball and T. T. Chen, *J. Biol. Chem.*, **102**, 691 (1932).

(6) I. M. Kolthoff and E. F. Orleman, THIS JOURNAL, **63**, 664 (1941).

(7) Technical Bulletin No. 2661, E. H. Sargent and Co., Chicago, 1949, p. 20.

(8) H. T. S. Britton, "Hydrogen Ions," D. Van Nostrand Co., Inc., New York, N. Y., 1932, Ch. XII.

(9) W. M. Clark, "Determination of Hydrogen Ions," Williams and Wilkins Co., Baltimore, Md., 1928, Ch. IX.

(10) L. F. Fieser and M. Peters, THIS JOURNAL, **53**, 797 (1931).

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Vapor Pressure of Thorium Oxide from 2050 to 2250°K.[1,2]

BY EDWARD SHAPIRO[3]

RECEIVED JUNE 7, 1952

F. Born's[2] reported values of the vapor pressure of thorium oxide, calculated from estimates of the heat of vaporization and of the chemical constant, are the only published references to thorium oxide vapor pressures. In the course of some studies of factors affecting the life of thorium oxide cathodes, it was necessary to have rather accurate

(1) This work was supported by the U. S. Navy, Bureau of Ships, under Contract NObs-34141.

(2) F. Born, *Z. Elektrochem.*, **31**, 309 (1925).

(3) Tracerlab, Inc., Boston, Mass.

vapor pressure data, and it was decided to make an experimental determination of the vapor pressure curve for thorium oxide. The method used was to determine the vacuum evaporation rate of thorium oxide from coated tungsten filaments by direct weight loss measurements and to correlate these rates to vapor pressures by use of the equation[4]

$$p_{mm.} = 17.14G(T/M)^{1/2}$$

where $p_{mm.}$ is the vapor pressure in mm., G the evaporation rate in g. cm.$^{-2}$ sec.$^{-1}$, T the absolute temperature and M the molecular weight of the evaporated material. Use of this equation assumes an accommodation coefficient of 1. The advantages of this method are in the ease of obtaining the temperatures required in the experiment, and in the ease of comparing evaporation rates with and without thermionic emission.

Apparatus and Experimental

A weighed 10-mil tungsten filament, hairpin shaped, was coated with thorium oxide (Foote Mineral Company, 99% pure) by cataphoresis from a butyl alcohol suspension using Hanley's method.[5] The coated filament was dried at 100° for 10 minutes and weighed. During these steps, the filament was held in a small aluminum sleeve by a set screw. A hook on one end of the sleeve was used to suspend the filament in the balance. Weighings, made on an Ainsworth Microbalance Model FDJ, were reproducible to within 20 micrograms. The glass system was assembled after attaching the filament to the filament lead-in wires by sleeves and set screws (Fig. 1, S_1 and S_2) and attaching the anode at S_3. The anode was a cylinder 1" diam. × 2" long rolled from a sheet of 10-mil tantalum. Holes were in it to permit sighting the filament for temperature measurements. After evacuation of the system to a pressure less than 10^{-5} mm., the filament was heated to the desired temperature and held at that temperature for a measured time interval. Electron emission from the thorium oxide was obtained by applying high voltage to the anode. After the heating period, the system was disassembled, and the filament removed and weighed. The thoria coating was wiped off and the clean filament weighed. The weight of thoria which had evaporated during the run was taken as the difference between the initial and final weights of the coating. Filament brightness temperatures were measured with a Leeds and Northrup optical pyrometer and were corrected to true temperatures by use of a calibration curve obtained on a thoria-coated filament to which a W–Mo thermocouple[6] was welded.

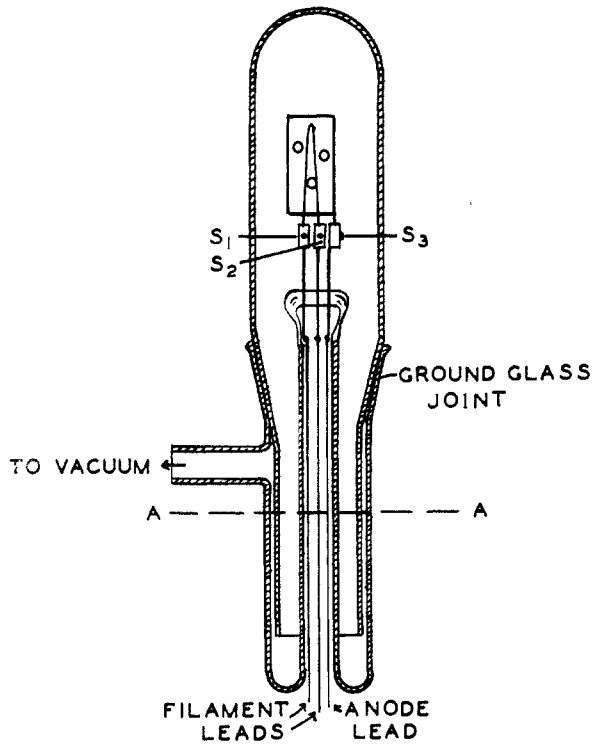

Fig. 1.—Evaporation apparatus: section below AA immersed in liquid N_2 during experiments.

Results and Discussion

The data are plotted in Fig. 2, as a log p *vs.* $1/T$ plot. The equation of the straight line, as obtained by the method of least squares, is

$$\log p_{mm.} = 3.71 \times 10^4/T + 11.53$$

The vapor pressure at 2000°K. is 10^{-7} mm. which is much lower than Born's value of 3×10^{-3} mm. The slope of the line corresponds to a heat of vaporization of 171 kcal./mole, in fair agreement with Fan's value of 184 kcal./mole obtained by an entirely different method.[7] Born's estimated value of about 100 kcal./mole is greatly in error.

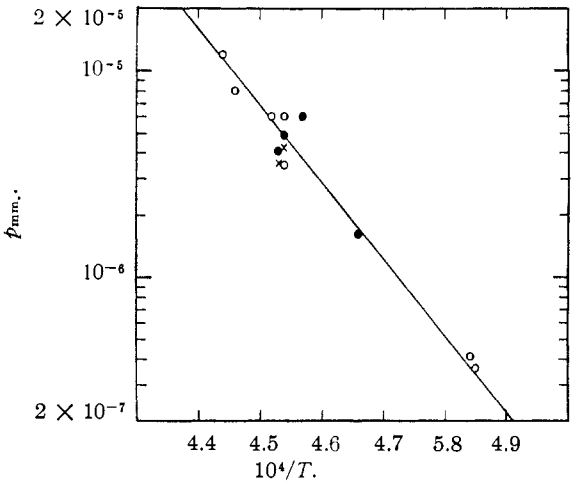

Fig. 2.—Vapor pressure of thoria: O, ThO_2 on W with electron emission; ●, ThO_2 on W without electron emission; ×, ThO_2 on Mo without electron emission.

The results showed no difference between evaporation rates from tungsten or molybdenum or between evaporation rates with or without electron emission currents to 1 amp. cm.$^{-2}$ from the thoria. The latter comparison was made to determine qualitatively whether electrolytic decomposition arising from the passing of current through the coating was appreciable. The results indicated that this fraction was less than 10^{-4}.

The largest source of error was in the temperature measurements. It was extremely difficult to get pyrometer readings reproducible to within ±20°, particularly at the higher temperatures. Errors in temperature readings of 10–15° could readily account for the observed scatter of the experimental points. The temperature used for a given run was determined as the average of a series of 10–30 temperature readings taken during the

(4) S. Dushman, "Vacuum Technique," John Wiley and Sons, Inc., New York, N. Y., 1949, p. 20.

(5) T. E. Hanley, *J. Applied Phys.*, **19**, 583-584 (1948).

(6) F. H. Morgan and W. E. Danforth, *ibid.*, **21**, 112 (1950).

(7) H. Y. Fan, *ibid.*, **20**, 689 (1949).

run. Improvement might have been effected by the use of coated ribbons to increase the area pyrometered.

At temperatures above 2400°K., relatively large losses of tungsten were noted. These losses were more than could be accounted for by evaporation, and were assumed to be the result of a reaction between thorium oxide and tungsten in which volatile tungsten oxides were formed.

Acknowledgment.—Mr. F. H. Morgan's help in obtaining the calibration curve with the W–Mo thermocouple and Mr. H. Bleecher's technical assistance are gratefully acknowledged.

BARTOL RESEARCH FOUNDATION
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Ethyl β-Morpholinocrotonate

BY J. F. TINKER AND T. E. WHATMOUGH

RECEIVED JUNE 9, 1952

Monoalkylation of acetoacetic ester is seldom clean and sometimes difficult. Alkylation of β-aminocrotonic ester[1] stops cleanly after a single alkyl group. A most satisfactory member of this series is the one derived from morpholine, using directions for the preparation of β-anilinocrotonate.[2]

Ethyl β-Morpholinocrotonate.—A mixture of 511 g. (3.93 moles) of ethyl acetoacetate, 400 cc. (4.60 moles) of morpholine, 10 cc. of 85% formic acid, and 2.5 l. of benzene was refluxed, and the water separated.[2] In 8 hours 75 cc. had been collected. The solution was then distilled, and yielded 592 g., 76%, of the product, b.p. 120–124° (0.5 mm.), d^{25}_{25} 1.099, $n^{23.5}D$ 1.5162. A sample was redistilled (b.p. 116° (0.35 mm.)) and analyzed.

Anal. Calcd. for $C_{10}H_{17}NO_3$ (199.24): C, 60.28; H, 8.60. Found: C, 60.20; H, 8.65.

Treatment of the aminoester with either propargyl bromide or propargyl *p*-toluenesulfonate, followed by treatment with hot water,[1] yielded **3-carbethoxy-5-hexynone-2**, b.p. 69–73° (1 mm.), in excellent yield. A single redistillation gave a sample of analytical purity (b.p. 71° (1 mm.)).

Anal. Calcd. for $C_9H_{12}O_3$ (168.19): C, 64.27; H, 7.19. Found: C, 63.60; H, 7.20.

3-Carbethoxy-5-hexynone-2, 2,4-dinitrophenylhydrazone, m.p. 97–98°.[3]

Anal. Calcd. for $C_{15}H_{16}N_4O_3$ (348.31): C, 51.72; H, 4.63; N, 16.09. Found: C, 51.74; H, 4.69; N, 15.94.

Acid hydrolysis yields **5-hexynone-2**,[4] b.p. 62–64° (12 mm.). The **2,4-dinitrophenylhydrazone** of 5-hexynone-2 melts at 138–139°.

Anal. Calcd. for $C_{12}H_{12}N_4O_4$ (276.25): N, 20.28. Found: N, 20.34.

Treatment of ethyl β-morpholinocrotonate with 2,3-dichloropropene, followed by refluxing with water, yielded directly **5-chloro-5-hexenone-2**, b.p. 74–77° (16 mm.) in 86% yield. **The 2,4-dinitrophenylhydrazone** has m.p. 84–85°.

Anal. Calcd. for $C_{12}H_{13}ClN_4O_4$ (312.71): C, 46.09; H, 4.19; N, 17.92. Found: C, 46.12; H, 4.31; N, 18.34.

Treatment of the chloroketone with sodium amide in liquid ammonia, in an attempt to effect the condensation of two molecules to a derivative of 1,6-cyclodecadiyne, yielded no detectable tertiary alcohol.

Acknowledgment.—We wish to thank Dr. M. C. Whiting for informative discussions during the course of this work.

(1) (a) R. Robinson, *J. Chem. Soc.*, **109**, 1043 (1916); (b) W. M. Lauer and G. W. Jones, THIS JOURNAL, **59**, 232 (1937).

(2) C. S. Hamilton, ed., *Org. Syntheses*, **29**, 42 (1949).

(3) All melting points taken with Anschütz thermometers in a Hershberg apparatus.

(4) T. E. Gardner and W. H. Perkin, *J. Chem. Soc.*, **91**, 851 (1907).

CONVERSE LABORATORY
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COMMUNICATIONS TO THE EDITOR

THREE NEW NEUTRON DEFICIENT ISOTOPES OF YTTRIUM

Sir:

Three new yttrium isotopes have been discovered by proton bombardment of spectroscopically pure yttrium oxide[1] in the Rochester 130-inch cyclotron. Targets of yttrium oxide were placed in an aluminum foil envelope which was mounted on the end of a probe and placed inside the tank of the cyclotron. The target was bombarded with both 240 and 130 Mev. protons for exposure times of one and two hours.

The yttrium oxide was dissolved in hot nitric acid and inert carriers of zirconium, strontium, rubidium and bromine were added to the solution. The yttrium fraction was purified from all the spallation products and the sample was followed under a Geiger-Müller tube for gross decay. The activities found had half lives of: 2–4 hours, 14 hours, 38 hours, 80 hours, 25.5 days and finally 65 days. In one experiment 105-day Y^{88} was also observed. The half-lives of the known[2] yttrium isotopes in this region are: Y^{88} 2 hours, 105 days; Y^{87} 14 hours, 80 hours; Y^{86} 14.6 hours; and Y^{84} 3.7 hours. The 38-hour, 25.5-day, and 65-day activities found in the yttrium gross decay curve can be identified with Sr^{83}, Sr^{82}, and Sr^{85}, respectively. This means that these strontium isotopes found in the purified yttrium sample are the daughters of their respective yttrium parents which are previously unreported yttrium isotopes. Thus, Y^{82} decayed to 25.5-day Sr^{82}, Y^{83} decayed to 38-hour Sr^{83}, and Y^{85} decayed to 65-day Sr^{85}.

Since the yttrium gross decay curve was so complex, it was impossible to resolve the half lives of these new isotopes directly. Therefore, a series of isolation experiments were performed in which the strontium daughter isotopes were removed from the yttrium at periodic intervals. These strontium

(1) The yttrium oxide was supplied through the courtesy of Ames Laboratory, Iowa State College.

(2) Nuclear Data by K. Way, *et al.*, Circular of the National Bureau of Standards 499; General Electric Research Laboratory Chart of the Nuclides.