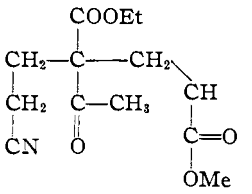
NOTES

So-called 5-Carbethoxy-9-methyl-2-oxo-1-azabicyclo[3.3.1]nonane. A Correction

By Noel F. Albertson

Reduction of ethyl (2-carbomethoxyethyl)-(2-cyanoethyl)-acetoacetate (I) with Raney nickel catalyst has been reported to give ethyl 3-(2-carbomethoxyethyl)-2-methylnipecotate (II) and 5-carbethoxy-9-methyl-2-oxo-1-azabicyclo[3.3.1]-nonane (III).[1] Structure III was assigned largely on the basis of the fact that a sample of II, on standing, partially crystallized with formation of more of this solid material. In a review article[2] on Bredt's rule, Fawcett pointed out that compound III was the first reported example of a bridgehead amide.[3] This fact, together with the "low" hydrogen analysis[4] obtained for the solid product, suggested that this compound should be re-examined. An ultraviolet absorption spectrum showed that conjugated unsaturation was present. The compound was found to absorb bromine readily and to absorb two moles of hydrogen in the presence of a palladium or platinum catalyst. These facts suggested that the solid was actually 4a-carbethoxy-1,2,3,4,4a,5,6,7-octahydro-7-quinolone (IV).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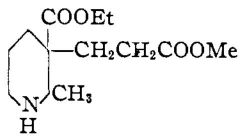
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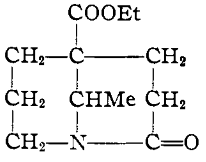
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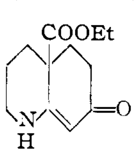
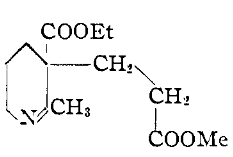

IV


V

Such a product could not arise from a sample of II unless II contained V as an impurity.[5,6] Other work in this Laboratory has shown that there is a tendency to form unsaturated piperidines by Raney nickel reduction of certain 5-oxonitriles.[7]

The infrared spectrum showed the presence of an ester group, and failed to disclose any evidence of a hydroxyl. On the basis of the evidence cited, it is apparent that reduction of I has led to ring closure between the methyl and ester groups to give IV rather than between the amine and ester groups to give III.

Although these data permit only one interpretation for the carbon–nitrogen skeleton of the reduction product, caution (after one mistake) led to additional experiments to confirm structure IV.

When IV was refluxed with methanolic potassium hydroxide and the resulting potassium salt acidified, carbon dioxide was evolved from the cold solution as was expected from the vinylog of a β-oxo ester. Heating the resulting octahydro-7-quinolone with sulfur gave 7-quinolinol the identity of which was confirmed by melting point, color test with ferric chloride and ultraviolet absorption spectrum. Incidentally, the same quinolone was obtained as one product of the reduction of benzyl (2-carbomethoxyethyl)-(2-cyanoethyl)-acetoacetate.

As anticipated for the vinylog of an amide, IV did not give a 2,4-dinitrophenylhydrazone or a semicarbazone under the usual reaction conditions.

An examination of structure IV indicates that reduction of the 8,8a double bond would lead to a Mannich base type. Thus, reduction under different conditions should lead to different results. Such was found to be the case. Reduction of IV with a palladium catalyst in acetic acid solution gave 4a-carbethoxy-decahydro-7-quinolinol. This reacted with thionyl chloride to give 4a-carbethoxydecahydro-7-chloroquinoline hydrochloride.

Reduction of IV using Raney nickel catalyst in ethanol at 110° proved to be very exothermic and the temperature rose rapidly to 155°.[8] The product, $C_{12}H_{21}NO_2$, was neutral and water soluble indicating that amide formation between the amine and ester functions had occurred. Since the product contained two more carbon atoms than had been expected, these must have come from the solvent. Confirmatory evidence was obtained by

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(1) N. F. Albertson, This Journal, **72**, 2594 (1950).

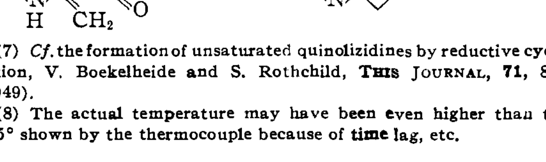
(2) F. S. Fawcett, *Chem. Revs.*, **47**, 259 (1950).

(3) G. M. Badger, J. W. Cook and T. Walker (*J. Chem. Soc.*, 1141 (1949)) postulated the existence of 5-phenyl-1-azabicyclo[3.3.1]nonan-2-one as an intermediate. This compound was not isolated, however, a compound containing a carbonyl joined to a bridgehead nitrogen, namely, 5-ethyl-1,3-diaza-2,4,9-trioxobicyclo[3.3.1]nonane, has recently been reported by J. Baumler, E. Sorkin and H. Erlenmeyer in *Helv. Chim. Acta*, **34**, 459 (1951). Ring closure to the oxygen to give 1,3-dioxo-8a-ethyl-decahydropyrano[2,3-d]pyrimidine would appear to be an equally plausible explanation for the product.

(4) Actually the published data agree with the correct formula, $C_{12}H_{17}NO_3$, rather than with the assigned structure, III.

(5) It should be noted that although a sample of II had partially crystallized in five months, no further crystallization occurred in several years.

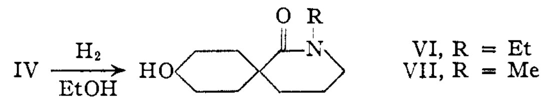
(6) Dr. W. S. Johnson suggested that IV was formed *via* the following:



(7) *Cf.* the formation of unsaturated quinolizidines by reductive cyclization, V. Boekelheide and S. Rothchild, This Journal, **71**, 879 (1949).

(8) The actual temperature may have been even higher than the 155° shown by the thermocouple because of time lag, etc.

carrying out the reduction in methanol. The resulting sirup (VII?) could not be seeded by the solid obtained in ethanol. The properties of the latter product agree with its formulation as 2-ethyl-9-oxy-2-azaspiro[5.5]hendecanone (VI). Its formation from IV involves (a) hydrogenation of the 8,8a-double bond, (b) ethylation of the nitrogen by the solvent, (c) hydrogenolysis of the C–N bond which is β not only to a carbonyl but also to a carbethoxy group, (d) cyclization of the amine and ester groups, and (e) reduction of the keto group.



Reduction of IV with sodium and 2-methylpentanol-4 gave decahydro-7-quinolinol.

It was originally planned to convert VI or VII to 2-alkyl-2-azaspiro[5.5]hendecane and to compare this with a synthetic specimen. This was later deemed unnecessary. However, the sirup, VII, was reduced with lithium aluminum hydride to a strong base having the properties expected of 2-methyl-2-azaspiro[5.5]hendecan-9-ol. Also, ethyl 1-(2-cyanoethyl)-cyclohexane-2-onecarboxylate ethylene glycol ketal was reduced to 2-azaspiro[5.5]hendecan-1,7-dione.

In the paper in which the synthesis of IV is described,[1] two other compounds have been identified only by empirical formula. After the paper was submitted for publication, the structure of these two compounds was established by synthesis. The compound, $C_9H_{13}NO_4$, obtained by hydrolysis of ethyl 2-(2-cyanoethyl)-cyclopentanone-2-carboxylate and distillation of the hydrolysis product is 3-(3-carboxypropyl)-glutarimide. The by-product obtained in the preparation of 4a-carbethoxyoctahydro-1-pyridine is 3-(3-carbethoxypropyl)-2-piperidone. Both of these products are readily obtained from cyclopentanone-2-carboxylic esters by treatment with acrylonitrile in alcohol with sodium ethylate as a catalyst. If the temperature is allowed to rise during the addition of acrylonitrile, the cyclopentanone ring is opened and the product is a 2-(2-cyanoethyl)-adipic acid diester.

Experimental[9]

4a-Carbethoxy-1,2,3,4,49,5,6,7-octahydro-7-quinolone (IV).—Reduction of 389 g. of ethyl (2-carbomethoxyethyl)-(2-cyanoethyl)-acetoacetate in 1500 ml. of alcohol at 100° using Raney nickel catalyst required four hours. This was worked up as previously described[1] to give 151 g. of IV after the ether wash and 45 g. more from the distillation residue. This compound gave a definite, though not intense, red color with aqueous or alcoholic ferric chloride. It also absorbed bromine. It showed an absorption maximum at 303 mμ (ϵ 30,215) and a minimum at 250 mμ (ϵ 471). The infrared spectrum showed a band at 5.83 μ (ester) and one at 6.15 μ (amide?).[9a] A sample recrystallized from methanol gave the following analytical data. Found: C, 64.53; H, 7.38; N(AP), 6.30. A sample from ethanol–ether gave: C, 64.78, 64.70; H, 7.43, 7.54. Calcd. for $C_{12}H_{17}NO_3$: C, 64.54; H, 7.68; N, 6.27.

4a-Carbethoxydecahydro-7-quinolinol.—A solution of 10 g. of IV in 100 ml. of acetic acid was reduced using 10% palladium-on-carbon catalyst at 50 lb. initial pressure and 50°. Reduction took six hours. Filtration and concentration gave a sirup which was taken up in water. Addition of potassium carbonate gave an oil which was extracted once with ether. The product soon crystallized from the ether. A sample, recrystallized from water, melted at 101.6–104.4° cor. The same compound (2.2 g. crude yield) was obtained by reducing 2.6 g. of IV with Adams platinum oxide catalyst in ethanol at 50°.

Anal. Calcd. for $C_{12}H_{21}NO_3$: C, 63.41; H, 9.31; N, 6.16. Found: C, 63.20; H, 9.34; N(K), 6.09.

4a-Carbethoxy-7-chlorodecahydroquinoline Hydrochloride.—Treatment of 2 g. of 4a-carbethoxydecahydro-7-quinolinol with 1.0 ml. of thionyl chloride in chloroform gave 2.0 g. of product. A sample, recrystallized twice from isopropyl alcohol–ether, melted at 199.0–199.4° cor.

Anal. Calcd. for $C_{12}H_{20}ClNO_2 \cdot HCl$: Cl, 25.13; N, 4.96. Found: Cl, 25.07; N(D), 4.92.

Octahydro-7-quinolone.—Ten grams of IV was refluxed 13 hours with 5 g. of potassium hydroxide in 40 ml. of methanol. The solvent was removed *in vacuo*, the solid dissolved in water and acidified with hydrochloric acid. The solution was again taken to dryness and extracted with hot isopropyl alcohol. The first crop, 2.5 g., melted at 210–212°. Concentration of the filtrate gave a second crop of 2.0 g. The combined crops were treated with aqueous potassium carbonate to give the base, m.p. 182.2–184.2° cor. from ethyl acetate. No attempt was made to locate the double bond in this quinolone.

Anal. Calcd. for $C_9H_{13}NO$: N, 9.26. Found: N(D), 9.11.

This compound was also prepared (in poor yield) by reduction of 65 g. of benzyl (2-carbomethoxyethyl)-(2-cyanoethyl)-acetoacetate in 100 ml. of methanol with Raney nickel catalyst at 1900 lb. initial pressure and 85°. Reduction took six hours. Removal of the catalyst and solvent gave 42 g. of red brown sirup soluble in dilute hydrochloric acid but insoluble in water and ammonium hydroxide. The sirup was stirred with about 100 ml. of ether and the ether layer decanted. The remaining heavy oil partially crystallized, the crystals being identical with the octahydro-7-quinolone prepared above.

The benzyl (2-carbomethoxyethyl)-(2-cyanoethyl)-acetoacetate was prepared by adding 18 ml. of acrylonitrile to 62 g. of benzyl-(2-carbomethoxyethyl)-acetoacetate to which had been added a ml. of methanolic potassium hydroxide. The reaction product was washed with water and used directly.

Benzyl (2-Carbomethoxyethyl)-acetoacetate.—A mixture of 108 g. of ethyl (2-carbomethoxyethyl)-acetoacetate[10] and 53 ml. of benzyl alcohol was heated in a flask equipped for distillation. When the liquid temperature reached 170°, ethanol distilled over. In less than two hours 62% of the theoretical amount of ethanol was collected. Distillation gave 85.2 g. (61%) of product boiling at 165–168° (1.8 mm.) and 33 g. of recovered starting material. The product gave an intense violet color with alcoholic ferric chloride.

Anal. Calcd. for $C_{15}H_{18}O_5$: C, 64.73; H, 6.52. Found: C, 64.97; H, 6.73.

7-Quinolinol.—A mixture of 0.63 g. of octahydro-7-quinolone and 0.40 g. of sulfur was immersed in a bath at 135° and heated to 230° over 15 minutes. The temperature of the bath was increased to 240° over the next ten minutes. Long needles sublimed to the upper surface of the flask. These decomposed at 231° after softening at 226°. With ferric chloride in aqueous alcohol a red brown color was observed. The ultraviolet absorption spectrum of a sample recrystallized from aqueous ethanol checked the curve published by Ewing and Steck.[11]

2-Ethyl-9-oxy-2-azaspiro[5.5]hendecanone (VI).—A suspension of 22.3 g. of IV in 130 ml. of ethanol was heated with Raney nickel catalyst to 110° and 980 lb. of hydrogen pressure. Reduction started and the heat was turned off. The temperature rose to 155° after 20 minutes and the reduction was over. Removal of the catalyst and solvent

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[9] N(AP) refers to nitrogen determined by titration with perchloric acid in acetic acid; N(K) refers to Kjeldahl nitrogen; and N(D) refers to Dumas nitrogen.

[9a] A referee has pointed out that the band at 6.15μ (equivalent to 1627 cm.$^{-1}$) actually is characteristic of the vinylog of an amide and supports the assigned structure. *Cf.* N. H. Cromwell, *et al.*, THIS JOURNAL, **71**, 3337 (1949).

[10] N. F. Albertson THIS JOURNAL, **70**, 669 (1948).

[11] G. Ewing and E. Steck, *ibid.*, **68**, 2181 (1946).

left 20.4 g. of crystals. These were extracted with hot benzene to remove the product from 3.9 g. of solid melting above 250°. Concentration of the benzene extracts and addition of Skellysolve B precipitated the product; m.p. 111–114°. It was very soluble in water and neutral to litmus. There was no absorption in the ultraviolet. The infrared spectrum showed the presence of an amide linkage and possibly an OH group. A sample, recrystallized from ethyl acetate, melted at 114–115.5°.

Anal. Calcd. for $C_{12}H_{21}NO_2$: C, 68.21; H, 10.02; N, 6.63; ethoxyl, none. Found: C, 67.86; H, 10.03; N(D), 6.85; ethoxyl, none.

2-Methyl-2-azaspiro [5.5] hendecan-9-ol.—When an equivalent amount of methanol was substituted for ethanol in the above experiment there was obtained 2.4 g. of by-product melting above 290° and 17.9 g. of sirup which could not be induced to crystallize even on seeding with the product melting at 115°. The crude sirup was reduced with lithium aluminum hydride to give 3 g. of very viscous pale yellow sirup distilling at 110–120° (0.7 mm.).

Anal. Calcd. for $C_{11}H_{21}NO$: N, 7.64. Found: N(AP), 7.54.

Decahydro-7-quinolinol.—Reduction of 45.1 g. of IV with 39.0 g. of sodium and 87.6 g. of 2-methylpentanol-4 in toluene gave 39.8 g. of oil most of which crystallized while still hot. Trituration with ether gave about 12 g. melting at 162–165°. This was a strong base in water and reacted with acetic anhydride to give a viscous oil. A mixed m.p. with the starting material was depressed (m.p. 137–157°). A sample, recrystallized from ethyl acetate, melted at 170.3–171.4° cor.

Anal. Calcd. for $C_9H_{17}NO$: C, 69.65; H, 11.04; N, 9.03. Found: C, 69.60; H, 10.98; N(AP), 8.94.

Ethyl 2-(2-Cyanoethyl)-cyclohexanone-2-carboxylate Ethylene Glycol Ketal.—A mixture of 22.3 g. of ethyl 2-(2-cyanoethyl)-cyclohexanone-2-carboxylate, 38 g. of ethylene glycol, 1.5 g. of toluenesulfonic acid monohydrate and 100 ml. of benzene was refluxed overnight using a water separator. The benzene phase was washed with water, aqueous potassium carbonate and water. The product (22.5 g.) was collected at 110–139° at 0.07 mm., but most boiled at the higher temperature; n^{25}D 1.4818.

Anal. Calcd. for $C_{14}H_{21}NO_4$: N, 5.24. Found: N(K), 5.21.

2-Aza-spiro [5.5] hendecan-1,7-dione.—Reduction of 21 g. of the above ketal in 70 ml. of ethanol with a Raney nickel catalyst at 60° required two hours. It was necessary to distil out some 4a-carbethoxydecahydroquinoline, b.p. 82–84° at 0.09 mm. before the product (11.3 g.) crystallized. After trituration with a small amount of benzene and three recrystallizations from isopropyl alcohol–ether, the product melted at 226.5–228.5°.

Anal. Calcd. for $C_{10}H_{15}NO_2$: N, 7.73. Found: N(K), 7.67.

The picrate of 4a-carbethoxydecahydroquinoline was prepared. It melted at 181.7–183.2° cor., from ethanol.

Anal. Calcd. for $C_{12}H_{21}NO_2 \cdot C_6H_3N_3O_7$: N, 12.72. Found: N(D), 12.82.

Methyl Ethyl 2-(2-Cyanoethyl)-adipate.—To 0.1 g. of sodium in 35 ml. of ethanol was added 38 g. of methyl cyclopentanone-2-carboxylate. Then 20 ml. of acrylonitrile was added slowly at an initial temperature of 30°. The reaction mixture was allowed to heat up to 75° and was then kept from heating up further by cooling as required. After two hours several milliliters of acetic acid was added, the solvent removed and the residue washed with water. Fractionation gave 7.9 g. of starting material and 45.4 g. of product boiling at 137–156° (0.6 mm.). It gave no color with ferric chloride.

Anal. Calcd. for $C_{12}H_{19}NO_4$: C, 59.73; H, 7.94; N, 5.81. Found: C, 60.18; H, 7.73; N, 5.65.

By using 105 g. of ethyl cyclopentanone-2-carboxylate, there was obtained 148 g. of diethyl 2-(2-cyanoethyl)-adipate; b.p. 158–162° at 0.2 mm.; n^{25}D 1.4442.

Anal. Calcd. for $C_{13}H_{21}NO_4$: N, 5.49. Found: N(K), 5.45.

3-(3-Carbethoxypropyl)-2-piperidone.—Reduction of 90.5 g. of methyl ethyl-2-(2-cyanoethyladipate) in 500 ml. of methanol with Raney nickel catalyst at 80° and 700 lb. initial hydrogen pressure required five hours. Removal of the catalyst and solvent left 76 g. of oil which crystallized in several hours. Recrystallization from ether gave a solid melting at 54–56°. The same compound was obtained by reduction of 132 g. of diethyl 2-(2-cyanoethyladipate) in ethanol, and was shown by means of mixed melting point to be identical with the by-product previously reported.[1]

Anal. Calcd. for $C_{11}H_{19}NO_3$: N, 6.57. Found: N(K), 6.56.

3-(3-Carboxypropyl)-glutarimide.—A mixture of 4 g. of methyl ethyl-2-(2-cyanoethyl)-adipate, 4 g. of sodium carbonate and 36 ml. of water was refluxed for six hours, acidified to congo paper with hydrochloric acid and extracted with ethyl acetate. Concentration gave 2.9 g. of sirup which was dried over phosphorus pentoxide–potassium hydroxide. Some of the sirup was warmed in a test-tube for several minutes over a free flame to effect cyclization. Upon cooling and addition of water white crystals readily formed in good yield; m.p. 149–151.5° after recrystallization from water. The m.p. was not depressed on admixture with the $C_9H_{13}NO_4$ compound previously reported[1] to result from hydrolysis of ethyl 2-(2-cyanoethyl)-cyclopentanone-2-carboxylate, followed by distillation of the intermediate.

Acknowledgment.—We are happy to have had the opportunity of discussing this problem with Dr. W. S. Johnson. We are indebted to Mrs. C. Diacetis for technical assistance, to Mr. Morris Auerbach and Kenneth Fleischer and staff for analytical results, and to Dr. Frederick Nachod, Miss Catherine Martini and Mrs. M. Becker for measuring and interpreting absorption spectra.

STERLING-WINTHROP RESEARCH INSTITUTE
RENSSELAER, N. Y. RECEIVED JULY 16, 1951

The Separation of Mixtures of *cis*- and *trans*-Estradiols

BY NORMAN BARSEL

Estrone on reduction with Raney nickel in aqueous potassium hydroxide, forms a mixture of estradiol-17-β, m.p. 178° (85–90%) and estradiol-17-α, m.p. 223° (10–15%). Recrystallization from aqueous ethanol usually removes the 17-β and leaves a residue in solution that is enriched in estradiol-17-α. Originally, a separation of the 17-beta compound as its slightly soluble digitonide[1] was suggested. Later, an insoluble urea complex was used to separate this same epimer.[2]

We have found that sharp separations may be more easily accomplished through the dipropionates of this mixture.[3] The 17-β dipropionate crystallizes from hot methanol before the 17-α dipropionate which melts at 76–77°, $[\alpha]^{25}$D + 36, 1% in dioxane. *Anal.* Calcd. for $C_{24}H_{32}O_4$: C, 74.95; H, 8.40. Found: C, 75.04; 8.50. The latter separates as an oil only after the solution had been concentrated.

We further noted that propionation of such a mixture of diols in pyridine below 95° forms the 17-monopropionates whereas above 105° the dipropionates are produced.

Saponification of the dipropionates in methanolic potassium hydroxide yields the pure diols.

RESEARCH DEPT., INTERNATIONAL HORMONES, INC.
BROOKLYN, NEW YORK RECEIVED SEPTEMBER 17, 1951

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(1) O. Wintersteiner, THIS JOURNAL, **59**, 765 (1937).

(2) H. Priewe, U. S. Patent 2,300,134 (1942).

(3) K. Miescher and C. R. Scholz, *Helv. Chim. Acta*, **20**, 268 (1937).

The Paper Chromatography of Imidazoles

BY BRUCE N. AMES AND H. K. MITCHELL[1]

During the course of investigations on the accumulation of imidazole-like substances by histidineless mutants of *Neurospora*, methods have been developed for paper chromatography and detection on the paper of compounds of this type. Dent[2] reported the use of the Pauly reagent (diazosulfanilic acid) for this purpose. Using the modification of this reagent described below and the method of Jorpes[3] in which the acidic diazo reagent is mixed with the imidazole before developing the color with Na_2CO_3, excellent results have been obtained with a variety of imidazole derivatives.

Procedure and Results.—Air-dried chromatograms are sprayed so as just to wet the paper with the diazosulfanilic acid reagent, and then the color is developed by a light spray of 5% sodium carbonate solution. The diazo reagent is made by adding slowly and with stirring 25 ml. of a freshly made up 5% sodium nitrite solution to 5 ml. of a stock sulfanilic acid solution (0.9 g. sulfanilic acid and 9 ml. of concentrated HCl made up to 100 ml. with distilled water). Both the nitrite and sulfanilic acid solution must be brought to 0° before mixing.

The diazo reagent will keep for about 4–5 days at 0° but decomposes rapidly at higher temperatures. The stock sulfanilic acid solution keeps indefinitely at room temperature.

TABLE I

R_f VALUES ON 3.5 HOURS, ASCENDING,[10] WHATMAN #1 CHROMATOGRAMS AT 25°

Compound	Diazo spot color	R_f with 3:1 propyl alcohol–0.2 *N* ammonia	R_f with 3:1 propyl alcohol–1 *N* acetic acid[11]	2537 Å. absorption	Ninhydrin color
Histidine	Red	0.22	0.12	−	Violet
4(5)-Carboxyimidazole[a]	Yellow	.23	.29	−	....
Carnosine	Red	.24	.06	−	Violet
2-Thiol histidine[b]	Red	.25	.15	+	Violet
[Imidazolyl-4(5)]-lactic acid	Red	.26	.27	−	....
Ergothionine	Red	.27	.26	+	....
Guanine	Orange	.27	.35	+	....
[Imidazolyl-4(5)]-pyruvic acid[c]	Red	.31	.31	−	....
[Imidazolyl-4(5)]-acrylic acid	Red	.34	.69	+	....
Ammonium chloride	Yellow	.39	.41	−	....
4(5)-Amino-5(4)-carboxamide imidazole[d]	Blue	.52	.51	+	Yellow-Orange
Histamine	Red	.65	.10–0.28	−	Violet
Histidinol[e]	Red	.65	.10– .28	−	Violet
Histidine methyl ester[b]	Red	.75	.45	−	Violet
4(5)-Hydroxymethylimidazole[f]	Red	.75	.56	−	....
Imidazole	Red-Orange	.88	.58	−	....

The compounds indicated were kindly supplied by [a] Dr. R. G. Jones, [b] Dr. M. Fling, [c] Mr. P. Thayer, [d] Dr. E. E. Snell, [e] Dr. B. Davis,[12] [f] Dr. P. M. Ruoff.

This method is considerably more sensitive than the ninhydrin method for histamine and histidine. The diazo reagent will indicate 0.3 of a microgram of histamine or histidine on a chromatogram. The sensitivity of the reagent is about the same for other imidazoles.

Using this procedure with known imidazoles several differently colored spots have been observed. In general imidazoles with a side chain at the 4-position, such as histidine, give a red color with the reagent. Substituents in addition to a side chain may alter the color considerably. Guanine gives a bright orange color and 4(5)-amino-5(4)-carboxamide imidazole gives first an orange color with the acid diazo solution and then a bright blue when the sodium carbonate is sprayed on.[4] This blue color is unique[5] and probably can be used for the quantitative estimation of this natural base.

The coupling reaction is not general for all imidazoles. Imidazoles with alkyl substituents on one of the ring nitrogens do not give the reaction[7]; *e.g.*, 1-methylhistidine and anserine. Some imidazoles with a carbonyl group next to the ring at the 4 position do not react; *e.g.*, [imidazolyl-4-(5)]-formaldehyde and [imidazolyl-4(5)]-glyoxylic acid. A weak yellow color is given by 4(5)-carboxyimidazole. Some condensed ring systems containing an imidazole nucleus also do not give the Pauly reaction; *e.g.*, most purines and benzimidazole.

In addition to imidazoles other compounds have been encountered in biological materials which react with diazosulfanilic acid giving colored dyes. Ammonium chloride as well as other ammonium salts gives yellow spots in fairly high dilution. Tyrosine has been found to give a red color under the conditions stated but only at much greater concentrations. Many phenols other than tyrosine are also known to couple with diazosulfanilic acid. This reaction has been used for their identification on paper chromatograms by Evans, *et al.*,[8] who reported various orange, brown and yellow colors from biochemically important phenols. A non-imidazole base that gives a red diazo reaction has been encountered by Hunter[9] in maize.

The R_f values and diazo colors of a number of imidazoles of biochemical and preparative importance are listed in Table I. Absorption spots under 2537 Å. ultraviolet and ninhydrin reaction color are also listed as they are useful in characterization.

Chromatograms have been made from the reaction mixture of the Parrod[13] synthesis of imidazoles from glucose.[14]

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(1) This work was supported in part by funds from the Rockefeller Foundation and by funds from the Atomic Energy Commission administered through contract with the Office of Naval Research, U. S. Navy, Contract N6 onr-244, Task Order V.

(2) C. E. Dent, *Biochem. J.*, **43**, 169 (1948).

(3) E. Jorpes, *ibid.*, **26** 1507 (1932).

(4) A darker color is obtained if the sodium carbonate is sprayed on before the diazo reagent.

(5) A blue diazotization product has also been reported by Hunter[6] with 4(5)-guanidinoimidazole.

(6) G. Hunter, *Biochem. J.*, **30**, 1183 (1936).

(7) M. Guggenheim, "Die Biogenen Amine," S. Karger, Basel, 1940, p. 407.

(8) R. A. Evans, W. Parr and W. Evans, *Nature*, **164**, 674 (1949).

(9) G. Hunter, *Biochem. J.*, **48**, 265 (1951).

(10) R. J. Williams and H. Kirby, *Science*, **107**, 481 (1948).

(11) Histamine and histidinol give streaks with this solvent.

(12) H. J. Vogel, B. D. Davis and E. S. Mingioli, THIS JOURNAL, **73**, 1897 (1951).

(13) J. Parrod, *Ann. Chim.*, **19**, 233 (1933).

(14) A modification of the Parrod procedure is listed in ref. 15 for the synthesis of 4(5)-hydroxymethylimidazole, an intermediate in histidine synthesis.

(15) *Org. Syntheses*, **24**, 64 (1944).

Parrod reported imidazole and 4(5)-(*D-arabino*)-tetrahydroxybutaneimidazole as the products. The chromatograms indicate that fair quantities of 4(5)-hydroxymethylimidazole and two other diazo reacting substances were obtained as well.

Chromatograms have been made of many other complex materials, such as deproteinized liver fractions, the products of the action of L-aminoacid oxidase on DL-histidine, and culture filtrates from *Neurospora* and *Penicillium* histidineless mutants, with good separation of imidazoles and reproducible colors and R_f values.

KERCKHOFF LABORATORIES OF BIOLOGY
CALIFORNIA INSTITUTE OF TECHNOLOGY
PASADENA, CALIFORNIA RECEIVED SEPTEMBER 12, 1951

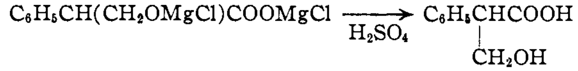
The Preparation of Tropic Acid

BY F. F. BLICKE, HAROLD RAFFELSON AND BOHDAN BARNA

It has been found that tropic acid, which is required for the synthesis of atropine and certain synthetic medicaments, can be obtained very conveniently, and in good yield, by the addition of formaldehyde to the Ivanov reagent[1] prepared from phenylacetic acid and isopropylmagnesium chloride

$$C_6H_5CH_2COOH + 2(CH_3)_2CHMgCl \longrightarrow C_6H_5CH(MgCl)COOMgCl + 2C_3H_8$$

$$\underset{\text{(Ivanov reagent)}}{C_6H_5CH(MgCl)COOMgCl} + CH_2O \longrightarrow$$



$$C_6H_5CH(CH_2OMgCl)COOMgCl \xrightarrow[H_2SO_4]{} \underset{\displaystyle CH_2OH}{C_6H_5\overset{}{C}HCOOH}$$

Magnesium (97.3 g.) and 2 liters of anhydrous ether were placed in a 5-liter, 3-necked flask fitted with a stirrer, dropping funnel and a 2-ft. reflux condenser. About 2 cc. of ethyl bromide and 10 cc. of isopropyl chloride were added, and the mixture was warmed to initiate the reaction. Isopropyl chloride (330 g.) was then added, dropwise, at such a rate that the mixture refluxed. After all of the chloride had been added, the mixture was refluxed for one-half hour.

Phenylacetic acid (240 g.), dissolved in 2 liters of dry benzene, was added to the stirred solution at such a rate that the mixture refluxed. After the addition was completed, the material was refluxed (about 12 hours) until no more gas was evolved. Since a large volume of propane was evolved during and after the addition of the phenylacetic acid, this operation should be carried out in a hood or the gas should be passed through a tube which carries it out of the laboratory.

The mixture was cooled in an ice-bath, and the dropping funnel was replaced by the side-arm of a distillation flask. The side-arm was made of wide glass tubing and was bent at a right angle. The horizontal section of the side-arm should be about 6 inches long and the vertical section should be long enough so that after it has been inserted into the reaction flask the end of the side-arm is about 1 inch above the surface of the stirred liquid. Paraformaldehyde (140 g.) (Mallinckrodt), which had been dried for two days in a desiccator over phosphorus pentoxide, was placed in the distillation flask which was heated in an oil-bath at 180-200°. The formaldehyde was carried into the vigorously-stirred mixture by a slow stream of dry nitrogen. The latter operation required from three to three and one-half hours. The reaction mixture was then poured into a mixture of 300 cc. of concd. sulfuric acid and 3 liters of finely crushed ice which had been placed in a 2-gal. crock, and the mixture was stirred for one-half hour. The solid material was removed by filtration, the organic layer separated, and the aqueous layer, and also the filtered solid, were placed in the original reaction flask. The mixture was warmed on a steam-bath for one-half hour, or until most of the solid had disappeared, then thoroughly cooled, filtered, and extracted with three 300-cc. portions of ether. The ether extracts and the organic layer were combined, and the solvents were removed under reduced pressure until the volume in the distillation flask had been reduced to about 500 cc. The mixture was then cooled for 12 hours, the precipitated tropic acid filtered, the filtrate concentrated to one-half of its original volume, cooled and more tropic acid removed by filtration. The crude tropic acid was heated with 500 cc. of benzene to dissolve unchanged phenylacetic acid, cooled, filtered, and washed with a small amount of cold benzene. The air-dried acid melted at 116-117°; yield 207-245 g. (71-83%).

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ANN ARBOR, MICHIGAN RECEIVED SEPTEMBER 18, 1951

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[1] D. Ivanov and S. Spassov, *Bull. soc. chim.*, [4] **49**, 19 (1931).

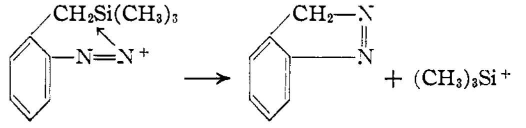
Aminoaryltrialkylsilanes

BY ROBERT A. BENKESER AND PHILIP E. BRUMFIELD

The successful isolation and identification of the isomeric nitro compounds from phenyltrimethylsilane and benzyltrimethylsilane[1] has provided a convenient approach to the preparation and study of the corresponding amines. Very few reports[2] of such amines are found in the literature, probably because compounds of this type suffer easy fission of their aromatic carbon-silicon bond which renders their preparation rather difficult. This tendency for cleavage of the silicon group becomes especially pronounced in acidic media, when the amine group is situated on the aromatic nucleus either *ortho* or *para* to the silicon. The instability of these aromatic silanes to strong acid renders the so-called "wet" reductions of the corresponding nitro compounds rather difficult since these procedures normally employ an acidic medium. In the work herein reported low pressure hydrogenation over a Raney nickel catalyst was found quite satisfactory for obtaining the aminosilanes. These compounds can be acetylated in the usual manner with little or no cleavage of the silicon group.

Five of these amines (*o*-aminophenyltrimethylsilane excepted) were diazotized and then coupled with β-naphthol to yield the corresponding azo compound. The formation of considerable amounts of tar *during* the diazotization indicated that the diazonium salts were unstable.

During the diazotization and subsequent reaction of *o*-aminobenzyltrimethylsilane there was isolated a 16% yield of indazole (I). This product can be explained if one assumes an intramolecular displacement of the trimethylsilyl group.



I

Experimental

Aminosilanes.—Weighed portions of up to 50 g. of the nitrosilanes[1] obtained from phenyltrimethylsilane and benzyltrimethylsilane were dissolved in 95% or absolute ethanol and reduced with hydrogen over Raney nickel. A Parr hydrogenator was used, with maximum pressures of 60

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[1] R. A. Benkeser and P. E. Brumfield, THIS JOURNAL, **73**, 4770 (1951).

[2] See F. S. Kipping and N. W. Cusa, *J. Chem. Soc.*, **79**, 1088 (1935); also B. N. Dolgov and O. K. Panina, *J. Gen. Chem.*, **18**, 1129 (1948), *C. A.*, **43**, 1737 (1949); and R. F. Fleming, U. S. Patent 2,386,452 (1945).

TABLE I

	Aminophenyltrimethylsilanes							Acetyl derivatives		
	B.p. (10 mm.)	$n^{20}D$	d^{20}_4	M_D (obsd.)	M_D (calcd.)	Si, % Calcd.	Si, % Found	M.p., °C.	Si, % Calcd.	Si, % Found
Ortho	101	1.5388	0.952	54.38	54.45	16.98	16.99	130–130.5	13.53	13.70
Meta[a]	111	1.5362	.947	54.44	54.45	16.98	16.96	114–115	13.53	13.83
Para	113	1.5393	.947	54.73	54.45	16.98	16.57	169–170	13.53	13.72

[a] It must be kept in mind that the nitro compound here was adjudged to be only 95% pure.

	β-Naphthol coupling products							
	M.p., °C.	Si, % Calcd.	Si, % Found	N, % Calcd.	N, % Found	Yield, %	Color	Crystallizing solvent
Meta	94–95	8.76	8.68	8.74	8.95	58	Red needles	Acetic acid
Para	94–95	8.76	8.48	8.74	8.94	50	Red-orange	Acetic acid

TABLE II

	Aminobenzyltrimethysilanes							Acetyl derivatives		
	B.p. (10 mm.)	$n^{20}D$	d^{20}_4	M_D (obsd.)	M_D (calcd.)	Si, % Calcd.	Si, % Found	M.p., °C.	Si, % Calcd.	Si, % Found
Ortho	114	1.5345	0.939	59.41	59.01	15.66	15.47	117–117.5	12.69	12.40
Para	119	(m.p. 33.5–34°)		...	...	15.66	15.85	132–133	12.69	12.84

	β-Naphthol coupling products							
	M.p., °C.	Si, % Calcd.	Si, % Found	N, % Calcd.	N, % Found	Yield,[a] %	Color	Crystallizing solvent
Ortho	97–98	8.39	8.15	8.38	8.31	12	Orange	Acetic acid
Para	126–127	8.39	8.25	8.38	8.82	19	Red	Acetic acid

[a] It is entirely possible that these yields can be improved since the optimum conditions were not investigated.

p.s.i. After absorption of the calculated amount of hydrogen, the catalyst was removed by filtration through a layer of Celite and the alcohol was removed by distillation. The residual amine was fractionally distilled through an efficient column at 10 mm. pressure. All amines were initially clear colorless liquids, but darkened on standing. The properties of these amines are given in Tables I and II.

The reduction of *o*-nitrophenyltrimethylsilane required careful control, in order to avoid excessive cleavage to give aniline. By carrying out the reduction in 95% ethanol, wrapping the reduction bottle in damp cloths, and terminating the reduction as soon as the calculated amount of hydrogen was absorbed, it was possible to obtain an 83% yield of *o*-aminophenyltrimethylsilane, with minor amounts of aniline and tarry pot residue.

The reduction of *m*-nitrophenyltrimethylsilane (95% pure)[1] and *p*-nitrophenyltrimethylsilane was carried out with no unusual precautions to give 75–85% yields of *m*-aminophenyltrimethylsilane and *p*-aminophenyltrimethylsilane, respectively. Very small amounts of aniline and tars were formed.

The reduction of *o*-nitrobenzyltrimethylsilane was found to take place very slowly, requiring 20 to 50 hours to obtain complete reduction. A maximum yield of 90% of *o*-aminobenzyltrimethylsilane was obtained from 39 g. of the nitrosilane in 50 ml. of absolute ethanol.

The reduction of *p*-nitrobenzyltrimethylsilane proceeded in a normal manner, requiring about 4 to 8 hours and giving about 85% yields of *p*-aminobenzyltrimethylsilane.

Acylation of Aminosilanes.—Small portions (0.5 g.) of the amines were dissolved in 3 to 5 ml. of acetic anhydride, with slight cooling. After solution was complete, 20 to 30 ml. of water was added and the mixture was cooled in an ice-bath. The waxy solids obtained were crystallized from hot petroleum ether (90–100°). Virtually quantitative yields of the acetyl derivatives were obtained, with properties as shown in Tables I and II.

Diazotization of Aminosilanes and Coupling with β-Naphthol.—The following procedure is typical of that employed in the diazotization and coupling of the amines.

Weighed portions (4 to 12 g.) of the aminosilanes were added to a mixture of 50 to 100 g. of crushed ice and a slight excess of dilute hydrochloric acid. In all cases the amine hydrochloride separated as a white solid. A dilute ice cold solution of the calculated amount of sodium nitrite was added rapidly (2 to 5 min.) with vigorous stirring. Most of the precipitated hydrochloride reacted in a short time, giving an orange diazonium solution. The solution darkened rapidly and formed dark tarry material. Within 10 min. of the start of the reaction, the diazonium solution was filtered rapidly through a glass wool plug into a cold dilute solution of the calculated amount of β-naphthol, containing a slight excess of sodium hydroxide. This reaction mixture was stirred rapidly and red solid particles separated usually along with dark tarry material. After about 20 min., acetic acid was added, if required, to give a slightly acid solution, and the product was filtered. The red gummy solid was dissolved in a small amount of benzene and poured into a chromatographic column, packed with activated alumina and Celite (50–50 by volume). The silicon-containing dye was collected in the first red area carried through the column by the benzene used as the elution solvent. Subsequent fractions obtained from the column contained mixtures of cleavage products, tars and unreacted β-naphthol. The product was crystallized from acetic acid, containing small amounts of water. Properties and yields of the azo compounds are given in Tables I and II.

Several attempts to obtain a coupling product from the ortho amine were not successful.

Action of Nitrosyl Chloride on *o*-Aminobenzyltrimethylsilane.—An ethereal solution of 25.6 g. (0.14 mole) of *o*-aminobenzyltrimethylsilane was cooled to −10° in an ice-salt-bath. With mechanical stirring, a cold solution of 9.6 g. (0.15 mole) of nitrosyl chloride in ether was added through a condenser cooled with Dry Ice. Addition was carried out slowly, the reaction mixture becoming orange and cloudy and finally forming black tar. After reaction was complete, the ether and any unreacted nitrosyl chloride were removed by vigorous suction with a water-pump. Ice cold water was added and one portion of the black solution resulting was added to boiling water in an attempt to form the phenol. The remainder of the diazonium solution was added to a solution of excess potassium iodide. Steam distillation of both portions of the reaction gave small amounts of dark oil and some yellow solid. Distillation of the organic material from either phase of the reaction gave no identifiable material other than this solid. Combination of the solid from both phases gave 2.7 g. (16%) of indazole, m.p. 147–148°, identified by an undepressed melting point with an authentic sample.[3]

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(3) See *Org. Syntheses*, **20**, 73 (1940).

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RECEIVED JULY 23, 1951

The Ethanolysis of Allyl Benzenesulfonate

BY CLARENCE G. BERGSTROM AND SAMUEL SIEGEL

In connection with another investigation[1] information on the kinetics of the ethanolysis of allyl

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(1) C. G. Bergstrom and S. Siegel, THIS JOURNAL, **73**, 145 (1951).

benzenesulfonate was needed. The displacement of the benzenesulfonate group from a saturated carbon atom is analogous to the displacement of the chloro group[2] and the ethanolysis of allyl benzenesulfonate was expected to be faster than ethyl benzenesulfonate[3] and to be markedly accelerated by the ethoxide ion.[4] This was found to be the case.

Bimolecular rate constants for the reaction of the ester with sodium ethoxide in anhydrous ethanol were obtained at three temperatures. The constants were reproducible to ±2%. There was no noticeable drift in the constants calculated for a run, which suggests that the reaction of the ester with the solvent was negligible. However, at the concentrations of sodium ethoxide used in this study, the first-order reaction with the solvent, measured independently, does contribute about 4 to 5%[5] to the over-all solvolysis of allyl benzenesulfonate. This indicated correction was not made in calculating the second-order rate constants because the correction would be of the order of magnitude of the uncertainty in the measurements. Furthermore, the correction is small compared with the variation in the constant (k_2) which is expected if the initial concentration of reactants was varied over a wider range.[5] The rate was essentially unchanged in a medium containing one per cent. of water. This is a behavior typical of the S_N2 type of displacement reaction.[4]

The preparation of allyl benzenesulfonate from allyl alcohol and benzenesulfonyl chloride was improved by the use of 2,4,6-collidine in place of pyridine.[6] Apparently the formation of quaternary ammonium salts is minimized by the use of a more sterically hindered base.

Experimental

Allyl Benzenesulfonate.—Allyl alcohol, obtained from the Paragon Chemical Company, was dried by an azeotropic distillation with carbon tetrachloride. The physical properties of the purified material were b.p. 95.0°; d^{25}_4 0.850; n^{25}_D 1.4113; (lit.[7] b.p. 96–97°; d^{20}_4 0.857; n^{20}_D 1.4134). Benzenesulfonyl chloride was distilled *in vacuo* before it was used; b.p. 85.0–86.5° (1.5 mm.).

To a mixture of allyl alcohol (19.2 g.) and 2,4,6-collidine (80 ml.) cooled to −4°, benzenesulfonyl chloride (53.0 g.) was added dropwise, at a rate which permitted the temperature of the reactants to remain between 0 and −5°. The mixture was stirred for one hour after the acid chloride had been added and the internal temperature dropped to −10°. Sulfuric acid (75 ml. of 10 *N*) was added at such a rate that the temperature remained between −10 and 0°. The ester separated from the solution and was taken up in chloroform, was washed with 2.5 *N* sulfuric acid and was dried over anhydrous potassium carbonate. The chloroform was evaporated and the ester was distilled; b.p. 98° (0.4 mm.); $d^{25.3}_4$ 1.204; n^{25}_D 1.5177; yield 39.6 g. (66% theoretical). The product gave no precipitate with an alcoholic solution of silver nitrate; sapn. equiv. calcd., 198.2; found, 196.2, 195.9.

Measurement of the Reaction of Allyl Benzenesulfonate with Sodium Ethoxide.—All volumetric apparatus was calibrated at the various temperatures used in the usual manner. The temperature, controlled to ±0.05°, was measured by thermometers calibrated by comparison with a platinum resistance thermometer. The solvent, anhydrous ethanol, was prepared from a commercial grade of absolute alcohol and was distilled from a mixture of sodium ethoxide and diethyl phthalate[8] directly into the volumetric flasks in which the various solutions were prepared. All exits of the distilling apparatus were closed with tubes containing indicating Drierite. A solution of sodium ethoxide in absolute alcohol was prepared by dissolving sodium in 100 ml. of alcohol to give a solution of double the concentration desired for the rate study. To standardize this solution, two samples were removed with a 10-ml. pipet and titrated against 0.02 *M* hydrochloric acid using phenolphthalein as the indicator. Fifty ml. of the standardized solution was transferred by pipet to a 100-ml. volumetric flask, and alcohol was distilled into the flask until the calibration mark was almost reached. The sodium ethoxide solution was then brought to the desired temperature in the thermostat. The sample of ester was injected into the flask from a weight pipet. The time at which the ester sample was injected was taken as the starting time of the reaction. After the sample was added, the contents of the flask were mixed and alcohol was added to bring the liquid to the calibration mark. One-tenth aliquots were withdrawn and the samples were placed in stoppered six-inch test-tubes which had previously been brought to the temperature of the thermostat.

The reaction was quenched when the contents of a tube was poured into an iodine flask containing a cold mixture of 10 ml. of carbon tetrachloride, phenolphthalein indicator and a slight excess of standard 0.02 *M* hydrochloric acid solution. The excess acid was titrated as rapidly as possible with 0.04 *N* sodium hydroxide. The end-point faded slowly.

Measurement of the Reaction of Allyl Benzenesulfonate with Ethyl Alcohol.—The solutions were prepared in 100-ml. volumetric flasks in the manner described previously but omitting the sodium ethoxide. At suitable intervals a 10-ml. aliquot was removed by pipet and introduced into 20 ml. of cold carbon tetrachloride. This effectively stopped the reaction. Cold water (25 ml.) was added and the mixture shaken to extract the acid and alcohol from the carbon tetrachloride. The mixture was then titrated quickly with standard 0.04 *N* sodium hydroxide to the phenolphthalein end-point. To obtain a value of the titer for complete reaction, an aliquot was transferred to a flask containing 20 ml. of water and heated for eight hours at 70°. This value was taken to be equivalent to the initial concentration of the ester (a).

Treatment of Results.—The second-order rate constants k_2 were calculated from the formula

$$k_2(t_2 - t_1) = \frac{2.303}{(b - a)} \log \frac{(a - x_1)}{(a - x_2)} - \log \frac{(b - x_2)}{(b - x_1)}$$

where k is the rate constant, a and b the initial concentrations, x the transformation variable and t the time.

The rate constant is a weighted average of all of the possible point combinations and is given by

$$k_2 = \frac{k_i w_i}{w_i}$$

$$w = (t_2 - t_1)(x_2 - x_1)$$

Hydrolysis of the sample of allyl benzenesulfonate used shows that somewhat more than the theoretical amount of acid is produced. This is assumed to be due to the presence of benzenesulfonyl chloride. In calculating the rate constants, it was assumed that the benzenesulfonyl chloride reacted before the first point was taken to give ethyl benzenesulfonate, which was considered inert. The reaction of benzenesulfonyl chloride has the effect of decreasing the initial ethoxide concentration by an amount equal to the amount of benzenesulfonyl chloride in the ester sample. Actually, the correction was insignificant.

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[2] H. R. McCleary and L. P. Hammett, *ibid.*, **63**, 2254 (1941).

[3] M. S. Morgan and L. H. Cretcher, *ibid.*, **70**, 375 (1948).

[4] E. D. Hughes, *Trans. Faraday Soc.*, **37**, 603 (1941).

[5] J. D. Roberts, W. G. Young and S. Winstein, THIS JOURNAL, **64**, 2157 (1942).

[6] R. S. Tipson, *J. Org. Chem.*, **9**, 235 (1944).

[7] R. Delaby and P. Dubois, *Compt. rend.*, **188**, 710 (1929).

[8] R. H. Manske, THIS JOURNAL, **53**, 1106 (1931).

TABLE I

RATE OF REACTION OF ALLYL BENZENESULFONATE WITH NaOEt IN ETHANOL AT 19.7°

Allyl benzenesulfonate, 0.0317 *M*; sodium ethoxide, 0.0398 *M*

Time, min.	Reacted, %	$k_2 \times 10^3$ (l. mole^{-1} sec.$^{-1}$)
39.2	19.6	2.67
52.7	27.9	3.07
69.3	32.2	2.80
83.5	35.0	2.62
101.7	41.0	2.73
151.2	52.1	2.75
220.3	61.6	2.67
307.1	71.2	2.73
	Weighted average	2.68
	Average	2.76 ± 0.09

The first-order rate constants were calculated from the equation

$$k_1 = \frac{2.303}{t} \times \log \frac{a}{(a - x)}$$

and the recorded value is an average of the individual values for k_1. The initial concentration of ester is represented by *a*, the other symbols are as given above. The variation in the rate constants for the runs at 20° was greater than those measured at higher temperatures. However, the estimated deviation in the constants is approximately 2 to 4%.

TABLE II

FIRST ORDER REACTION OF ALLYL BENZENESULFONATE WITH ABSOLUTE ETHANOL AT 25.10°

Allyl benzenesulfonate, 0.0345 *M*

Time, min.	Reacted, %	$k_1 \times 10^6$ (sec.$^{-1}$)
165	7.4	7.71
495	21.5	8.15
1213	44.5	8.10
1707	56.1	8.03
2702	72.4	7.93
4109	86.1	8.00
	Average	8.00 ± 0.11

TABLE III

REACTION RATES FOR THE ETHANOLYSIS OF ALLYL BENZENESULFONATE

Temp., °C.	Ester, mole/l.	NaOEt, mole/l.	$k_1 \times 10^6$, sec.$^{-1}$	$k_2 \times 10^3$, l. mole^{-1} sec.$^{-1}$
25.36	0.0469	0.0432	..	4.90
25.36	.0287	.0440	..	5.18
25.36	.0346	.0430	..	5.23^a
19.70	.0317	.0398	..	2.68
19.70	.0304	.0445	..	2.63
19.70	.0317	.0422	..	2.73
14.70	.0250	.0448	..	1.57
14.70	.0287	.0418	..	1.52
34.79	.0344	....	23.3	..
34.79	.0492	....	23.8	..
25.10	.0345	....	8.0	..
25.10	.0419	....	7.9	..
20.15	.0408	....	4.5	..
20.15	.0332	....	4.2	..

^{a} Solvent: 99% ethanol and 1% water.

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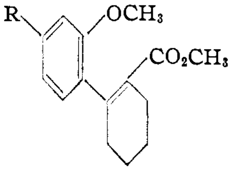
RECEIVED JANUARY 31, 1951

Coumarins as Possible Synthetic Intermediates[1]

BY V. BOEKELHEIDE AND A. P. MICHELS

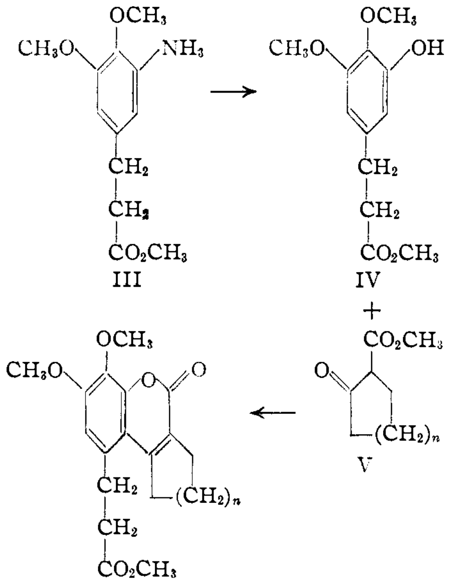
The von Pechmann coumarin condensation[2] is a convenient method for linking substituted aromatic compounds with alicyclic derivatives. Since the lactone ring of the resulting coumarins is susceptible to cleavage, intermediates can readily be obtained which would appear to have some value for the synthesis of certain natural products. It is the purpose of this note to describe some preliminary experiments directed toward this end.

As a model study directed toward the synthesis of morphine analogs, the intermediates I and II were prepared and treated with ethyl cyanoacetate in an attempt to obtain a Michael condensation. In each case the Michael condensation failed completely. Our work which was completed prior to recent publications on the limited reactivity of phenylcyclohexenone derivatives in the Michael condensation,[3,4,5] is further evidence of the limitations of the Michael reaction when applied to highly substituted molecules.



I, R = $-CH_3$
II, R = $-OCH_3$

Another possible application of coumarins as synthetic intermediates would be the synthesis of colchicine analogs. Thus, the condensation of a suitable phenol (IV) with β-keto esters, such as V, would yield intermediates of some promise for the synthesis of colchicine analogs in which the nature of ring C might readily be varied.[6] When



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[1] Abstracted from the M.S. Thesis of A. P. Michels, 1949.

[2] H. von Pechmann and C. Duisberg, *Ber.*, **16**, 2119 (1883).

[3] G. F. Woods, THIS JOURNAL, **69**, 2549 (1947).

[4] W. E. Bachmann and E. J. Fornefeld, *ibid.*, **72**, 5529 (1950).

[5] C. F. Koelsch, *ibid.*, **73**, 2951 (1951).

[6] For a discussion of ring C of colchicine, see H. R. V. Arnstein, D. S. Tarbell, G. P. Scott and H. T. Huang, *ibid.*, **71**, 2448 (1949).

the synthesis of III was attempted for this purpose, it was found that vanillin could be converted by the successive steps of nitration, condensation with malonic acid, and reduction to III, but that III could not be successfully diazotized to yield IV. However, other approaches utilizing coumarins for the synthesis of colchicine analogs are under investigation.

Experimental[7]

Methyl 2-(2'-Methoxy-4'-methylphenyl)-1-cyclohexenecarboxylate (I).—In accordance with the method of Canter and Robinson,[8] 14.3 g. of 3-methyl-7,8,9,10-tetrahydro-6-dibenzopyrone[9] was dissolved in a boiling solution of 100 ml. of methanol and 100 ml. of 20% aqueous sodium hydroxide. The solution was cooled to 50° and 60 g. of dimethyl sulfate was added slowly with stirring followed by 200 ml. of a 20% sodium hydroxide solution. An additional 30 g. of dimethyl sulfate was then added dropwise, the solution was made basic and the mixture was extracted with ether. After the ethereal extract had been washed with water and dried, the ether was removed and the residue was distilled yielding 11.0 g. (62%) of a light yellow oil; b.p. 165–175° at 5 mm., $n^{27}\mathrm{D}$ 1.5465.

Anal. Calcd. for $C_{16}H_{20}O_3$: C, 73.84; H, 7.69. Found: C, 73.70; H, 7.71.

2-(2'-Methoxy-4'-methylphenyl)-cyclohexenecarboxylic Acid.—A solution of 4.0 g. of I in 30 ml. of methanol containing 5.0 g. of potassium hydroxide was boiled under reflux for two hours. When the cold reaction mixture was acidified with dilute hydrochloric acid, a white solid separated. This, on recrystallization from an ethanol–water mixture, gave 3.0 g. (85%) of white crystals, m.p. 175–176°.

Anal.[10] Calcd. for $C_{15}H_{18}O_3$: C, 73.17; H, 7.32. Found: C, 73.12; H, 7.35.

Methyl 2-(2',4'-Dimethoxyphenyl)-cyclohexenecarboxylate (II).—This was prepared in the same manner as described for I. From 6.0 g. of 3-hydroxy-7,8,9,10-tetrahydro-6-dibenzopyrone)[9] there was obtained 2.5 g. (39%) of a light yellow oil, b.p. 175–180° at 5 mm.

Anal. Calcd. for $C_{16}H_{20}O_4$: C, 69.53; H, 7.21. Found: C, 69.01; H, 7.06.

Attempts to obtain a condensation of either I or II with ethyl cyanoacetate under the usual conditions of the Michael condensation[11] were entirely unsuccessful and resulted in recovery of starting material. Also, hydrogen cyanide would not add to I.

3-Methoxy-4-hydroxy-5-nitrocinnamic Acid.—A solution of 32.5 g. of 5-nitrovanillin,[12] 88.0 g. of malonic acid and 2 ml. of piperidine in 100 ml. of dry pyridine was heated on the steam-bath for three hours, and then poured into a mixture of 100 g. of cracked ice and 80 ml. of concd. hydrochloric acid. The dark yellow solid, which separated, was washed with water and recrystallized from ethanol. There was obtained 36.0 g. (91%) of light yellow crystals, m.p. 230–231°.

Anal. Calcd. for $C_{10}H_9NO_6$: C, 50.25; H, 3.76; neut. equiv., 119. Found: C, 50.36; H, 3.80; neut. equiv., 124.

3-Methoxy-4-hydroxy-5-aminocinnamic Acid.—A solution of 10.0 g. of 3-methoxy-4-hydroxy-5-nitrocinnamic acid in 150 ml. of absolute ethanol was subjected to hydrogenation in the presence of Raney nickel catalyst at room temperature and 3 atm. pressure of hydrogen. Three moles of hydrogen was readily absorbed (90 min.). After removal of the catalyst and concentration of the solvent, there separated 8.3 g. (95%) of white crystals, m.p. 185–186°.

Attempts to convert this product to the corresponding phenol, 3-methoxy-4,5-dihydroxycinnamic acid, by means of the diazonium salt gave only intractable tars. Also attempted hydrogenation to the corresponding hydrocinnamic acid, using Raney nickel catalyst in the presence of base, failed.

Anal. Calcd. for $C_{10}H_{11}NO_4$: C, 57.41; H, 5.30. Found: C, 57.39; H, 5.20.

Methyl 3,4-Dimethoxy-5-nitrocinnamate.—A solution of 7.0 g. of 3,4-dimethoxy-5-nitrocinnamic acid[13] in 120 ml. of a saturated solution of methanolic hydrogen chloride was allowed to stand until separation of a yellow solid occurred. This was removed, washed with water and recrystallized from methanol. There was obtained 3.5 g. (48%) of creamy white crystals, m.p. 105–106°.

Anal. Calcd. for $C_{12}H_{13}NO_6$: C, 53.92; H, 4.87. Found: C, 54.22; H, 4.70.

Methyl 3,4-Dimethoxy-5-aminohydrocinnamate Hydrochloride (III).—A solution of 10.0 g. of methyl 3,4-dimethoxy-5-nitrocinnamate in 100 ml. of methyl acetate was subjected to low pressure hydrogenation using Adams catalyst. Four molar equivalents of hydrogen were rapidly absorbed. After removal of the catalyst and solvent, the residue was taken up in ether and treated with dry hydrogen chloride. This caused the separation of 8.9 g. (92%) of hygroscopic white crystals, m.p. 208–209° dec.

Attempts to convert III to IV by the usual procedures through the diazonium salt yielded only black intractable tars.

Anal. Calcd. for $C_{12}H_{18}NO_4Cl$: C, 52.27; H, 6.57. Found: C, 52.87, 51.60; H, 6.30, 6.21.

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[7] Analyses by Mrs. G. L. Sauvage.

[8] F. W. Canter and R. Robinson, *J. Chem. Soc.*, 1 (1931).

[9] H. K. Sen and U. Basu, *J. Indian Chem. Soc.*, **5**, 467 (1928).

[10] We are indebted to Mr. Nicholas Parente for the first preparation of this compound.

[11] R. Connor and W. R. McClellan, *J. Org. Chem.*, **3**, 570 (1939).

[12] K. H. Slotta and G. Szyska, *Ber.*, **68**, 184 (1935).

Certain Derivatives of 2,5-Dihydroxyphenylacetic Acid

BY R. W. BOST[*] AND C. A. HOWE

Since 2,5-dihydroxybenzoic acid, gentisic acid, has been reported to exhibit anti-rheumatic activity,[1] it seemed desirable to establish whether 2,5-dihydroxyphenylacetic acid, homogentisic acid, and certain of its derivatives showed similar action.

2,5-Dimethoxyphenylacetic acid was synthesized through the Willgerodt reaction from 2,5-dimethoxyacetophenone by the procedure of Abbott and Smith.[2] Similar procedures were utilized to synthesize the 2,5-diethoxy-, 2,5-di-*n*-propoxy- and 2,5-di-*n*-butoxyphenylacetic acids. The amides and methyl esters of these four 2,5-dialkoxyphenylacetic acids were prepared by standard procedures. 2,5-Dihydroxyphenylacetic acid was synthesized by the demethylation of 2,5-dimethoxyphenylacetic acid[2] and also by the method of McElvain and Cohen.[3] The intermediate 2,5-dialkoxyacetophenones were prepared from the appropriate 1,4-dialkoxybenzene by Friedel–Crafts acylation.[2]

The molar refractions of the 2,5-dialkoxyacetophenones and methyl 2,5-dialkoxyphenylacetates show a considerable and fairly constant exaltation.

None of the compounds tested exhibited appreciable anti-rheumatic activity.

Experimental

2,5-Dialkoxyacetophenones.—The general method of Abbott and Smith[2] for the preparation of 2,5-dimethoxyacetophenone by the Friedel–Crafts acylation of 1,4-dimethoxybenzene was used. In the case of the di-*n*-propoxy- and di-*n*-butoxy-compounds, better yields were obtained if the aluminum chloride complex was hydrolyzed three hours after combination of the reactants was completed rather than allowing the mixture to stand overnight.

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[*] Deceased.

[1] K. Meyer and C. Ragan, *Science*, **108**, 281 (1948).

[2] L. DeF. Abbott and J. D. Smith, *J. Biol. Chem.*, **179**, 365 (1949).

[3] S. M. McElvain and H. Cohen, THIS JOURNAL, **64**, 264 (1942).

TABLE I

General name	Alkoxy groups	Yield, %	B.p., °C.[a] or crystn. solv. °C.	Mm.	M.p.,[b] °C.	Molecular formula	Analyses, % Carbon		Analyses, % Hydrogen	
							Calcd.	Found	Calcd.	Found
2,5-Dialkoxyacetophenone	CH_3O	68	116	2	21[c,d]	$C_{10}H_{12}O_3$				
	C_2H_5O	52	129	3	41[e]	$C_{12}H_{16}O_3$				
	n-C_3H_7O[f]	63	138	2	19[c]	$C_{14}H_{20}O_3$	71.1	70.8	8.53	8.67
	n-C_4H_9O[g]	72	152	2	26[c]	$C_{16}H_{24}O_3$	72.7	72.6	9.15	9.08
2,5-Dialkoxyphenylacetic acid	CH_3O	64	Water		123[h]	$C_{10}H_{12}O_4$				
	C_2H_5O	37	37% EtOH		89	$C_{12}H_{16}O_4$	64.3	64.3	7.22	7.25
	n-C_3H_7O	63	Pet.[i]		66	$C_{14}H_{20}O_4$	66.6	66.3	7.99	8.17
	n-C_4H_9O	29	30% EtOH		53	$C_{16}H_{24}O_4$	68.6	68.5	8.63	8.44
2,5-Dialkoxyphenylacetamide	CH_3O	82	Water		133	$C_{10}H_{13}O_3N$	31.8[j]	32.1[j]	7.18[k]	7.01[k]
	C_2H_5O	70	Water		111	$C_{12}H_{17}O_3N$			6.28[k]	6.19[k]
	n-C_3H_7O	88	C_6H_6–Pet.[i]		115	$C_{14}H_{21}O_3N$			5.57[k]	5.55[k]
	n-C_4H_9O	86	C_6H_6–Pet.[i]		88	$C_{16}H_{25}O_3N$			5.02[k]	4.99[k]
Methyl 2,5-dialkoxyphenylacetate	CH_3O	93	128	3	44[l]	$C_{11}H_{14}O_4$				
	C_2H_5O	69	127	2	[m]	$C_{13}H_{18}O_4$	65.5	65.0	7.60	7.54
	n-C_3H_7O	84	134	2	[m]	$C_{15}H_{22}O_4$	67.6	67.3	8.32	8.49
	n-C_4H_9O[n]	50	178	3	18[c]	$C_{17}H_{26}O_4$	69.4	69.2	8.90	9.24

[a] Uncorrected; lower limit of 2 degree range listed. [b] Taken in apparatus calibrated with standard compounds. [c] Freezing point. [d] Lit.: 20–22° (ref. 4). [e] Lit.: 42° (ref. 4.) [f] 2,4-Dinitrophenylhydrazone, m.p. 107°. *Anal.* Calcd. for $C_{20}H_{24}O_6N_4$: N, 13.45. Found: N, 13.68. [g] 2,4-Dinitrophenylhydrazone, m.p. 116°. *Anal.* Calcd. for $C_{22}H_{28}O_6N_4$: N, 12.61. Found: N, 12.61. [h] Lit.: 123–124° (ref. 2). [i] Pet. ether, b.p. 60–90°. [j] Methoxyl. [k] Nitrogen %. [l] Lit.: 45° (ref. 5). [m] Did not solidify after 4 hr. in Dry Ice-bath. [n] n^{25}_D 1.4954.

TABLE II

Alkoxy groups	T. °C.	n^t_D	d^t_4	Molar refraction Found[a]	Molar refraction Calcd.[c]
		2,5-Dialkoxyacetophenones			
CH_3O	20	1.5430	1.1401[b]	49.82	48.77[c]
n-C_3H_7O	25	1.5150	1.0368	68.72	67.24[c]
n-C_4H_9O	30	1.5067	1.0076	78.07	76.47[c]
		Methyl 2,5-dialkoxyphenylacetates			
C_2H_5O	25	1.5070	1.0997	64.38	63.57
n-C_3H_7O	25	1.4991	1.0564	74.05	72.81

[a] From Lorentz–Lorenz equation. [b] Lit.: 1.1385 (ref. 4). [c] Includes exaltation of 0.69 for conjugation of carbonyl and aromatic double bonds.

The yields, physical constants and analyses are listed in Tables I and II.

2,5-Dialkoxyphenylacetic Acids.—The general method of Abbott and Smith[2] for the preparation of 2,5-dimethoxyphenylacetic acid from 2,5-dimethoxyacetophenone by the Willgerodt reaction was used. In the case of the di-*n*-propoxy- and di-*n*-butoxy-compounds, acidification of the basic hydrolysis solution yielded a dark oil which was dissolved in ether and extracted repeatedly with potassium bicarbonate solution followed by acidification of the aqueous extracts. The yields, physical constants, analyses and crystallization solvents are listed in Table I.

2,5-Dialkoxyphenylacetamides.—One-tenth of a mole of the 2,5-dialkoxyphenylacetic acid and 22 ml. of thionyl chloride were refluxed for 30 minutes. The resulting solution was poured slowly into 100 ml. of ice-cold concentrated ammonium hydroxide. The crude product was filtered off and recrystallized. The yields, physical constants, analyses and crystallization solvents are listed in Table I.

Methyl 2,5-Dialkoxyphenylacetates.—One-tenth of a mole of the 2,5-dialkoxyphenylacetic acid and 22 ml. of thionyl chloride were refluxed for 30 minutes. Then 150 ml. of absolute methanol were added dropwise with cooling. After addition was complete, the reaction mixture was allowed to stand at room temperature for 30 minutes and then refluxed for 30 minutes. Excess volatile reagents and by-products were removed by evaporation, and the residual oil was fractionated twice through a 15-cm. Vigreux column. The yields, physical constants and analyses are listed in Tables I and II.

2,5-Dihydroxyphenylacetic Acid.—This compound was prepared in a yield of 76% by the demethylation of 2,5-dimethoxyphenylacetic acid[2] and in yields of 38–47% by the condensation of *p*-quinone with ketene diethylacetal followed by hydrolysis.[3]

Acknowledgments.—The authors are indebted to The Wm. S. Merrell Co., Cincinnati, Ohio, for a grant in support of this work and for the pharmacological testing of some of the compounds synthesized, and to the Tennessee Eastman Corporation, Kingsport, Tennessee, for a generous supply of the 1,4-dialkoxybenzenes used as starting materials.

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(4) I. M. Heilbron and H. M. Bunbury, "Dictionary of Organic Compounds," Vol. III, Oxford University Press, New York, N. Y., 1938, p. 568.

(5) *Ibid.*, Vol. II, p. 194.

(6) H. Gilman, "Organic Chemistry," 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1943, p. 1751.

The Preparation of Di- and Triphenylacetonitrile and Their Cuprous Halide Complexes

BY WALTER M. BUDDE AND SYLVESTER J. POTEMPA

Although a good preparation for diphenylacetonitrile (II) has been described[1] it was decided to attempt a method which would involve fewer time-consuming steps and no lachrymatory intermediates. The process developed was the reaction of benzhydryl bromide (I) with anhydrous cuprous cyanide.

$$\underset{\text{I}}{(C_6H_5)_2CHBr} + CuCN \longrightarrow \underset{\text{II}}{(C_6H_5)_2CHCN} + CuBr$$

I was prepared in 70–75% yield by the action of phosphorus tribromide on benzhydrol. Heating I with a slight molar excess of oven-dried cuprous cyanide at 125° produced pure II in 75–80% yield after distillation. It was noticed that if impure I was used there was a pronounced tendency to form a stable complex molecule, III, dec. pt. 155°.

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(1) C. Robb and E. Schultz, *Org. Syntheses*, **28**, 55 (1948).

$$(C_6H_5)_2CHC{\equiv}N \longrightarrow CuBr$$
III

The chief impurities present in impure I were presumably benzhydrol and dibenzhydryl ether. Compounds of the type III have been previously reported[2] but the ones investigated heretofore were somewhat less stable. Attempts in this Laboratory to synthesize III by other methods were unsuccessful. The methods tried were heating II with freshly prepared cuprous bromide, heating II with a mixture of cupric bromide and activated copper powder, and heating a mixture of II, cupric bromide, and activated copper powder with acetonitrile as a solvent.

The structure of III was fairly well established by two means: (1) analytical data checked very closely with calculated values; (2) vacuum distillation of pure III produced practically theoretical amounts of II in the distillate and cuprous bromide in the residue. The possibility that III was a complex of the isonitrile type (IV) was rejected for three reasons: (1) Compounds of the type IV

$$(C_6H_5)_2CH{-}N{=}C \longrightarrow CuBr$$
IV

have been prepared[3] and all are described as being deeply colored, while III is colorless; (2) vacuum distillation was not considered sufficient to convert the isonitrile into the nitrile form. In other instances of these transitions longer heating was required[4]; (3) heating III above its decomposition point did not produce, even momentarily, a characteristic isonitrile odor.

Attempts to substitute benzhydryl chloride for I were abandoned because poor yields of II were produced each time (40–50%). A high-melting nitrogen-containing organic compound was isolated as a by-product but was not further identified. Even with pure benzhydryl chloride the corresponding complex molecule $(C_6H_5)_2CHCN \rightarrow CuCl$ was formed in considerable proportion. It was isolated as a light tan crystalline solid, dec. pt. 119–121°.

Heating purified trityl chloride with dry cuprous cyanide at 125° affords triphenylacetonitrile,[5] (V) in 65–70% yield. When impure trityl chloride was employed the chief product was the corresponding complex molecule VI. This compound is

$$(C_6H_5)_3C{-}CN \longrightarrow CuCl$$
VI

colorless when pure, but assumes a purplish color when allowed to stand in air. Qualitative analysis showed the expected elements to be present; distillation of the dry material produced the theoretical amounts of residual cuprous chloride and distilled triphenylacetonitrile. In this case it was established that the chief impurity present in the trityl chloride was triphenylcarbinol.

Experimental

All melting and decomposition points are corrected.

Benzhydryl bromide (I) b.p. 150–155°, 2 mm., m.p. 46° was prepared by a modification of the method of Claisen.[6]

Diphenylacetonitrile (II).—In a flask subsequently used for a vacuum distillation, was placed pure I (35.2 g., 0.143 mole) which was heated with stirring to 125° in an oil-bath. Cuprous cyanide (14.1 g., 0.157 mole) (J. T. Baker Chemical Co.), dried at 110° for two hours, was then added all at once. The mixture quickly darkened, and a heavy precipitate of cuprous bromide began to separate. The stirring and heating were continued for 45 minutes, and then a vacuum stillhead and receiver were attached to the reaction flask, and the entire mixture vacuum distilled. Precautions were taken to avoid bumping, and solidification of the product in the delivery tube. The colorless oil which distilled solidified in the receiver. This solid melted at 74–75°, and amounted to 20.6 g. (75%) (b.p. 158° at 4 mm.). Recrystallization from isopropyl alcohol gave a product melting at 74.5–75°. When larger amounts of the starting materials were used the percentage yields were a little higher (75–78%).

Formation of Diphenylacetonitrile–Cuprous Bromide Complex (III).—The greatest tendency for this product to form was noted when, in the preparation of I, petroleum ether was used in place of ether as an extraction solvent, and the benzhydryl bromide was not vacuum distilled. When molar quantities of undistilled I and cuprous cyanide were used as described in the above experiment, it was observed that after about one-half hour of heating at 125° the whole mass solidified and stopped the stirrer. The solid mixture was cooled, ground to a powder and extracted for five hours with benzene in a soxhlet extractor. Evaporation of the benzene gave 7.0 g. of impure II. The benzene-insoluble residue was further extracted with chloroform for six hours. The hot chloroform deposited 21.1 g. of the complex III in the form of hard, gleaming white prisms. The residue in the soxhlet cup consisted almost entirely of cuprous bromide and excess cuprous cyanide. In the several runs of this sort that were made the ratio of complexed to uncomplexed II was variable, ranging from about 4:1 to 2:1 by weight.

Anal. Calcd. for $C_{14}H_{11}BrNCu$: C, 49.94; H, 3.29; Br, 23.74; N, 4.16; mol. wt., 336.73. Found: C, 49.98; H, 3.24; Br, 23.64; N, 4.16; mol. wt. (ebulliometrically in chloroform), 288.

Triphenylacetonitrile (V).—Purified trityl chloride (Eastman Kodak Co. product) m.p. 110° (15.8 g., 0.057 mole) was heated to 125° with mechanical stirring, and oven-dried cuprous cyanide (6.6 g., 0.0623 mole) was added. The mixture was heated and stirred for 1.5 hours, and it thickened slightly during this time. The cooled solid mixture was extracted with 100 ml. of boiling benzene, followed by two 30-ml. portions. The solid residue remaining weighed 5.94 g., which amounted to 98.5% of the theoretical amounts of cuprous chloride and excess cuprous cyanide. Upon evaporation of the filtered benzene extracts there remained 14.4 g. (94%) of impure triphenylacetonitrile, m.p. 101–104°. One recrystallization of this brown solid from isopropyl alcohol using decolorizing charcoal gave 9.5 g. (62%) of a white product which melted at 124–125°. The reported melting point[5] is 127.5°.

Formation of Triphenylacetonitrile–Cuprous Chloride Complex (VI).—When the above directions were followed using an old unpurified sample of commercial trityl chloride (m.p. 95–109°), the cooled benzene extract deposited 8.5 g. of a white solid. This material turned purple when exposed to the air. It was decomposed by dry distillation to give almost the theoretical amounts of triphenylacetonitrile in the distillate and cuprous chloride in the residue. The decomposition point of the complex was distinct, but above 190°. Qualitative analysis showed Cu, Cl and N to be present. The benzene extracts from which VI had been removed were evaporated. The residue consisted of triphenylacetonitrile, m.p. 101–105°.

Reaction of Benzhydryl Chloride with Cuprous Cyanide.—Benzhydryl chloride was prepared in 61% yield by a method analogous to that used for benzhydryl bromide. It distilled at 134–135° at 2 mm. A voluminous unidentified solid residue was left in the distillation flask. When benzhydryl chloride reacted with cuprous cyanide in the same manner as benzhydryl bromide (see above) the mixture partially solidified after one-half hour of heating. There could be isolated from the reaction mixture the complex of diphenyl-

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[2] H. Morgan, *J. Chem. Soc.*, 2901 (1923).

[3] I. Malatesta, *Gazz. chim. ital.*, **77**, 240 (1947).

[4] N. Sidgwick, "The Organic Chemistry of Nitrogen," Oxford Press, London, 1937, p. 318.

[5] E. Fischer and O. Fischer, *Ann.*, **194**, 261 (1878).

[6] L. Claisen, *Ann.*, **442**, 245 (1925).

acetonitrile and cuprous chloride by extraction with hot benzene, from which it crystallized on cooling.

Anal. Calcd. for $C_{13}H_{11}ClNCu$: C, 57.53; H, 3.79. Found: C, 57.34; H, 3.48.

Evaporation of the cooled benzene extracts afforded a 40–50% yield of II, admixed with the unidentified compound described below. If the original reaction mixture was distilled before extraction with benzene, there remained in the undistilled residue an organic compound of high melting point which contained nitrogen. In a run using the same amounts of starting materials as described for benzhydryl bromide, about 4–5 g. of this benzene-soluble compound was formed. Its identification was not undertaken.

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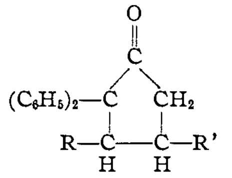
Synthesis of Diphenylalkylcyclopentanones

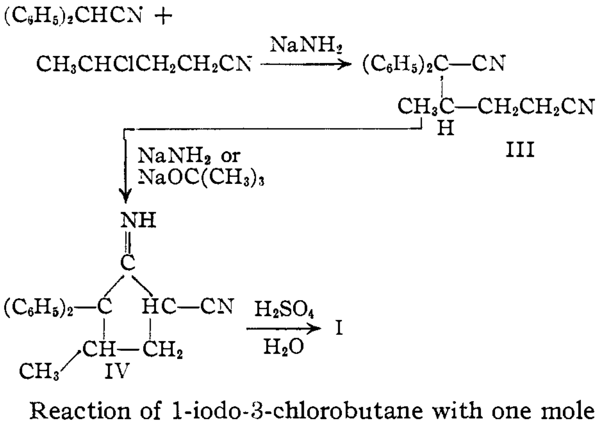
BY NELSON R. EASTON, HARRY E. REIFF, GEORGE SVARNAS AND VELMER B. FISH

No preparation of diphenylalkylcyclopentanones has been reported in the literature and due to their similarity to a deaminated, cyclized Methadone it seemed advisable to investigate the synthesis of compounds of this type.



I, R′ = H
R = CH_3
II, R′ = CH_3
R = H

Two examples—2,2-diphenyl-3-methylcyclopentanone (I) and 2,2-diphenyl-4-methylcyclopentanone (II) were selected. The synthesis of I is shown in the following scheme.



Reaction of 1-iodo-3-chlorobutane with one mole of sodium cyanide converted this compound to γ-chlorovaleronitrile, which was condensed with diphenylacetonitrile in the presence of sodamide to give III. However, considerable cyclization to IV occurred during this reaction. The linear compound III could then be cyclized with sodamide or in a better yield using sodium tertiary butoxide as the catalyst. The hydrolysis and decarboxylation of IV gave I.

The ketone II was prepared in a similar manner using γ-chloroisovaleronitrile.

γ-Chloroisovaleronitrile (V) was prepared from γ-chloroisobutyl bromide by treatment with an equivalent of sodium cyanide.

Experimental

The 1,3-dichlorobutane was prepared according to Clarke and Streight.[1] The 1-iodo-3-chlorobutane was prepared according to Hass and Huffman.[2]

Preparation of γ-Chlorovaleronitrile.—Into a three-neck one-liter flask equipped with a dropping funnel, a mechanical stirrer, and a gas trapped reflux condenser was placed 10.1 g. (0.206 mole) of sodium cyanide and 60 cc. of water. After solution of the sodium cyanide 200 cc. of 95% ethyl alcohol was added, followed by 37.5 g. (0.172 mole) of 1-iodo-3-chlorobutane. The mixture was refluxed for six hours and then cooled. The cooled solution was diluted with 225 cc. of water and the solution was then extracted with three 50-cc. portions of chloroform. The chloroform layers were separated and washed twice with an equal volume of half-saturated calcium chloride solution, and then washed twice with an equal volume of water. The organic layer was dried over calcium chloride and stored in the refrigerator in a container covered with aluminum foil to prevent decomposition. The solution was filtered and the filtrate subjected to a distillation to remove the chloroform. The residue was then distilled under reduced pressure and 14.6 g. (72.3% yield) of a clear colorless liquid with a boiling range of 95–110° at 40–44 mm. pressure was collected. Gresham[3] found the boiling point to be 55° at 2 mm.

Condensation of γ-Chlorovaleronitrile and Diphenylacetonitrile in the Presence of Sodamide.—Into a three-neck 500-cc. flask equipped with a dropping funnel, a mechanical stirrer, and a reflux condenser with attached calcium chloride drying tube was placed 250 cc. of dry benzene followed by 5.3 g. (0.136 mole) of sodamide. To this mixture was added with stirring, 25 g. (0.129 mole) of diphenylacetonitrile. The mixture was refluxed for three hours, during which time evolution of ammonia occurred (during this period the drying tube was removed for the condenser), and then cooled to room temperature. To the resulting mixture was added dropwise 14.6 g. (0.124 mole) of γ-chlorovaleronitrile. The mixture was refluxed for four hours, cooled and then poured into 300 cc. of water. The layers were separated, the benzene layer washed three times with an equal volume of water and then dried over anhydrous magnesium sulfate. After filtration of the magnesium sulfate, the benzene was removed from the solution by distillation. The resulting oil was placed in the refrigerator. Within 48 hours, partial crystallization had occurred. The oil was filtered and the crystalline solid was carefully washed with ether. Approximately 1.5 g. of a solid was obtained which, when recrystallized from methanol, yielded white crystals melting at 164–166°.

The balance of the oil and the ethereal washings when concentrated and then subjected to a series of fractional distillations at one mm. pressure, yielded 8.5 g. of diphenylacetonitrile from the fraction distilling at 0–150° and 1.5 g. of the cyclic ketimine from the fraction distilling at 150–210°. The total yield of 2,2-diphenyl-3-methyl-5-cyanocyclopentanone imine was 3 g. (8.8% yield).

Anal. Calcd. for $C_{19}H_{18}N_2$: N, 10.22. Found: N, 10.10.

Preparation of 2,2-Diphenyl-3-methylcyclopentanone.—Into a one-neck 200-cc. flask equipped with a reflux condenser was placed 1.4 g. (0.00511 mole) of finely divided 2,2-diphenyl-3-methyl-5-cyanocyclopentanone imine and a cold sulfuric acid solution made up of 1.5 cc. of water and 5 cc. of concentrated sulfuric acid. After the addition was complete, the flask was heated on a water-bath until solution occurred and then for 15 minutes longer. The solution was cooled and 25 cc. of water added. The mixture was then heated to reflux, at which time 30 cc. of glacial acetic acid was added to increase the miscibility of the two layers present, and the solution was refluxed for 25 hours. The reaction mixture was then cooled, diluted with 200 cc. of water, and extracted with three 40-cc. portions of ether. The ether layers were combined and washed with several portions of 5% sodium hydroxide solution, and dried over anhydrous magnesium sulfate. The solution was filtered and the filtrate concentrated under reduced pressure until the volume was reduced to 5–8 cc. (at this point some nearly white solid had formed) and was then stored in the

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[1] R. H. Clarke and H. R. L. Streight, *Trans. Roy. Soc. Can. Series* 3, Vol. 23, Sec. III (77) 1929.

[2] H. B. Hass and H. C. Huffman, THIS JOURNAL, **63**, 1233 (1941).

[3] Wm. F. Gresham, U. S. Patent 2,405,948.

refrigerator. Within 24 hours a crystalline mass had formed in the flask. The supernatant liquid was decanted and the solid was recrystallized from methanol. The one gram of product (78.3 yield) was then sublimed at one mm. pressure for further purification, and this procedure gave a white crystalline product melting at 92.5–94°.

Anal. Calcd. for $C_{18}H_{18}O$: C, 86.36; H, 7.25. Found: C, 86.20; H, 7.26.

Preparation of γ-Chloroisovaleronitrile.—γ-Chloroisobutyl bromide was prepared according to Hearne, *et al.*[4]

Into a three-neck three-liter flask equipped with a gas-trapped reflux condenser, a mechanical stirrer, and a dropping funnel were placed 100 ml. of water and 103 g. (2 moles) of sodium cyanide. After solution of the cyanide, 700 ml. of 95% ethyl alcohol was added, followed by 305 g. (1.78 moles) of γ-chloroisobutyl bromide. The mixture was refluxed for two hours, cooled, and 600 ml. of water was added, followed by 200 ml. of chloroform. The layers were separated, and the chloroform layer was washed with an equal volume of water. After drying over calcium chloride, the chloroform was removed from the solution at atmospheric pressure, and the residue was fractionated at 15 mm. pressure. The fraction boiling at 79–83° and weighing 58 g. (27.7% yield) was collected. Cloke, *et al.*,[5] found the boiling point to be 82–83° at 16 mm.

Condensation of γ-Chloroisovaleronitrile with Diphenylacetonitrile.—The sodium salt of 19.3 g. (0.1 mole) of diphenylacetonitrile was prepared by refluxing 4.3 g. (0.11 mole) of sodamide with diphenylacetonitrile in 300 ml. of dry benzene for 90 minutes. The mixture was cooled, and 22 g. (0.2 mole) of γ-chloroisovaleronitrile was added dropwise with stirring. The resulting mixture was refluxed for 12 hours, cooled and poured into an equal volume of water. The organic layer was separated, washed with water and dried over anhydrous magnesium sulfate. After removal of benzene under vacuum, the mixture was distilled until the vapor temperature reached 80° at 15 mm. Distillation at 2 mm. pressure gave as a first fraction diphenylacetonitrile, secondly an oil which was a mixture of diphenylacetonitrile and the product VI and a third fraction which was VII. The second fraction was cyclized as shown below.

Cyclization to 2,2-Diphenyl-4-methyl-5-cyanocyclopentanone Imine.—Into a three-neck 200-ml. flask equipped with a mechanical stirrer and a reflux condenser was placed 50 ml. of dry *t*-butyl alcohol and 0.2 g. of sodium metal. The mixture was refluxed until complete solution of the sodium occurred, and 8 g. of the second fraction from the preceding reaction, dissolved in 20 ml. of dry *t*-butyl alcohol, was added all at once. The mixture was refluxed for four hours, cooled and one ml. of water was added. The solution was evaporated to 50 ml., whereupon trituration with petroleum ether caused crystallization. After two recrystallizations from methanol, white crystals of 2,2-diphenyl-4-methyl-5-cyanocyclopentanone imine, melting at 133–135°, were obtained.

Anal. Calcd. for $C_{19}H_{18}N_2$: N, 10.22. Found: N, 10.12.

Preparation of 4-Methyl-2,2-diphenylcyclopentanone from the Iminonitrile VII.—A mixture of 2.3 g. of the iminonitrile (VII) 4.5 ml. of concd. sulfuric acid and 1.3 ml. of H_2O was warmed on a steam-bath until the solid dissolved and the resulting solution was heated on the steam-bath for 20 minutes. The solution was cooled and a mixture of 20 ml. of water and 20 ml. of acetic acid was added. The resulting mixture was refluxed for 20 hours. It was then cooled and extracted with ether. The ether layer, after being washed with water and then with a solution of sodium bicarbonate, was dried over magnesium sulfate. After distillation of the solvent an oily residue remained. This was dissolved in petroleum ether and the solution was cooled with Dry Ice, the crystals which separated were recrystallized from a mixture of methanol and water and gave 1.4 g. (66.3%) of product which melted at 58.5–59.5°.

Anal. Calcd. for $C_{18}H_{18}O$: C, 86.36; H, 7.25. Found: C, 86.55; H, 7.33.

The 2,4-dinitrophenylhydrazone melted at 191–192° after being recrystallized from ethyl acetate.

Anal. Calcd. for $C_{24}H_{22}N_4O_4$: N, 13.03. Found: N, 13.10.

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RECEIVED AUGUST 8, 1951

Dipole Moments and Structure of Acid Amides

BY W. D. KUMLER

In a recent paper Bates and Hobbs[1] imply that they were unable to calculate the dipole moment of acetamide from our data[2] because it scattered so widely. In Fig. 1 is a graph of the data showing that all three points fall near a straight line. The dipole moment of acetamide calculated from this line by the method of Halverstadt and Kumler[3] has a value of 3.92 *D* in good agreement with the value of 3.90 *D* reported by Bates and Hobbs.

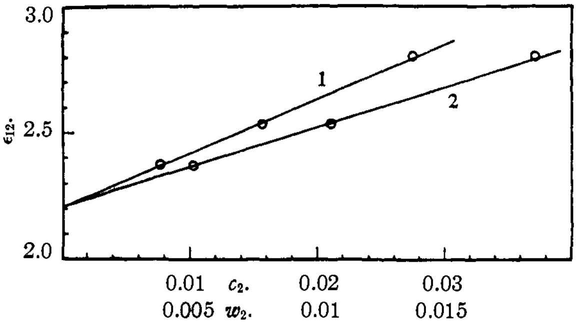

Fig. 1.—Plot of ϵ_{12} *vs.* c_2 (curve 1) for acetamide taken directly from Kumler and Porter's paper THIS JOURNAL, **56**, 2549 (1934), and a plot of ϵ_{12} *vs.* w_2 (curve 2) for the same solutions.

These authors claim the usual polar resonance form makes a negligible contribution to the structure of amides because the theoretical moment of acetamide of 3.1 *D* which they calculate from the dimensions and angles obtained in the crystalline state, is near the gas value of 3.4–3.5 *D*.[4] This argument can have validity only if the molecule has the same configuration in the gas as it has in the crystal. No evidence has been given that this is the case. If it is assumed that the molecule does have the same configuration in the gas as in the crystal, it becomes pertinent to inquire how the molecule could be so held in the gas. The structure they have assumed is coplanar with one of the N–H dipoles pointing in nearly the same direction as the C=O dipole. This structure is opposed by both dipole or electrostatic forces and steric effects, since these would cause both amino hydrogens to be as close as possible to the oxygen atom and as far as possible from the methyl hydrogens. The absence of crystal forces leaves only resonance to account for the molecule having a planar configuration in the gas. Furthermore, the resonance must be of considerable magnitude to overcome both the dipole interaction and steric effects and, hence

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[4] G. Hearne, Ervin Stehr, T. R. Steadman and L. C. Westcott, *Ind. Eng. Chem.*, **33**, 385 (1941).

[5] J. B. Cloke, Ervin Stehr, T. R. Steadman and L. C. Westcott, THIS JOURNAL, **67**, 1587 (1945).

(1) W. W. Bates and M. E. Hobbs, THIS JOURNAL, **73**, 2151 (1951).

(2) W. D. Kumler and C. W. Porter, *ibid.*, **56**, 2549 (1934).

(3) I. F. Halverstadt and W. D. Kumler, *ibid.*, **64**, 2988 (1942).

(4) They do not state how this gas value was obtained, but presumably it is an estimate obtained by analogy with the known gas and solution values of formamide.

the polar resonance form must make an appreciable contribution to the over-all structure of the molecule.

Bates and Hobbs claim that the low basicity of the amide group is due mainly to dipole interaction. Since dipole interaction opposes a coplanar configuration, it is logical to conclude that if this effect is stronger than the resonance effect, the structure they have assumed for their calculations would not exist.

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RECEIVED JULY 3, 1951

The Infrared Spectrum of Disulfur Decafluoride

BY D. EDELSON

Disulfur decafluoride, S_2F_{10}, is one of the fluorides of sulfur formed when sulfur is heated in a fluorine atmosphere; its properties have been described by Denbigh and Whytlaw-Gray.[1] It may be obtained as a by-product in the production of sulfur hexafluoride and is frequently present in the latter as impurity. In this work the infrared spectrum of this compound is reported as a means of comparing its structure to that of SF_6 of which it may be considered a dimer.

Measurements[2] were made on a double-beam spectrophotometer using a four-inch cell with potassium bromide windows. A sodium chloride prism was used to cover the range 2.5–15 μ, and a potassium bromide prism for 15–22 μ. The spectrum was measured at two pressures, 4 mm. and 37 mm. Results are shown in Fig. 1. The bands and their intensities are given in Table I.

TABLE I

INFRARED BANDS OF S_2F_{10} (CM.$^{-1}$)

vs, very strong; s, strong; m, medium; w, weak; vw, very weak

544	s	1182	w
576	s	1206	w
605	w	1242	m
683	m	1256	s
733	w	1299	w
827	vs	1323	w
890	s	1404	w
917	s	1497	s
940	vs	1550	w
988	m	1629	w
1107	vw	1736	w
1130	vw		

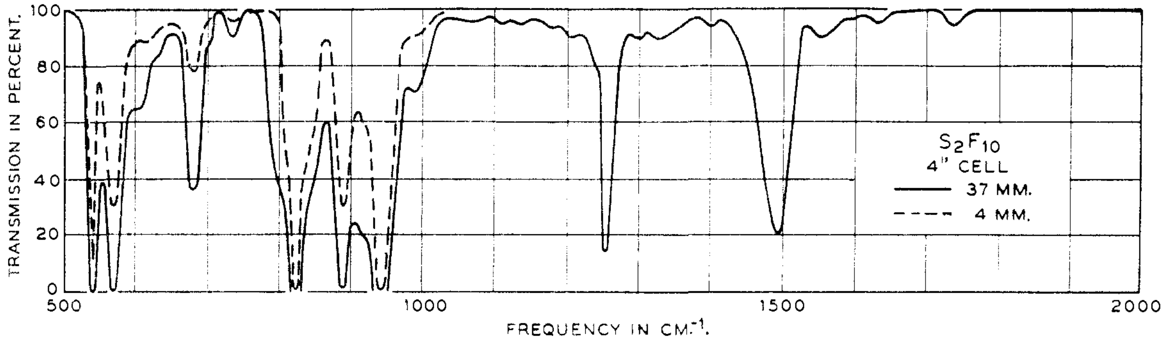

Fig. 1.—The infrared spectrum of S_2F_{10}.

S_2F_{10} may be assumed to consist of two half-octahedra of five fluorine atoms about a central sulfur atom, in analogy with the structure of SF_6, joined by a S–S bond. Although the fundamentals cannot be definitely assigned without further knowledge of the extent of rotation about the S–S bond,[3] and without the Raman spectrum, some tentative assignment may be made by a comparison with the spectrum of SF_6. The vibration of the plane of four fluorine atoms with respect to the central sulfur atom in SF_6 is given by the F_{1u} fundamental[4] at 940 cm.$^{-1}$; the corresponding vibration in S_2F_{10} may be assigned to the very strong band at 940 cm.$^{-1}$. This band in S_2F_{10} is considerably stronger than that in SF_6, undoubtedly because there are twice as many vibrating groups per molecule.

It is questionable whether a S–S vibration should be expected to appear in the infrared; if this may be assumed, however, the bands at 544 or 576 cm.$^{-1}$ may be attributed to this in comparison with the value 512 cm.$^{-1}$ reported by Venkateswaran[5] for this frequency in S_2Cl_2.

The assistance of Mr. K. H. Storks and Mrs. M. H. Read in the experimental work is gratefully acknowledged.

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(1) K. G. Denbigh and R. Whytlaw-Gray, *J. Chem. Soc.*, 1346 (1934).

(2) The sample used in these experiments was obtained through the courtesy of the Pennsylvania Salt Mfg. Co., Chestnut Hill, Phila., Pa.

(3) NOTE ADDED IN PROOF: S. H. Bauer, in a paper presented at the 120th meeting of the American Chemical Society at New York, September 6, 1951, Symposium on Bond Strengths, reported the existence of some hindered rotation despite an abnormally long S-S bond distance.

(4) R. T. Lagemann and E. A. Jones, *J. Chem. Phys.*, **19**, 534 (1951).

(5) S. Venkateswaran, *Ind. J. Phys.*, **6**, 275 (1931).

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RECEIVED AUGUST 27, 1951

Silicon Disulfide and Silicon Diselenide[1a]

BY HENRY GABRIEL[1b] AND C. ALVAREZ-TOSTADO

The fact that silicon and the sulfur family elements react to form binary compounds has been known since the discovery of these elements and

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[1a] Extract from a dissertation prepared under the direction of Prof. Alvarez-Tostado and submitted to the Dept. of Chemistry of Stanford University by Henry Gabriel in partial fulfillment of the requirement for the degree of Doctor of Philosophy.

[1b] Fisk University, Nashville, Tenn.

the reaction was described by Wöhler and Berzelius.[2] Although silicon disulfide has been prepared by various methods and extensively investigated, silicon diselenide has never been prepared pure and described. An attempt to prepare the latter by a reaction between hydrogen selenide and silicon resulted in evidence of compound formation but the material was apparently impure.[3]

When Sabatier[4] first investigated a large number of metal sulfides, he prepared silicon disulfide and measured its heat of reaction with water. By the use of the Hess law he determined the heat of formation of this compound from amorphous silicon as 40.4 kcal./fw. and from crystalline silicon as 31.7 kcal./fw. No redetermination of the heat of hydrolysis of silicon disulfide has been carried out but by using more modern values for the other reactions, the value could change slightly. However, there is a wide divergence in the reference literature for the heat of formation of this compound. Lange's Handbook[5] gives 32.02 kcal., Mellor[6] gives 10.4 kcal. as the value reportedly obtained by Sabatier, while the International Critical Tables[7] give a value for a "yellow" silicon disulfide, which, according to Sabatier's original article[4] was an impure mixture of varying composition. It was the purpose of this investigation to resolve this disagreement and to obtain similar information about silicon diselenide.

Experimental

(1) **The Preparation and Purification of Silicon Disulfide and Silicon Diselenide.**—The preparation of the two compounds was based on the observation of Berzelius that silicon and sulfur combine directly at elevated temperatures.[2] One mole of iron-free crystalline silicon and two and a half moles of sulfur were ground together in a mortar. Portions of this mixture were introduced into an 8 inch Pyrex glass test-tube, containing Pyrex glass wool, in such a manner that the mixture was distributed on the fibers of the wool and not in a compact mass at the bottom. The tube was filled about one third full and constricted in order to facilitate sealing. The material was then spot heated with a glass-blowing torch, care being taken that the spot did not blow out. Just about at the softening temperature of the glass, a violent reaction was observed with incandescence spreading through the entire mixture when it was properly distributed. Whenever the reaction was only local, the tube was spot-heated until the entire quantity of material had exhibited this incandescence. The excess sulfur vaporized and burned at the top of the tube. The tube was then sealed until needed for purification. The omission of glass wool inhibited the reaction completely, at least at the temperature below the softening point of the Pyrex glass. The apparent catalytic effect of the glass wool should be noted.[8]

Silicon diselenide was prepared in the same manner as described above. However, the reaction between silicon and selenium is not very evident and it was necessary to bring the entire content of the tube to a temperature of about 650°. Again the catalytic action of Pyrex glass wool was in evidence.

The purification was carried out by means of a Lindberg Tube Furnace, using a $^3/_4$ inch inside diameter Vitroseal combustion tube connected to a high vacuum pump system. The crude material, including the walls of the test-tube which were often covered with active material was crushed and placed into a large porcelain boat. This was placed in the combustion tube and the open end closed by means of a rubber stopper sealed in with commercial gasket cement. The gasket cement produced a satisfactory seal and made the removal of the stopper at the end of the run quite easy. The air was exhausted from the system and the oven allowed to reach a temperature from 900–1150°, which was maintained for about two hours. The vacuum was maintained at less than 0.1 mm. during the entire time and while the tube was cooling back to room temperature. It was essential to allow the material to return to room temperature as immediate decomposition of the compounds took place when they were permitted to come into contact with air at an elevated temperature.

The white crystalline, very porous silicon disulfide which collected in the cooler portion of the tube was removed and immediately sealed into glass vials (sulfur analysis 69.7%, theory 69.6%; hydrolysis and ignition to silica, 0.1221 g. yielded 0.0794 g. of silica, theory 0.0796 g.).

The purified silicon diselenide was also a white, crystalline solid (selenium analysis: 83.9%, theory 84.91%; hydrolysis and ignition to silica, 0.1490 g. yielded 0.0507 g. SiO_2; theory 0.0481 g.).

(2) **Density of Silicon Disulfide and Silicon Diselenide.**—Since the density of silicon disulfide had not been reported previously in the literature, it was measured by means of immersion in dry, thiophene-free benzene. A pycnometer, having a capacity of 10 cc., and closed by a thermometer fitted ground-glass stopper, was used. The average of three determinations at 25° was 1.875 ± 0.01 g./cc. A similar determination for silicon diselenide gave an average value of 2.63 ± 0.05 g./cc. The relatively large uncertainty factor is due to the fact that even sealed silicon diselenide will react with the enclosed oxygen so that it is almost impossible to maintain a purity of more than 98%.

(3) **Heat of Hydrolysis and Heat of Formation of Silicon Disulfide and Silicon Diselenide.**—In order to settle the difference in the values given in the various reference works, the measurement of the heat of reaction of silicon disulfide, and subsequently that of silicon diselenide, was carried out in 6 *M* sodium hydroxide. In this manner the formation of gaseous hydrogen sulfide and selenide would be minimized and the precipitation of hydrated silica could be suppressed in favor of the formation of sodium metasilicate.

The heats of reaction were measured in a small calorimeter employing a five junction thermocouple thermometer balanced by a potentiometer circuit. These measurements were complicated by the fact that both compounds tend to decompose on exposure to moisture of the air, the characteristic odor of hydrogen sulfide and hydrogen selenide becoming noticeable immediately upon breaking of the sealed vials in which the material was kept. Four determinations made on fresh material analyzing 99$^+$% SiS_2, gave 45.38, 46.57, 45.92, 46.38 kcal./fw. for an average of 46.1 kcal./fw. A similar series of determinations on silicon diselenide gave an average value of 391.3 cal./g. and 72.8 kcal./fw. It was noted that whenever two successive determinations of the heat of hydrolysis were made using silicon diselenide from the same vial, the value dropped 4–5 kcal. although remainders were kept only for short periods in tightly stoppered weighing bottles and in a desiccator containing magnesium perchlorate.

The heat of formation of silicon disulfide was calculated from the following reaction, using heat of formation, values from the Handbook of Chemistry and Physics, 32d Edition, except for the value of Na_2SiO_3(aq), as explained below.

$$\begin{array}{llll} SiS_2 + 6NaOH\ (aq.) & \longrightarrow & Na_2SiO_3\ (aq.) & \\ -x \quad -6(112.04) & & +362.25 & \\ & & +2Na_2S\ (aq.) + 3H_2O & +46.1\ kcal. \\ & & +2(105.4) \quad +3(68.4) & = 46.1 \end{array}$$

$$-x = -59.91\ \text{kcal. or}$$

$$Si + 2S \longrightarrow SiS_2 + 59.9 \pm 0.5\ \text{kcal.}$$

For $SiSe_2$:

$$\begin{array}{lll} SiSe_2 + 6NaOH\ (aq.) & \longrightarrow & Na_2SiO_3\ (aq.) \\ -x \quad -6(112.04) & & +362.25 \end{array}$$

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(2) H. Moissan, "Traite de chemie minérale," Masson et Cie., Paris, 1904, Metalloides II, pp. 450 ff.

(3) P. Sabatier, *Compt. rend.*, **113**, 132 (1903).

(4) P. Sabatier, *Ann. chim.*, [v] **22**, 86 (1881).

(5) N. A. Lange, ed., "Handbook of Chemistry," 5th Edition, Handbook Publishers, Inc., Sandusky, Ohio, 1944.

(6) J. W. Mellor, "Comprehensive Treatise on Inorganic and Theoretical Chemistry," Longmans Green and Co., London, 1931, Vol. VI, p. 859.

(7) "International Critical Tables," Vol. V, McGraw-Hill Book Co., New York, N. Y., 1929.

(8) Observation of this effect was first made by Dr. Tostado and Mr. Harlow, while attempting this synthesis at the Chemistry Laboratories of Stanford University. Patent applied for.

$$+ 2Na_2Se\,(aq.) + 3H_2O + 72.78\text{ kcal.}$$
$$+ 2(88.12) + 3(68.4) = 72.78$$
$$-x = 1.33\text{ kcal. or}$$
$$Si + 2Se \longrightarrow SiSe_2 - 1.33 \pm 0.5\text{ kcal.}$$

Thomsen[9] investigated the reaction between aqueous sodium hydroxide and aqueous silicic acid; he found the heat of reaction for aqueous sodium metasilicate to be +5.23 kcal., at the exact equivalence point. Excess reagents produced different results so that the figure is of uncertain reliability. However, it is the only figure available and the calculation of the heat of formation of $Na_2SiO_3(aq)$ when compared to that of $Na_2SiO_3(s)$ is a reasonable one, giving a negative heat of solution of about 6 kcal. per mole.

$$2NaOH\,(aq.) + SiO_2 \longrightarrow Na_2SiO_3\,(aq.) + H_2O + 5.23\text{ kcal.}$$
$$-2(112.04) - 201.34 + x + 68.4 = 5.23$$
$$x = 362.25$$

To account for the differences between the figures obtained by this calculation and those of Sabatier, the latter's equation must be considered.

$$SiS_2 + 2H_2O \longrightarrow SiO_2(diss) + 2H_2S(g) + 38\text{ kcal.}$$
$$-x - 2(68) + 201 + 10 = 38$$

in round figures using recent values $-x = -37$ kcal. Sabatier considered the heat of solution of silica a negligible quantity and failed to consider the formation of a saturated solution of hydrogen sulfide. It is also possible that the dissolved silica was a mixture of silicic acids. The use of 6 *M* sodium hydroxide in this study resulted in the formation of dissolved salts of predictable composition, especially since a large excess of sodium hydroxide was always present.

Properties of Silicon Diselenide.—The freshly sublimed silicon diselenide was a white, crystalline solid, which was deposited in a hard compact mass on the wall of the tube.

Silicon diselenide reacts with the oxygen of the air at room temperature in a simple replacement reaction.

$$SiSe_2 + O_2 \longrightarrow SiO_2 + 2Se\text{ (red).}$$

It reacts vigorously with water, forming hydrogen selenide and silica. With strong bases, the corresponding selenides and silicates are formed. Evidence of the reaction in the crude material was obtained by the formation of zinc selenide and the odor of hydrogen selenide immediately evident when the material was in contact with moist air. Due to its instability and the nature of its decomposition products, extreme caution should be exercised in its preparation and handling.

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(9) J. Thomsen, "Thermochemische Untersuchingen," Vol. II, Johan Ambrosius Barth, Leipzig, 1882, p. 413.

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RECEIVED JUNE 11, 1951

Preparation of Radioactive Sodium Metal by Exchange of Na^{23} and $Na^{22}Cl$

BY NORMAN H. NACHTRIEB, JOHN A. WEIL AND EDWARD CATALANO

In the course of investigating diffusion phenomena among the alkali metals, we have found it convenient to prepare metallic radioactive sodium by means of the reaction

$$Na^{23}(l) + Na^{22}Cl(s) \longrightarrow Na^{22}(l) + Na^{23}Cl(s)$$

The distribution of Na^{22} between the metal and salt should stand in the approximate ratio of the weights of sodium in the two phases. Under the conditions of our experiments, when the ratio of sodium to sodium chloride was about 10^4, essentially quantitative conversion was obtained. No effort was made to determine the distribution coefficient. On the face of it, it looks as if the reaction occurs between solid sodium chloride and liquid sodium metal, but the detailed nature is not known. The high conversion rate rules out the possibility that the reaction involves only the contact surfaces. Conceivably, the sodium chloride may dissolve in the metal; alternatively, reaction may take place by diffusion of sodium through sodium chloride.

Experimental

The exchange reaction and the subsequent distillation of the metal took place in a specially designed Pyrex tube. An iron thimble made from a 6″ length of 7/8″ dia. seamless tubing, with a bottom plug pressed into place, was sealed into one end of the tube. Adjacent to the thimble was a U shaped section with a seal-off tube connected at the bottom. The other end of the tube led to a vacuum line. 1.00 ml. of a tracer solution,[1] having an activity of 1.13×10^7 disintegrations min.^{-1} and containing a total of 2.39 mg. of carrier sodium chloride, was transferred to the thimble. The water was removed by evacuation of the tube with an oil diffusion pump through an intervening liquid nitrogen trap. A quantity of freshly cut sodium, estimated to weigh about 10 g., was then placed in the thimble and the system was again evacuated. A cylindrical electric furnace was slipped over the end of the tube and the contents of the thimble maintained at 250° overnight.

A thin iridescent metal mirror appeared on the walls of the tube beyond the thimble. Since its thickness did not increase with time, it was assumed to be a trace of potassium and was flamed out of the tube. When the temperature was raised to 525°, all of the sodium distilled from the thimble and condensed in the U section. Careful flaming transferred almost all of the metal into the seal-off tube. The 7.60 g. of sodium thus recovered was found to have a specific activity of 1500 disintegrations $\text{min.}^{-1}\ \text{mg.}^{-1}$. The possibility that $Na^{22}Cl$ was carried over mechanically was ruled out by the fact that redistillation did not diminish the activity of the metal. Some discoloration of the U section appears to be unavoidable, but can be minimized by care in flaming. Five preparations have been carried out in this manner.

This work was supported in part by the United States Air Force under contract AF-33(038)-6534.

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(1) Supplied by Isotopes Division, United States Atomic Energy Commission, Oak Ridge, Tennessee.

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RECEIVED JULY 3, 1951

Thallous Salts as Derivatives of Sulfonic Acids. II

BY HENRY GILMAN AND H. SMITH BROADBENT

The present report is an extension of previous preliminary studies[1] on the use of thallous salts for the characterization of some sulfonic and other acids or their soluble salts. Several advantages of these salts as derivatives of sulfonic acids were mentioned in the earlier reports.[1] Among the salts now reported is found additional support

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(1) (a) Gilman and Abbott, THIS JOURNAL, **65**, 123 (1943); (b) Gilman and Abbott, *ibid.*, **71**, 659 (1949).

TABLE I

THALLOUS SALTS OF SUBSTITUTED BENZENESULFONATES

No.	Substituents	M.p., °C.	Rel. solubility	Formula	Tl analyses, % Found	Calcd.
1	2,5-Dimethyl-[a]	217–219	Extremely sol.	$C_8H_9O_3STl$	52.8	52.5
2	3-Biphenyl-[b,c]	454–457 dec.	Quite insol.	$C_{18}H_{13}O_3STl$		
3	4-Biphenyl-[b,c]	> 532	Very insol.	$C_{18}H_{13}O_3STl$		
4	4-Chloro-[b]	258–260	Moderately sol.	$C_6H_4O_3ClSTl$	52.0	51.6
5	2,5-Dichloro-[a]	326–328	Quite insol.	$C_6H_3O_3Cl_2STl$	47.4	47.5
6	3,4-Dichloro-[b]	273–275	Moderate	$C_6H_3O_3Cl_2STl$	47.65	47.5
7	3-Chloro-4-methyl-[b]	198–200	Moderate	$C_7H_6O_3ClSTl$	49.45	49.9
8	4-Chloro-3-methyl-[b]	227–229	Moderate	$C_7H_6O_3ClSTl$	50.2	49.9
9	4-Hydroxy-[b,d]	266	Very sol.	$C_6H_5O_4STl$	54.6	54.2
10	4-Hydroxy-5-isopropyl-2-methyl-[e] [Thallous thymolsulfonate]	243–244	Very sol.	$C_{10}H_{13}O_4STl$	49.2[e]	47.2
11	2-Hydroxy-3,4-dichloro-[b]	270–272	Moderate	$C_6H_3O_4Cl_2STl$	45.8	45.8
12	2-Nitro-[a,f]	226–228	Moderate	$C_6H_4O_5NSTl$	49.95	50.3
13	4-Nitro-[a]	284–285	Moderate	$C_6H_4O_5NSTl$	50.7	50.3
14	2,4-Dinitro-[a]	241	Moderate	$C_6H_3O_7N_2STl$	44.9	45.3
15	2-Methyl-5-nitro-[b]	305–308 dec.	Moderate	$C_7H_6O_5NSTl$	48.5	48.6
16	2-Chloro-5-nitro-[a]	323–324 dec.	Quite insol.	$C_6H_3O_5NClSTl$	46.3	46.4
17	4-Bromo-3-nitro-[a]	308–309	Quite insol.	$C_6H_3O_5NBrSTl$	41.7	42.1
18	4-Chloro-3-methyl-5-nitro-[b]	363–364	Quite insol.	$C_7H_5O_5NClSTl$	44.62[g]	44.9
19	2-Amino-[a]	169–171	Quite sol.	$C_6H_6O_3NSTl$	54.1	54.3
20	5-Amino-2-methyl-[a]	187–188	Quite sol.	$C_7H_8O_3NSTl$	52.5	52.35
21	4-Amino-3-methyl-[a]	212–213	Moderate	$C_7H_8O_3NSTl$	51.8	52.35
22	2-Amino-5-(4-aminophenyl)-[a] [Thallous benzidine-3-sulfonate]	269–271	Moderate	$C_{12}H_{11}O_3N_2STl$	44.1[g]	43.7
23	2-Anilino-5-nitro-[b] [Thallous 4-nitrodiphenylamine-2-sulfonate]	277–280 dec.	Very insol.	$C_{12}H_9O_5N_2STl$	40.7[g]	41.1
24	4-Hydrazo-[a]	Dec. *ca.* 245	Moderate	$C_7H_7O_3N_2STl$	52.0	52.2
25	4-(4-Aminonaphthylazo)-[b]	Darkens 268 Dec. 275–280	Very insol.	$C_{16}H_{12}O_3N_3STl$	38.2[g]	38.5

[a] Prepared from the free sulfonic acid. [b] Prepared from the sodium salt of the acid. [c] Both *p*-terphenyl derivatives are very insoluble and highly refractory, particularly the *p*-terphenyl-4-sulfonate. Even heating with fuming nitric acid at 400° for 72 hours in a sealed tube failed to completely decompose the organic matter making a satisfactory analysis for thallium virtually impossible by this method. [d] The dithallous salt is not formed quantitatively. It seems best to use two equivalents of thallous formate and isolate the monothallous salt by recrystallizing it from ethanol–water (2:1). Otherwise products analyzing low for the monothallous salt are obtained. [e] The starting sulfonic acid was the Eastman Kodak Co. white label product (m.p. for the anhydrous product was 114–115°). Stebbins, THIS JOURNAL, **3**, 111 (1881), gives the melting point of the monohydrate as 91–92°. It is very difficult to prepare this very soluble thallous salt with a satisfactory melting point. An acceptable analysis was not obtained. Several values varying from 2 to 4% high for thallium were obtained. Some thallous sulfate was also isolated from the reaction. It appears likely that the sample of the sulfonic acid was impure. [f] A mixture of two types of crystals is obtained if the solution is boiled too long in the course of evaporation. One type is the bright, yellow crystals of the thallous sulfonate, and the other is the fine, white needles of thallous sulfate (m.p. 632°). The former is soluble in 95% ethanol while the latter is not. Both No. 13 and 14 would also likely undergo hydrolysis giving thallous sulfate under similar conditions. [g] These analyses required preliminary destruction of the organic matter by heating with fuming nitric acid at 300° in a sealed tube.

for the suitability of these derivatives for the separation and characterization of isomers.

As a result of the present more extensive study, it appears that about 20% of the thallous salts now reported are so high melting as to require temperatures above those conveniently attained with ordinary melting point apparatus (*ca.* 300–350°). However, in such cases one of the conventional melting point blocks described in the literature[2] may be used satisfactorily. Furthermore, we were unable to prepare pure, crystalline thallous salts from two acids (metanilic acid and 4-amino-3-hydroxynaphthalenesulfonic acid) and two sulfonates (sodium 3,4-dimethylbenzenesulfonate and sodium 2,4-dimethylbenzenesulfonate). The difficulty in the latter case appeared to be the only slightly lower solubility of the thallous sulfonates compared to the sodium salts from which they were obtained.

The results are summarized in Tables I and II.

The authors are grateful to R. K. Abbott, Jr., Gene Mock and Keith Brinker for assistance.

Experimental

Procedure.—In the preparations from the sulfonic acids, 0.01 mole of acid dissolved in the minimum amount of water is titrated with thallous hydroxide,[1,3] or the requisite amount of base is merely added to a weighed quantity of acid. In the preparations from the sodium sulfonates, a weighed quantity of sodium sulfonate dissolved in a small amount of water is treated with an equivalent quantity of thallous formate or malonate dissolved in a few drops of water. In either case, on cooling, the thallous sulfonate crystallizes out on standing. With the more soluble salts, evaporation to a smaller volume or to dryness may be necessary. The product is recrystallized from water or mixtures of ethanol and water. The principal point of importance in preparing the more soluble of these salts lies in adjusting the amount and ratio of these two recrystallizing solvents quite accurately to the properties of the sulfonate being prepared. No extensive study was made of other solvents, but none of the more common ones appeared to be more suitable.

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(2) Berl and Kullmann, *Ber.*, **60**, 811 (1927).

(3) Care must be taken not to expose the solution of thallous hydroxide unduly to light and air which oxidizes it slowly, precipitating the insoluble thallic hydroxide and oxide on the walls of the container, thus changing the titer of the solution.

TABLE II

THALLOUS SALTS OF OTHER SULFONIC ACIDS

No.	Thallous salt	M.p., °C.	Rel. solubility	Formula	Tl analyses, % Found	Tl analyses, % Calcd.
1	4-Methyl-1,3-benzenedisulfonate[b,e]	272–276[c] 295–297	Fairly insol.	$C_7H_6O_6S_2Tl_2$	60.5[c]	62.0
2	Benzidine-3,3'-disulfonate[a]	Chars above 350	Moderate	$C_{12}H_{10}O_6N_2S_2Tl_2$	54.8	54.4
3	D,L-Camphor-β-sulfonate[a,d]	259–260	Extremely sol.	$C_{10}H_{15}O_4STl$	46.7	46.9
4	D-Camphor-β-sulfonate (Reychler's)[a,d]	259–260	Extremely sol.	$C_{10}H_{15}O_4STl$	46.9	46.9
5	4-Amino-1-naphthalenesulfonate[a]	240–241	Quite insol.	$C_{10}H_8O_3NSTl$	47.9	47.9
6	8-Hydroxy-5,7-dinitro-2-naphthalenesulfonate[a] (dithallous salt)	Dec. *ca.* 376 explosively	Quite insol.	$C_{10}H_4O_8N_2STl_2$	56.95	56.7
7	1-Anthraquinonesulfonate[e]	475–480 dec	Moderate	$C_{14}H_7O_5STl$		
8	2-Anthraquinonesulfonate[b]	384–386	Quite insol.	$C_{14}H_7O_5STl$	41.9[g]	41.6
9	5-Nitro-1-anthraquinonesulfonate[a]	348–350	Fairly insol.	$C_{14}H_6O_7NSTl$	38.45	38.1
10	8-Nitro-1-anthraquinonesulfonate[a]	339–341	Fairly insol.	$C_{14}H_6O_7NSTl$	37.7	38.1
11	8-Hydroxy-5-quinolinesulfonate[a] (monothallous salt)	292–295	Quite insol.	$C_9H_6O_4NSTl$	47.3[g]	47.7
12	8-Hydroxy-5-quinolinesulfonate[a] (dithallous salt)	Darkens 400 Dec. 425	Quite insol.	$C_9H_5O_4NSTl_2$	64.8[g]	64.7
13	8-Hydroxy-7-iodo-5-quinolinesulfonate[a,f]	Dec. *ca.* 300	Quite insol.	$C_9H_4O_4NISTl_2$	56.0[f,g]	53.9

[a] Prepared from the free sulfonic acid. [b] Prepared from the sodium salt of the acid. [c] Part of the product always melted at 272–276° and the main part of it at 295–297° even after several recrystallizations. The analyses were consistently 1.5% low for the dithallous salt. Perhaps the original sulfonate contained a small amount of impurity not separable by the processes of preparation. [d] These thallous salts are exceedingly soluble in water, but they are very readily prepared by evaporating the solution to dryness under reduced pressure and recrystallizing from absolute ethanol. The melting point for thallous D-camphorsulfonate here recorded is somewhat lower than previously reported.[1a] The melting points for both the camphorsulfonates were determined on several different samples of these salts, and they were found to be unchanged after repeated crystallizations from absolute ethanol. The fact that both the D- and the D,L- salts have the same melting point and that a mixed-melting point of the two is undepressed indicates that the D- and L- salts form a continuous series of solid solutions in any proportion. To guarantee the identity of these salts they were examined polarimetrically. For thallous D-camphorsulfonate $[\alpha]^{25}D$ +11.8 ± 0.2°, in 5–8% aqueous solution. This value corresponds closely on the basis of equivalent D-camphorsulfonate ion concentration with the values reported for free D-camphorsulfonic acid in aqueous solution of +21.5° (Reychler, *Bull. soc. chim. France,* [3] **27,** 982 (1902)) and of +22.60° (Rewald, *Ber.,* **42,** 3137 (1909)). Our sample of thallous D,L-camphorsulfonate was found to be entirely optically inactive and, hence, uncontaminated with optically active salt. [e] It was very difficult to secure a crystalline thallous salt (fine, yellow needles) from the highly insoluble crude potassium sulfonate (Eastman Kodak Co.). This is a case of the initial salt being nearly as insoluble as the thallous salt product making isolation of the desired product very difficult. A satisfactory analysis was never obtained, although the product appeared to be pure. [f] No crystalline material could be isolated using one equivalent of thallous hydroxide. The crystalline dithallous salt decomposed so that no melting point check on purity was available. It was very difficult to analyze the product, but the analysis shown was checked. [g] These analyses required preliminary destruction of the organic matter by heating with fuming nitric acid at 300° in a sealed tube.

Melting Points.—The melting points of all compounds melting below 345° were determined on an electrically heated block similar to the Fisher–Johns melting point apparatus. All such melting points were uncorrected. The melting points of those compounds melting above 345° were determined in a Berl–Kullmann block[2] using a Weston dial type thermometer calibrated with a thermocouple.

Analyses.—Suitable modifications of the method of Meyer and Bertheim[4] were used for determining thallium content.

(4) Meyer and Bertheim, *Ber.,* **37,** 2051 (1904).

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RECEIVED MAY 24, 1951

The Reaction of Dibenzothiophene-5-oxide with *n*-Butyllithium

BY HENRY GILMAN AND DONALD L. ESMAY

The treatment of sulfoxides with organometallic compounds has resulted in reduction,[1] cleavage,[1a,2] cyclization,[1b,3] rearrangement,[3b,4] lateral metalation,[3b] sulfonium salt formation,[5] or complex formation.[3b,6] No nuclear metalation of aryl or heterocyclic sulfoxides has been reported, although metalation of the nucleus has been shown to occur with sulfides such as ethyl phenyl sulfide,[7] diphenylsulfide,[8] thiophene[9] and dibenzothiophene.[8,10]

We are reporting the reaction of dibenzothiophene-5-oxide with *n*-butyllithium[11] in diethyl ether to give upon carbonation 4-dibenzothiophenecarboxylic acid as the major product. The identity of the acid product was established by the method of mixed melting points and by comparison of spectra obtained by infrared absorption measurements.

An initial experiment at the temperature of refluxing ether gave a very small yield of 4-dibenzo-

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(1) (a) K. Fuchs and P. Gross, *Ber.,* **63,** 1009 (1930); (b) C. Courtot, M. Chaix and L. Nicholas, *Compt. rend.,* **194,** 1660 (1932); (c) H. Hepworth and H. W. Clapham, *J. Chem. Soc.,* **119,** 1188 (1921); (d) C. Courtot and C. Pomonis, *Compt. rend.,* **182,** 893 (1926).

(2) (a) E. Bergmann and M. Tschudnowsky, *Ber.,* **65,** 457 (1932); (b) E. P. Kohler and H. Potter, THIS JOURNAL, **57,** 1320 (1935).

(3) (a) A. Schönberg, *Ber.,* **56,** 2275 (1923); (b) K. Fuchs and F. Breuer, *Monatsh.,* **53,** 438 (1929); (c) C. Courtot, M. Chaix and J. Kelner, *Compt. rend.,* **194,** 1837 (1932).

(4) A. Schönberg and A. Stephenson, *Ber.,* **66,** 260 (1933).

(5) B. S. Wildi, S. W. Taylor and H. A. Potratz, THIS JOURNAL, **73,** 1965 (1951).

(6) H. Hepworth, *J. Chem. Soc.,* **119,** 1249 (1921).

(7) H. Gilman and F. J. Webb, THIS JOURNAL, **62,** 987 (1940); *ibid.,* **71,** 4062 (1949).

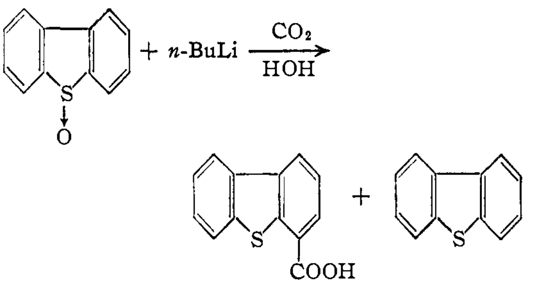
(8) H. Gilman and R. L. Bebb, *ibid.,* **61,** 109 (1939).

(9) H. Gilman and D. A. Shirley, *ibid.,* **71,** 1870 (1949).

(10) (a) H. Gilman and A. L. Jacoby, *J. Org. Chem.,* **3,** 108 (1938); (b) H. Gilman, A. L. Jacoby and H. A. Pacevitz, *ibid.,* **3,** 120 (1938).

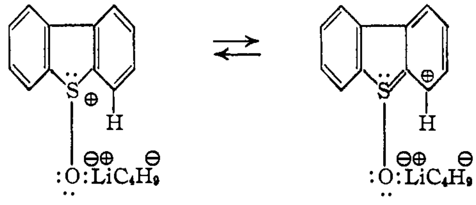
(11) H. Gilman, J. A. Beel, C. G. Brannen, M. W. Bullock, G. E. Dunn and L. S. Miller, THIS JOURNAL, **71,** 1499 (1949).

thiophenecarboxylic acid, about an equal yield of dibenzothiophene, a considerable amount of an acidic gum, and a large recovery of dibenzothiophene-5-oxide (equation 1). Since reaction at a low temperature has been shown to be the method of choice for the metalation of certain reactive heterocycles,[12] it was considered of interest to determine the effect of lowering the reaction temperature in the present case. Metalation at −10° increased the yield of crude 4-dibenzothiophenecarboxylic acid to 55.4% (35.7% pure), while the yield of dibenzothiophene remained about the same (10.8%) and no starting material was recovered. It was found necessary to add 1.8 equivalents of *n*-butyllithium before a Color Test II[13] was positive and to add 3.2 equivalents before the test was positive after prolonged stirring. Color Test I[14] was positive throughout the entire reaction period. It is interesting to note that the yield of 4-dibenzothiophenecarboxylic acid compares favorably with that obtained when dibenzothiophene itself is metalated with *n*-butyllithium in diethyl ether.[8,10a,15]



(1)

Regardless of the mechanism assumed, the overall reaction involves both reduction of the sulfoxide group and metalation ortho to the carbon–sulfur linkage. Nuclear metalation ortho to a hetero atom is well-known[16]; however, in view of the established meta-directing influence of the sulfoxide group in dibenzothiophene-5-oxide,[17] ortho-substitution in the present case was somewhat unexpected. The isolation of dibenzothiophene in substantial yields would seem to indicate an initial reduction of the dibenzothiophene-5-oxide to dibenzothiophene with subsequent metalation of the reduced compound to yield 4-dibenzothienyllithium. However, two attempts to metalate dibenzothiophene under analogous low-temperature conditions were unsuccessful as evidenced by the quantitative recovery of starting material after carbonation. In addition, only a trace of acidic material was isolated when the same reaction was carried out with dibenzothiophene in the presence of a catalytic amount of dibenzothiophene-5-oxide. The demonstration that the addition of organometallic compounds to nitriles[18] and ketones[19] proceeds through the initial formation of a complex suggests the possibility that a similar complexation occurs in the present instance between the metal end of the *n*-butyllithium dipole and the unshared electrons of the oxygen atom (equation 2). The electron shift induced by such a complex formation would then facilitate the removal of a proton by the carbanion end of the attacking molecule with subsequent (or concerted) rearrangement of the lithium cation to give the observed ortho metalation.[20] An initial, simultaneous complexing between the remaining unshared electrons of the oxygen atom and at least one additional molecule of *n*-butyllithium would explain the fact that Color Test II did not remain positive until three equivalents of *n*-butyllithium had been added and the fact that complete solution did not occur until two equivalents were present. Decomposition of this complex on termination of the reaction would then lead to the observed reduction and metalation. Furthermore, decomposition of the complex without metalation would yield dibenzothiophene. Although *n*-butanol would be the most probable reduction by-product,[21] none has been isolated as yet.



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Experimental

Metalation of Dibenzothiophene-5-oxide. Run I.—To a stirred suspension of 14.0 g. (0.07 mole) of dibenzothiophene-5-oxide[17] in 100 ml. of dry ether was added 64.4 ml. of a 1.308 *M* ether solution of *n*-butyllithium[11] (0.084 mole; 20% in excess of 1.0 equivalent) at such a rate that a spontaneous, gentle reflux was maintained. Twenty minutes was required for the addition of the *n*-butyllithium, during which time the initial light orange color gradually deepened to a dark orange. The mixture, which contained undissolved dibenzothiophene-5-oxide, was refluxed for six hours and carbonated by pouring jetwise into a slush of ether and Dry Ice.[12] Color Test I[14] was positive throughout, but Color Test II,[13] initially positive, gradually became weaker until the final test was negative. After hydrolysis with water, considerable insoluble material was filtered off and the ether and alkaline layers were separated. Acidification of the aqueous layer yielded 1.4 g. (8.7%) of nearly white acid melting at 240–245°. Recrystallization from dilute methanol raised the melting point to 254–255°. A mixed melting point with authentic 4-dibenzothiophenecarboxylic acid[10a] showed no depression. The neutral, ether-insoluble material weighed 5.4 g. (35.7% recovery), melted at 185–187°, and was established as being dibenzothiophene-5-oxide by a mixed melting point with an authentic specimen. The ether layer was dried over sodium sulfate and the solvent was removed by distillation. The gummy residue was crystallized from dilute ethanol to yield 1.0 g. (7.7%) of

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[12] H. Gilman and J. A. Beel, This Journal, **71**, 2328 (1949); *ibid.*, **73**, 774 (1951).

[13] H. Gilman and J. Swiss, *ibid.*, **62**, 1847 (1940).

[14] H. Gilman and F. Schulze, *ibid.*, **47**, 2002 (1925).

[15] H. Gilman and C. G. Stuckwisch, *ibid.*, **67**, 877 (1945).

[16] H. Gilman, "Organic Chemistry," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 536.

[17] R. K. Brown, R. G. Christiansen and R. B. Sandin, This Journal, **70**, 1748 (1948).

[18] C. G. Swain, *ibid.*, **69**, 2306 (1947).

[19] C. G. Swain and L. Kent, *ibid.*, **72**, 598 (1950).

[20] For a complete discussion of a similar mechanism proposed to explain the high reactivity toward metalation or halogen–metal interconversion of a nuclear position ortho to oxygen, see S. V. Sunthankar and H. Gilman, *J. Org. Chem.*, **16**, 8 (1951).

[21] (a) V. Grignard and L. Zorn, *Compt. rend.*, **150**, 1177 (1910); (b) H. Gilman and R. E. Fothergill, This Journal, **51**, 3501 (1929).

nearly pure dibenzothiophene in three fractions melting within the range of 97–99°. Identity was established by the method of mixed melting points.

Run II.—A stirred suspension of 5.0 g. (0.025 mole) of dibenzothiophene-5-oxide in 250 ml. of dry ether was cooled in an acetone–Dry Ice-bath to −10 ± 5° (internal) while a total of 57.9 ml. of a 1.378 *M* ether solution of *n*-butyllithium (3.2 equivalents) was added over a period of 5.5 hours. The addition of the *n*-butyllithium was interrupted at predetermined intervals in order to follow the course of the reaction with color tests. A Color Test II was not positive until after 1.8 equivalents of *n*-butyllithium had been added. The mixture did not give a positive Color Test II after prolonged stirring until 3.2 equivalents of *n*-butyllithium were present. Color Test I was positive throughout. There was definite evidence of undissolved starting material until 2.0 equivalents of *n*-butyllithium had been added, at which point a finely divided precipitate began to form and the undissolved platelets of dibenzothiophene-5-oxide disappeared. Carbonation and hydrolysis were effected as in Run I. The ether and aqueous layers were easily separated as no insoluble material was present. Acidification of the aqueous layer yielded 3.1 g. (55.4%) of 4-dibenzothiophenecarboxylic acid; m.p. 232–246°. Recrystallization from dilute methanol yielded 2.0 g. of pure acid (35.7%) which melted at 256–256.5°. Infrared absorption measurements of this acid showed its spectrum to be identical with that of an authentic sample of 4-dibenzothiophenecarboxylic acid.[10a] From the ether layer there was isolated 0.5 g. (10.8%) of dibenzothiophene.

Run III.—The procedure for this run was exactly the same as that followed in Run II except that only 1.0 equivalent of *n*-butyllithium was added and that the mixture was stirred for seven hours. By working up the carbonated mixture as described in Run II there was obtained 0.2 g. (3.5%) of 4-dibenzothiophenecarboxylic acid, 2.8 g. (56.0%) of recovered dibenzothiophene-5-oxide and 0.2 g. (4.4%) of dibenzothiophene.

Metalation of Dibenzothiophene.—A solution of 4.6 g. (0.025 mole) of dibenzothiophene was treated at −10° with 1.4 equivalents of *n*-butyllithium in exactly the same manner as reported in Run II above. On working up the carbonated reaction mixture, no acidic material was found in the aqueous layer and the ether layer yielded 4.0 g. (89.4% recovery) of dibenzothiophene. Identical results were obtained in a check run with 89.3% of the starting material being recovered. When dibenzothiophene is treated with *n*-butyllithium for 24 hours at the temperature of refluxing ether, yields of 4-benzothiophenecarboxylic acid of 50–60% are obtained after carbonation.[8,10a,15]

A third run was made in which 0.5 g. (0.0025 mole) of dibenzothiophene-5-oxide was added to the initial solution of 4.6 g. (0.025 mole) of dibenzothiophene. Only a trace of acidic material was isolated and 91.3% of the starting dibenzothiophene was recovered.

The low-temperature metalation of sulfones, other sulfoxides and related types is being examined in order to determine the mechanism and scope of the reaction.

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Mechanism of Aquation of Carbonatopentaamminocobaltic Ion in Acid Solution

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The transformation of $[Co(NH_3)_5Co_3{}^+]$ to $[Co(NH_3)_5H_2O^{+++}]$ takes place rapidly in water, and even more rapidly when the solution is acidified.[1] The net change in acid solution is described by the equation

$$Co(NH_3)_5CO_3{}^+ + 2H^+ = Co(NH_3)_5H_2O^{+++} + H_2CO_3$$

Interest in this reaction developed out of research which is in progress on the mechanisms of substitution in hexacoördinated complex ions. We have performed some tracer experiments to learn whether the metal ion–oxygen bond or the carbon–oxygen bond breaks in the removal of carbonate from the complex ion. In the former event but not in the latter, the oxygen found in the resulting aquo ion will be derived from the solvent. The results obtained show that at least 99% of the change proceeds leaving the Co(III)–O bond intact. The mechanism is therefore of the type observed in the hydrolysis of certain esters.[2]

Kinetic experiments[1] have shown that the rate of aquation in acid is proportional to the concentration of the bicarbonato ion, $[Co(NH_3)_5Co_3H^{++}]$. This ion is analogous in structure to H_2CO_3, but has H^+ in the acid replaced by $Co(NH_3)_5{}^{+++}$. The tracer result shows that the mechanism of the aquation in acid is analogous to the change: $H_2CO_3 = H_2O + CO_2$, and a comparison of the specific rates of the two reactions is therefore of interest. From the work of Lamb and Mysels,[1] the specific rate of decomposition of $Co(NH_3)_5Co_3H^{++}$ at 0° is calculated as 0.19 min.$^{-1}$. Combining the value 0.0012 quoted by Faurholt[3] for the quotient $(H_2CO_3)/(CO_2)$ at equilibrium, with the specific rate measured by Mills and Urey[4] for the formation of H_2CO_3, the specific rate of decomposition of H_2CO_3 is calculated as 105 min.$^{-1}$. The higher value for H_2CO_3 as compared to $Co(NH_3)_5Co_3H^{++}$ is not unexpected in view of the greater acidity of H^+ as compared to $Co(NH_3)_5H_2O^{+++}$. ($Co(NH_3)_5H_2O^{+++}$ is a weak acid[5]—$K_{\text{diss.}} = 6 \times 10^{-7}$ at 15° and $\mu = 0.1$.)

The tracer result we have obtained demonstrates rather strikingly the inertia to substitution of the Co(III)–O bond in the complex ion. A mechanism similar in type to that established will come into question in other reactions involving replacement of a complex ligand from the central ion, for example in the aquation of acetatopentamminocobaltic ion. A system in which this type of mechanism probably operates is in the reaction of $Cr(H_2O)_6{}^{+++}$ with polymolybdates. Hall and Eyring[6] have shown the hexamolybdatochromic ion is formed rapidly. Substitutions on Cr(III) are in general slow, on Mo(VI) rapid. In the reaction therefore the Cr–O bond is probably preserved and the Mo–O bonds broken and re-established.

Experimental

The salt $[Co(NH_3)_5CO_3]NO_3 \cdot H_2O$ was prepared[7] following the method described by Lamb and Mysels.[1] A solution of the salt in water was found to give no precipitate of $CaCO_3$ initially when Ca^{++} was added but after a period of time a precipitate began to appear.

Two tracer experiments were performed. In one, 2 g. of salt was dissolved in 75 ml. of enriched water (mole fraction $O^{18} = N \simeq 8 \times 10^{-3}$) at room temperature. After a period of ten minutes the salt had dissolved, the solution was then cooled to 0° and *ca.* 1.5 ml. of concd. HCl was added. A few minutes later, the ion $Co(NH_3)_5H_2O^{+++}$ was precipitated as the salt $Co(NH_3)_5H_2OCl_3 \cdot HgCl_2$. This compound was filtered off, dried and heated to yield water. The iso-

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(1) A. B. Lamb and K. J. Mysels, THIS JOURNAL, **67**, 468 (1945).

(2) M. Polanyi and A. L. Szabo, *Trans. Faraday Soc.*, **30**, 508 (1934).

(3) C. Faurholt, *J. Chim. Phys.*, **21**, 400 (1924).

(4) G. A. Mills and H. C. Urey, THIS JOURNAL, **62**, 1019 (1940).

(5) J. N. Bronsted and K. Volquartz, *Z. physik. Chem.*, **134**, 97 (1928).

(6) H. T. Hall and H. Eyring, THIS JOURNAL, **72**, 782 (1950).

(7) We are indebted to Mr. John Below for preparing the compound.

topic composition of the water was established by equilibrating it with CO_2 and analyzing the CO_2 by means of a mass spectrometer. The second experiment differed only in that the reactant solution and the reagents needed to precipitate the double salt were not precooled before being added.

The results obtained are presented in Table I.

TABLE I

TRACER EXPERIMENTS ON THE AQUATION OF $Co(NH_3)_5CO_3^+$ IN ACID

	$N_{obsd.}$ in water from ion	$N_{calcd.}$ for H_2O from solvent
Experiment 1	2.197×10^{-3}	7.90×10^{-3}
Experiment 2	2.630×10^{-3}	7.52×10^{-3}
Blank; reaction in unenriched H_2O	2.158×10^{-3}	....

The result obtained in Expt. 1 is very close to that in the blank. The higher value in Expt. 2 can be attributed to the exchange[8] of $Co(NH_3)_5H_2O^{+++}$ with H_2O^* which took place when the solution warmed as the precipitating agents were added.

Acknowledgment.—This work was supported by the Office of Naval Research under contract N6-ori-02026. The funds for the purchase of the mass spectrometer used in this research were supplied by the Atomic Energy Commission under contract At(11-1)-92.

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[8] This exchange is at present under study (A. C. R. and H. T.). The method for isotopic sampling will be described in more detail when the data on the exchange are presented for publication.

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RECEIVED AUGUST 31, 1951

Spectrophotometry of Ferric Chloride Complexes with *m*-Cresol, Salicylaldehyde and Ethyl Acetoacetate

BY RALPH L. HERBST, JR., ROBERT H. CLOSE, FRANK J. MAZZACUA AND ROBERT F. DWYER

In 1934, the structure $Fe(OR)_6^{---}$, where OR represents the phenoxide or enolate ion, was postulated by Wesp and Brode[1] for the colored complex formed in the reaction of ferric chloride with phenols and enols. This postulation was based on the observation that the ferric chloride–phenol complexes gave absorption spectra similar to that found for the iron(III) ion–cyanate and monothiocyanate iron(III) ion complexes. At this time these latter complexes were described as $Fe(CN)_6^{---}$ and $Fe(CNS)_6^{---}$, respectively. More recent investigations by Bent and French,[2] Edmonds and Birnbaum,[3] and Vosburgh and associates[4] have shown the monothiocyanate iron(III) complex to be $Fe(SCN)^{++}$. These results prompted a study of the iron(III) ion–phenol and enol complexes by the method of continuous variations employed by Vosburgh.[4]

Experimental

Materials.—All the organic compounds were freshly distilled: *m*-cresol, b.p. 201°; salicylaldehyde, b.p. 196.5°; ethyl acetoacetate, b.p. 180°; reagent grade $FeCl_3 \cdot 6H_2O$ was used.

Method.—The experimental details have been described by Vssburgh.[4] For *m*-cresol and ethyl acetoacetate, the mixtures were made up by volume from a freshly prepared stock solution of 0.02003 *N* ferric chloride and a 0.02003 *M* stock solution of the organic compound. In the case of salicylaldehyde, it was necessary to use more dilute stock solutions of 0.0001 *M*. Optical densities were measured with a Beckman model B spectrophotometer within 10–15 minutes after the mixtures were prepared. Preliminary scanning of 1:1, 1:3 and 1:6 mixtures of ferric chloride–*m*-cresol, ferric chloride–salicylaldehyde, and ferric chloride–ethyl acetoacetate between 400 and 675 mμ showed that only one colored compound formed in each case since curves of the same shape resulted. Next a series of mixtures was measured at four arbitrarily selected wave lengths. The values of *y*, the difference between the optical density observed and the corresponding optical density calculated for no reaction, were plotted *versus* *x*, the volume of the phenol or ester solution added to the volume (1 − *x*) of the ferric chloride solution. The data are plotted in Figs. 1 and 2; the *y* terms have been multiplied by constants for clarity in presentation. The optical density of the blank ferric chloride solution showed no change within the time the measurements were made.

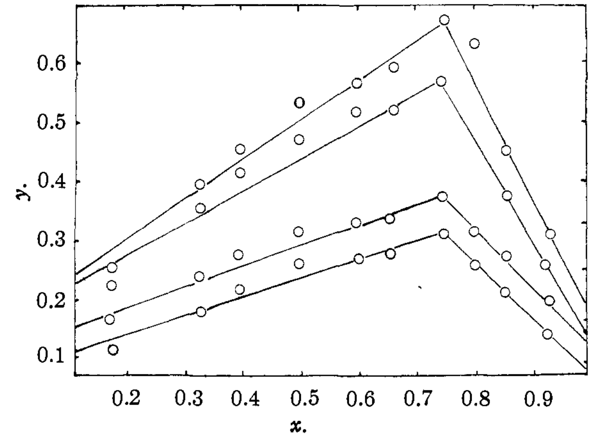

Fig. 1.—Ferric chloride-ethyl acetoacetate from top to bottom: 520, 475, 510, 490 mμ.

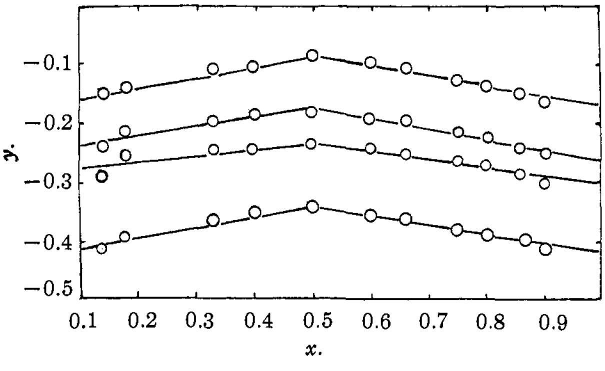

Fig. 2.—Ferric chloride–salicylaldehyde from top to bottom: 540, 520, 500, 560 mμ.

Results and Discussion

As shown in Figs. 1 and 2, the maxima for the colors occurred at 1 ferric chloride:3 ethyl acetoacetate and at a 1:1 ratio for ferric chloride–salicylaldehyde. A similar plot has also shown that the maximum occurs at 1 ferric chloride:3 *m*-cresol. At optical density readings of 0.704, 0.242 and 0.341 for ethyl acetoacetate, salicyladehyde and *m*-cresol, these maxima occurred at 510, 500 and 525 mμ, respectively Thus under the conditions used only one complex occurred for each pair of

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[1] E. F. Wesp and W. R. Brode, THIS JOURNAL, 56, 1037 (1934).

[2] H. B. Bent and C. L. French, *ibid.*, 63, 568 (1941).

[3] S. M. Edmonds and N. Birnbaum, *ibid.*, 63, 1471 (1941).

[4] W. C. Vosburgh and G. R. Cooper, *ibid.*, 63, 437 (1941); R. K. Gould and W. C. Vosburgh, *ibid.*, 64, 1631 (1942).

compounds and no evidence was found for Fe(OR)$_6^{---}$. It is possible that other maxima might be observed at different concentrations and wave lengths. For ethyl acetoacetate, the ferric chloride is believed to react with the cis enol form.[5] Letellier[6] has reported that the maximum of color exists at the ratio of 1 ferric chloride:2 ester in water. The existence of other complex ions has been demonstrated.[7]

The concentration of OR ions may be an important factor in determining which particular complex is formed.[1] It is of interest, therefore, to compare the ionization constants of the organic compounds used. The classical dissociation constants in water at 25° for salicylaldehyde and *m*-cresol are 1.53×10^{-5}[8] and 0.98×10^{-10},[9] respectively. Using the relationship[10]

$$K_a = K_g(1 + K_E)/K_E \qquad (1)$$

where K_a is the classical dissociation constant of the enol form, K_g is the classical dissociation constant, and K_E is the enol–keto equilibrium constant results in a value of 2.9×10^{-10} for K_a for ethyl acetoacetate in water at 25°. Values of 2.09×10^{-11}[10] for K_g and 0.078[5] for K_E were used. Thus it is the more acidic compound, salicylaldehyde, which forms the 1:1 complex. This may be due to steric influences between the ortho CHO group and the hydrated ferric ion.

In regard to electrolysis experiments, Wesp and Brode[1] reported that the phenol complex migrates toward the cathode, while Bent and French[2] claim the color migrates toward the anode. Our results show that the complexes for *m*-cresol and ethyl acetoacetate are neutral; the salicylaldehyde complex should migrate toward the cathode. The observed disappearance of color may be due to the instability of the complex. Due to the neutral nature of the *m*-cresol and ethyl acetoacetate complexes it is essential to establish the existence of the RO$^-$ complex rather than a possible ROH complex. A determination of the *p*H of the solutions as the complexes are formed may prove fruitful in establishing this fact.

Acknowledgment.—The authors are indebted to Mr. Joseph M. Rizzo for technical assistance.

[5] H. Henecka, *Chem. Ber.*, **81**, 179 (1948).

[6] L. Letellier, *Bull. Sci. Pharmacol.*, **38**, 145–217 (1931).

[7] B. Emmert and W. Seebode, *Ber.*, **71B**, 242 (1938).

[8] "International Critical Tables," McGraw-Hill Book Co., Inc., New York, N. Y., Vol. 6, 1929, p. 279.

[9] D. R. Boyd, *J. Chem. Soc.*, 1540 (1915).

[10] M. L. Eidinoff, THIS JOURNAL, **67**, 2072 (1945).

DEPARTMENT OF CHEMISTRY
UTICA COLLEGE OF SYRACUSE UNIVERSITY
UTICA, NEW YORK RECEIVED JULY 9, 1951

Cevine, a Correction

BY LÉO MARION, D. A. RAMSAY AND R. NORMAN JONES

In a previous study of the infrared absorption spectra of a number of alkaloids[1] we reported the presence of a carbonyl absorption band in the infrared spectrum of cevine and concluded that this alkaloid contained a carbonyl group. At the suggestion of Dr. H. L. Holmes we re-examined the base on which our observation had been made and found that it consisted not of cevine but of one of the minor alkaloids occurring with it. This alkaloid which is obtained like cevine by saponification of crude veratrine, crystallizes in short prismatic needles melting at 266–270.5° whereas cevine melts at 164–174°. The infrared absorption spectrum of an authentic sample of cevine *does not* contain a carbonyl absorption band.

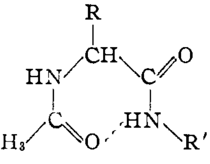
[1] L. Marion, D. A. Ramsay and R. N. Jones, THIS JOURNAL, **73**, 305 (1951).

CHEMISTRY DIVISION
NATIONAL RESEARCH COUNCIL
OTTAWA, CANADA RECEIVED SEPTEMBER 28, 1951

Additional Studies on the Intramolecular Hydrogen Bonding in Acetylglycine N-Methylamide

BY SAN-ICHIRO MIZUSHIMA, TAKEHIKO SHIMANOUCHI, MASAMICHI TSUBOI AND REISUKE SOUDA

In a previous paper[1] we reported our experimental results of near infrared absorption observed for CH$_3$CONHCHRCONHCH$_3$ and CH$_3$CONHCHRCONHC$_6$H$_5$ (R = H or C$_4$H$_9$) in dilute carbon tetrachloride solutions. All these compounds show two NH bands at about 2.9 μ and 3.0 μ of which the former is assigned to the vibrations of the NH group in the free state and the latter to that involved in the *intramolecular* hydrogen bonding of the structure



which corresponds to "B form" (one of the two unit structures of a polypeptide chain) proposed by us in 1947.[2] In view of the importance of proving the existence of B form in the structural chemistry of proteins we have recently made additional measurements of the near infrared absorption, the results of which will be reported in the present note.

In order to obtain further information concerning the relation between molar absorption coefficient κ and concentration *c* for these two NH bands measurements were made at 60° on carbon tetrachloride solutions of acetylglycine N-methylamide CH$_3$CONHCH$_2$CONHCH$_3$ of different concentrations *c* and absorption path-lengths *l*, keeping the product *c* × *l* constant. The results are shown in Fig. 1. If these two NH bands arise solely from single molecules and not from associated molecules (*intermolecular* hydrogen bonding), all the curves (1), (2) and (3) of Fig. 1 must be of the same form. Actually they are found almost of the same form, but differ slightly from one another.

Let us now consider to what extent these three absorption curves should differ from one another, if the 2.98 μ band were to be assigned solely to the *intermolecularly* hydrogen-bonded NH vibration (*i.e.*, solely to the NH association band). Since

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[1] S. Mizushima, T. Shimanouchi, M. Tsuboi, T. Sugita, E. Kato and E. Kondo, THIS JOURNAL, **73**, 1330 (1951).

[2] T. Shimanouchi and S. Mizushima, *Kagaku*, **17**, 24, 52 (1947); *Bull. Chem. Soc. Japan*, **21**, 1 (1948), see *C. A.*, **43**, 8843 (1949).

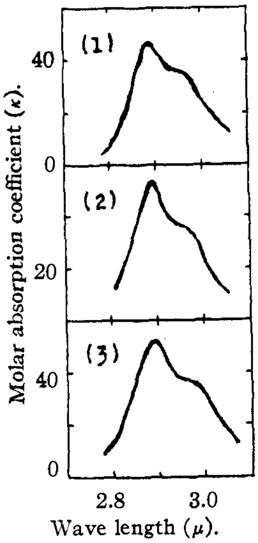

Fig. 1.—Near infrared absorption curves of acetylglycine N-methylamide in dilute carbon tetrachloride solutions at 60°. Concentrations and absorption path-lengths are: (1) 0.0006 mole/l. 5 cm.; (2) 0.0003 mole/l. 10 cm.; (3) 0.00015 mole/l. 20 cm.

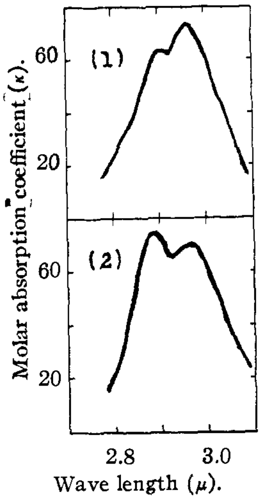

Fig. 3.—Near infrared absorption curves of acetylglycine N-methylamide in dilute carbon tetrachloride solutions at 30°. Concentrations and absorption path-lengths are: (1) 0.0003 mole/l. 5 cm.; (2) 0.00015 mole/l. 10 cm.

the first step of molecular association would be the formation of a dimer, only the monomer–dimer equilibrium is taken into consideration. Figure 2 shows the relation between concentration c and degree of association α calculated for the different values of equilibrium constant K from the law of mass action. (κ of the dimer band is proportional to α, and κ of the monomer band to $1 - \alpha$.) An inspection of this figure reveals that the effect of dilution upon the decrease of α is remarkable. Thus the dilution of a solution from 0.0006 mole/l. to 0.00015 mole/l. results in the decrease of α by one-third for $K = 55$, and by one-half for $K = 1097$.[3] (There is no need of taking the value of K greater than 1097, because κ corresponding to the 2.8 μ band for the 0.0006 mole/l. solution at 60° (Fig. 1) is about one-half of that for the 0.0003 mole/l. solution at 30° (Fig. 3) and, therefore, α cannot be greater than 50% for 0.0006 mole/l. solution at 60°.) For the smaller values of K the decrease in α is more pronounced.

On the other hand the changes in κ for the NH bands of acetylglycine N-methylamide actually observed on dilution from 0.0006 mole/l. to 0.00015 mole/l. at 60° are very small. This fact shows that the 2.98 μ band observed by us in dilute solutions at 60° arises almost solely from the intramolecularly hydrogen-bonded NH group.

We have made similar absorption measurements on dilute solutions of the same compound at 30°, again keeping $c \times l$ constant. On dilution of a solution from 0.0003 mole/l. to 0.00015 mole/l.

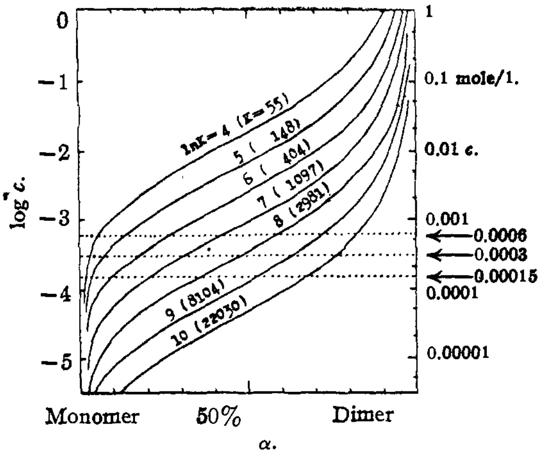

Fig. 2.—Relations between concentration c and degree of association α for different values of equilibrium constant K.

an appreciable increase of κ for the 2.90 μ band and an appreciable decrease of κ for the 2.98 μ band have been observed (see Fig. 3). This shows that at 30° even in a solution as dilute as 0.0003 mole/l. there is an appreciable molecular association in this compound and that the 2.98 μ band must be considered to arise partly from the NH group involved in the abnormally strong *intermolecular* hydrogen bonding. However, as the actually observed changes in κ are far smaller than those for the case in which the 2.98 μ band would solely arise from the *intermolecularly* hydrogen-bonded NH group, we can surely consider that even at 30° the 2.98 μ band arises for the most part from the NH group involved in the *intramolecular* hydrogen bonding.

According to what we have stated above we can confirm our previous conclusion that in dilute carbon tetrachloride solutions of acetylglycine N-methylamide the molecules take partly the "B form."

HONGO, TOKYO, JAPAN RECEIVED AUGUST 14, 1951

Camoquin Relatives[1]

BY H. J. NICHOLAS[2] AND J. H. BURCKHALTER[2]

Camoquin (I) and O-methyl Camoquin (II) are known to possess high antimalarial activity in birds, and the former is now marketed for the treatment of human malaria. Many close analogs of these compounds have already been described,[3] but none apparently possesses an advantage over Camoquin. We have been interested in making somewhat wider variations in structure in order to observe the effect upon antimalarial potency. Two such products, V and VIII, have now been prepared, but they also are inferior to Camoquin.

V was prepared by starting with 2-methoxy-5-nitrophenylacetonitrile (III), which was made from the corresponding benzyl chloride. III was reduced catalytically to the desired intermediate

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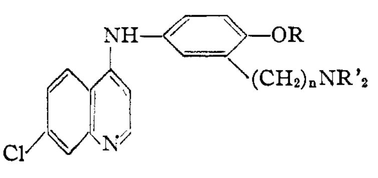
[3] For δ-valerolactam which forms a dimer with the double *intermolecular* hydrogen bond in its carbon tetrachloride solution K was found to be 45 at 60.7° (Tsuboi, *Bull. Chem. Soc. Japan*, **24**, 75 (1951).

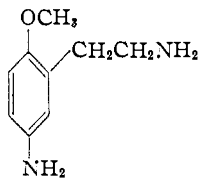
[1] Camoquin is a registered trademark name of Parke, Davis and Co., Detroit.

[2] University of Kansas, Lawrence, Kansas.

[3] (a) J. H. Burckhalter, F. H. Tendick, E. M. Jones, P. A. Jones, W. F. Holcomb and A. L. Rawlins, THIS JOURNAL, **70**, 1363 (1948); (b) J. H. Burckhalter, *J. Am. Pharm. Assoc.*, **38**, 658 (1949).



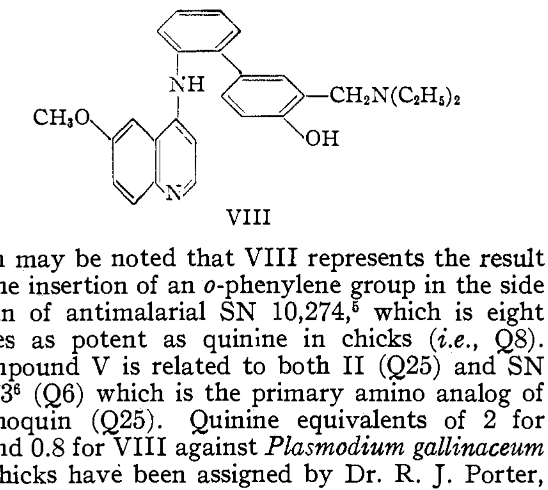
	n	R	R'
I,	1	H	C_2H_5
II,	1	CH_3	C_2H_5
V,	2	CH_3	H



IV

diamine IV, but only in very low yield. Condensation of IV dihydrochloride with 4,7-dichloroquinoline gave V in good yield.

In order to obtain VIII, 2-amino-4'-hydroxybiphenyl was acetylated to its O,N-diacetyl derivative (VI) which was converted to 4-(2-acetamidophenyl)-α-diethylamino-*o*-cresol (VII) by treatment with diethylamine and formaldehyde.[4] VII was then deacetylated with boiling concentrated hydrochloric acid, and after adjustment of the *p*H was condensed with 4-chloro-6-methoxyquinoline to give VIII.



VIII

In may be noted that VIII represents the result of the insertion of an *o*-phenylene group in the side chain of antimalarial SN 10,274,[5] which is eight times as potent as quinine in chicks (*i.e.*, Q8). Compound V is related to both II (Q25) and SN 1,603[6] (Q6) which is the primary amino analog of Camoquin (Q25). Quinine equivalents of 2 for V and 0.8 for VIII against *Plasmodium gallinaceum* in chicks have been assigned by Dr. R. J. Porter, of the University of Michigan, Ann Arbor. These results do not encourage further syntheses in this area.

Experimental

2-Methoxy-5-nitrophenylacetonitrile (III).—A solution of 100 g. of 2-methoxy-5-nitrobenzyl chloride[7] in 300 ml. of absolute alcohol was added slowly to a stirred solution of 32.2 g. of potassium cyanide in 100 ml. of water. Stirring was continued, and the mixture was kept at 75–80° for 2.5 hours while it darkened and potassium chloride separated out. The hot mixture was filtered and cooled whereupon the solid nitrile crystallized. Recrystallization first from benzene and then from alcohol yielded 65 g. (68%) of a yellow product; m.p. 111–113°.

Anal. Calcd. for $C_9H_8N_2O_3$: C, 56.25; H, 4.20. Found: C, 56.63; H, 4.25.

β-(5-Amino-2-methoxyphenyl)-ethylamine (IV) Dihydrochloride.—A mixture of 32 g. of III and 200 ml. of absolute methanol was subjected to three atmospheres of hydrogen in the presence of Adams catalyst. The solid was kept in solution by means of heat. After two hours, no more hydrogen was being taken up, and the amount consumed corresponded to a complete reduction of the nitro group to amino. After removal of the platinum catalyst, 0.6 g. of sodium hydroxide and Raney nickel was added and the clear brown solution reduced further. After 12 hours, the theoretical amount of hydrogen was consumed. The mixture was filtered through fritted glass and the volume of the filtrate reduced by evaporation. The residue was extracted with ether–benzene solution, and the extract was washed with water before it was dried over potassium carbonate. The desired product IV was precipitated as a yellow dihydrochloride from the filtered solution by means of alcoholic hydrogen chloride; m.p. 238–240° dec. Recrystallization from methanol elevated the melting point to 245–247° dec.; yield 7 g. (17%).

Anal. Calcd. for $C_9H_{14}N_2O \cdot 2HCl$: N, 11.72. Found: N, 11.94.

4-(3-β-Aminoethyl-4-methoxyanilino)-7-chloroquinoline (V).—A mixture of 8 g. of IV dihydrochloride, 6.7 g. of 4,7-dichloroquinoline, 50 ml. of water and 25 ml. of dioxane was heated at reflux temperature for 4 hours. A yellow solid separated when the mixture was cooled. After it was collected, washed with water and dried, 11 g. (a theoretical yield) of V was obtained as a light gray colored material; m.p. 185–190°. Recrystallization first from isopropyl alcohol and then from ethanol changed the melting point to 198–200°.

Anal. Calcd. for $C_{18}H_{18}ClN_3O$: C, 65.95; H, 5.53. Found: C, 66.03; H, 5.25.

2-(4-Acetoxyphenyl)-acetanilide (VI).—A mixture of 30 g. of 2-amino-4'-hydroxybiphenyl (92.6% purity),[8] 15 g. of acetic anhydride and 100 ml. of glacial acetic acid was heated to boiling for two hours. The liquid was then removed under reduced pressure and the oily residue dissolved in 100 ml. of hot alcohol. Upon cooling the solution, 30 g. (74% yield) of a crystalline product with a purplish tint was obtained; m.p. 183–185°. Recrystallization from isopropyl alcohol effected no change in melting point.

Anal. Calcd. for $C_{16}H_{15}NO_3$: C, 71.36; H, 5.62. Found: C, 71.86; H, 5.76.

4-(2-Acetamidophenyl)-α-diethylamino-*o*-cresol (VII) Hydrochloride.—A mixture of 8 g. of VI, 1 g. of paraformaldehyde, 5 g. of diethylamine and 75 ml. of isopropyl alcohol was heated to boiling for two hours and then evaporated to an oily consistency. An excess of alcoholic hydrogen chloride was added. After evaporation of the solvent and repeated triturations with mixtures of alcohol, acetone and ether, an off-white crystalline product was finally obtained; m.p. 235–240° dec. After recrystallization from methanol, 5 g. (36% yield) of the desired cresol was obtained; m.p. 245–250° dec.

Anal. Calcd. for $C_{19}H_{24}N_2O_2 \cdot HCl \cdot 2^1/_2H_2O$: C, 57.93; H, 7.68. Found: C, 57.74; H, 7.20.

4-[2-(6-Methoxy-4-quinolylamino)-phenyl]-α-diethylamino-*o*-cresol (VIII).—A mixture of 5 g. of VII hydrochloride and 25 ml. of concentrated hydrochloric acid was heated to boiling for two hours, and then cooled and brought to a *p*H of about 4 by the addition of concentrated ammonium hydroxide. A solution of 2.8 g. of 4-chloro-6-methoxyquinoline in 15 ml. of dioxane was added, and the mixture was heated to boiling for two hours. After cooling the solution, it was treated with an excess of ammonium hydroxide to precipitate an oil which soon solidified. Recrystallized with difficulty first from an ethanol–methanol mixture and then from methanol, the product VIII was obtained in a yield of 3 g. (55%); m.p. 208–210° dec.

Anal. Calcd. for $C_{27}H_{29}N_3O_2$: C, 75.85; H, 6.84. Found: C, 75.84; H, 6.86.

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(4) It will be noted that the basic conditions apparently liberated the phenolic group and allowed the Mannich reaction to occur.

(5) Ref. 3a, Table IX.

(6) Ref. 3a, Table XII.

(7) U. S. Patent 2,278,996.

(8) Kindly supplied by General Aniline and Film Corporation.

RESEARCH LABORATORIES
PARKE, DAVIS AND COMPANY
DETROIT 32, MICHIGAN

RECEIVED JULY 23, 1951

An Interpretation of Bond Lengths in Alkali Halide Gas Molecules

BY R. T. SANDERSON

Alkali halide gas molecules are considered to contain highly polar covalent bonds. The bond lengths in twelve of these compounds have been reported[1] to be generally less than the non-polar covalent radius sums, determined from diatomic gas molecules of the alkali metals and the halogens. They are less also than the internuclear distances in the crystals. Covalent bond "shortening" ascribed to electronegativity differences has been recognized and corrected for empirically,[2] but not clearly understood. The purpose of this note is to suggest a general explanation which for illustration is here applied to the alkali halide gas molecules.

The well-recognized tendency for the electronic sphere of an atom or ion to expand when it gains electrons and contract when it loses electrons need not be thought of as confined to complete electron transfer but may reasonably be expected of any atoms forming polar covalent bonds. From bond energies, Pauling[3] has derived "electronegativity" values which represent the relative attractions of atoms in a covalent bond for the valence electrons. It seems entirely reasonable to consider the electronegativities to become equalized in the process of covalent bond formation. If the atoms after combination have equal attraction for the valence electrons although before combination the attraction was unequal, then an adjustment must have occurred during the combining. Such an adjustment is easily visualized. Polarity of the bond results because the valence electrons spend more than half-time more closely associated with the atom initially attracting them more. In effect, this gives this atom a partial negative charge and results in expansion of its electronic sphere. Expansion of its electronic sphere diminishes the attraction of the nucleus for these valence electrons. Similarly, the atom initially having less attraction for the valence electrons gains a partial positive charge which results in contraction of its electronic sphere. This contraction results in increased attraction of its nucleus for the valence electrons. In combining to form a covalent bond, then, the more electronegative atom expands, thereby lessening its attraction for the valence electrons, and the less electronegative atom contracts, thereby increasing its attraction for the valence electrons, until the attractions of the two atoms are equal. The bond length is then the sum of the *adjusted radii*. If a relation between electronegativity and radius were known, the length of a bond between two atoms initially different in electronegativity could be calculated.

A relationship between electronegativity and radius has been found, by inquiring into the origin of the chemical differences between inert element atoms and isoelectronic ions. Such ions differ from the atoms of the inert elements not only in nuclear charge but also in the average packing of electrons. The degree of packing may be simply expressed as the "*average* electronic density (*ED*)," in number of electrons per cu. Å.

$$ED = Z/4.19r^3 \qquad (1)$$

where Z is the electronic number and r the ionic or non-polar covalent radius. *ED*'s of atoms of the inert elements, calculated from radii suggested by Pauling,[4] are: He 0.61, Ne 1.70, A 1.18, Kr 1.78, Xe 1.87, Rn 1.93. The electronic spheres of cations are more compact and of anions less compact than those of the isoelectronic inert atoms. The *ED*'s of all the active atoms are likewise different from those of the inert atoms, only the most active metals having less dense electronic spheres and the most active non-metals having spheres of much greater average density.

If it is assumed that the great chemical stability of the inert elements is associated not only with their atomic number but also with their *ED*, then the relative attraction for electrons, or in a sense the electronegativity, of an atom or ion of an active element may be expressed as the ratio of its *ED* to that of an isoelectronic inert atom (real, or determined by linear interpolation between real values). This ratio is called the "stability ratio (*SR*)." The *SR* values for some of the elements are compared with electronegativity values in Table I. The numerical similarity is of course fortuitous but the comparison indicates that *SR* values may be used for determining bond lengths as suggested above.

TABLE I

STABILITY RATIOS AND ELECTRONEGATIVITIES

	EN	*SR*		*EN*	*SR*		*EN*	*SR*
Li	1.0	0.39	Na	0.9	0.44	K	0.8	0.50
Be	1.5	1.45	Mg	1.2	0.82	Rb	0.8	0.53
B	2.0	2.10	Al	1.5	1.24	Br	2.8	3.22
C	2.5	2.68	Si	1.8	1.70	Cs	0.7	0.62
N	3.0	3.04	P	2.1	2.20	I	2.4	2.89
O	3.5	3.42	S	2.5	2.74			
F	4.0	3.66	Cl	3.0	3.35			

The adjusted radius, r, of each atom in a molecule may be determined by use of the equation

$$r = \sqrt[3]{\frac{Z}{4.19SR_{\mathrm{m}}ED_{\mathrm{i}}}} \qquad (2)$$

where SR_{m}, the stability ratio of the molecule, is the geometric mean of the SR's of all the atoms of the molecule before combination, and ED_{i} is the *ED* corresponding to inert atom stability for electronic number Z.

Application of this method to the alkali halide gas molecules is illustrated in Table II. For these particular molecules, the bonds were considered to be so polar that slightly greater accuracy would result from substituting the ionic rather than covalent values of Z. The difference is slight and such a correction is unnecessary for most molecules. It may be observed from a careful study of these data that if it is reasonable to expect fairly uniform differences among bond lengths of such similar molecules, then such discrepancies as shown for CsBr and RbI are more likely to be the result of errors in measurement rather than in calculation.

According to the ideas presented herein, bond

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(1) S. B. Hendricks and V. M. Mosley, *Phys. Rev.*, **51**, 1000 (1937); L. R. Maxwell, S. B. Hendricks and V. M. Mosley, *ibid.*, **52**, 968 (1937).

(2) V. Schomaker and D. P. Stevenson, THIS JOURNAL, **63**, 37 (1941).

(3) L. Pauling, "Nature of the Chemical Bond," 2nd Ed., Cornell University Press, Ithaca, N. Y., 1940.

(4) L. Pauling, "General Chemistry," W. H. Freeman and Co., San Francisco, Calif., 1948, p. 145.

TABLE II

BOND LENGTHS (Å.) IN ALKALI HALIDE GAS MOLECULES

Compound	Non-polar covalent radius[5]			Adjusted covalent radius			Reported bond length[1]
	r_m	r_x	Sum	r_m	r_x	Sum	
NaCl	1.54	0.99	2.53	1.05	1.44	2.49	2.51 ± 0.03
KCl	1.96	.99	2.95	1.41	1.41	2.82	2.79 ± 0.02
RbCl	2.11	.99	3.10	1.54	1.40	2.94	2.89 ± 0.01
CsCl	2.25	.99	3.24	1.69	1.36	3.05	3.06 ± 0.03
NaBr	1.54	1.14	2.68	1.06	1.59	2.65	2.64 ± 0.01
KBr	1.96	1.14	3.10	1.42	1.56	2.98	2.94 ± 0.03
RbBr	2.11	1.14	3.25	1.55	1.55	3.10	3.06 ± 0.02
CsBr	2.25	1.14	3.39	1.70	1.51	3.21	3.14 ± 0.03
NaI	1.54	1.33	2.87	1.08	1.83	2.91	2.90 ± 0.02
KI	1.96	1.33	3.29	1.45	1.79	3.24	3.23 ± 0.04
RbI	2.11	1.33	3.44	1.58	1.77	3.35	3.26 ± 0.02
CsI	2.25	1.33	3.58	1.73	1.73	3.46	3.41 ± 0.03

"shortening" results when the contraction of the less electronegative atom of a covalent bond exceeds the expansion of the more electronegative atom.

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(5) G. Herzberg, "Molecular Spectra and Molecular Structure. I. Spectra of Diatomic Molecules," 2nd Ed., D. Van Nostrand Co., Inc., New York, N. Y.

DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING
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RECEIVED AUGUST 24, 1951

An Improved Synthesis of 3-Acetimido-5-methyltetronic Acid[1]

BY THEODORE L. REBSTOCK AND HAROLD M. SELL

3-Acetimido-5-methyltetronic acid has recently become of added interest because of its chlorophyll inhibition and herbicidal action on several plants.[2] Since this publication numerous inquiries have been made concerning its preparation as several investigators[3] have often failed to realize the desired product. The method of synthesis described by Lecocq[4] in most cases leads to a sirup and other crystalline by-products or produces the substance in very low yields. The reason for these failures may be use of too high temperatures during the condensation, too rapid addition of α-bromopropionyl bromide, moist solvents and reagents, and not using the proper ratio of ethyl β-aminocrotonate and α-bromopropionyl bromide. Low temperature condensation may also aid in yielding the correct product by preventing internal heating and causing the ethyl β-aminocrotonate to react in the imino[5] form with the acid bromide.

The purpose of this report is to present a modification of Lecocq's method which will consistently give 3-acetimido-5-methyltetronic acid in better yields.

Experimental

A mixture containing 96 g. (0.74 mole) of ethyl β-aminocrotonate, 65.5 g. (0.83 mole) of anhydrous pyridine and 320 ml. of anhydrous ethyl ether was placed in a 1-liter three-necked round-bottom flask fitted with an efficient mercury-sealed mechanical stirrer, reflux condenser with a calcium chloride tube and a dropping funnel. The flask and contents were cooled in a Dry Ice–ethanol mixture to −60°; 180 g. (0.83 mole) of freshly distilled α-bromopropionyl bromide was added dropwise to the cooled solution over a period of two hours. The solution was stirred vigorously during the entire addition of the acid bromide and the temperature was maintained between −50 to −60°. After adding the α-bromopropionyl bromide, the stirring was continued and the solution was permitted to come to room temperature which required approximately two hours. To this mixture was added 160 ml. of chloroform and 400 ml. of water. The ether-chloroform phase (upper layer) was separated from the aqueous phase in a 2-l. separatory funnel and the organic layer dried over 20 g. of anhydrous sodium sulfate for two hours. The drying agent was removed by filtration upon a buchner funnel, the cake washed with ether, and the filtrate was concentrated under reduced pressure to a volume of 175 ml. The amorphous material which separated from the mixture was dissolved upon the addition of 50 ml. of absolute ethanol. The clear solution was placed in the refrigerator overnight for crystallization. Occasionally it was necessary to scratch the side of the flask containing the cooled mixture in order to induce crystallization. The product was collected on a dry filter paper in a buchner funnel. It was recrystallized by dissolving the material in 100 ml. of hot 30% methanol, decanting the supernatant liquid from the insoluble oil and permitting the solution to crystallize in the refrigerator overnight. The yield of white rectangular crystals was 28 g., m.p. 160–161°.[4] Upon further concentration of the mother liquor and crystallization by the method previously described, an additional 7 g., m.p. 160–161° is obtained. The total yield is 35 g. (30.2%).

Anal.[6] Calcd. for $C_7H_9O_3N$: N, 9.02. Found: N, 8.99.

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[1] Published as Journal Article No. 1275 of the Michigan Agricultural Experiment Station. This research was supported in part by a grant from the Rockefeller Foundation.

[2] Hamner and Tukey, *Bot. Gaz.*, **112**, 525 (1951).

[3] Personal communications to H. M. S. and T. L. R.

[4] Lecocq, *Compt. rend. acad. sci.*, **222**, 183 (1946).

[5] Knoevenagel, *Ber.*, **32**, 853 (1899).

[6] No analysis was given on this compound by Lecocq.[4]

DEPARTMENT OF AGRICULTURAL CHEMISTRY
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RECEIVED AUGUST 17, 1951

Stable Bromonium and Chloronium Salts

BY REUBEN B. SANDIN AND ALLAN S. HAY

Mascarelli and Benati[1] prepared diphenyleneiodonium iodide[2] by the addition of potassium iodide to tetrazotized 2,2′-diaminobiphenyl. More recently this reaction has been used, without any apparent difficulty, by various workers[3] for the preparation of derivatives of diphenyleneiodonium iodide. However, as far as the authors of this paper are aware no bromonium or chloronium compounds have been isolated as such. Nevertheless the concept of a three-membered positively charged cylic halonium ion has been proposed by Roberts and Kimball.[4] This concept has been used with much success by Winstein and Lucas and co-workers.[5] In their work, there is ample evidence for the existence of cyclic bromonium and chloronium intermediates. Bartlett and Tarbell[6] have demonstrated the existence of intermediate positive ions containing halogen atoms in the re-

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[1] L. Mascarelli and Benati, *Gazz. chim. ital.*, [II] **38**, 624 (1908).

[2] This compound is also called dibenziodolium iodide. For nomenclature see *C. A.*, **39**, 5938 (1945).

[3] N. E. Searle and R. Adams, THIS JOURNAL, **55**, 1649 (1933); W. C. Lothrop, *ibid.*, **63**, 1187 (1941); M. Rieger and F. H. Westheimer, *ibid.*, **72**, 28 (1950).

[4] I. Roberts and G. E. Kimball, *ibid.*, **59**, 947 (1937).

[5] S. Winstein and H. J. Lucas, *ibid.*, **61**, 1576, 2845 (1939); H. J. Lucas and C. W. Gould, *ibid.*, **63**, 2541 (1941); S. Winstein, *ibid.*, **64**, 2791, 2792 (1942); S. Winstein, E. Grunwald, R. E. Buckles and C. Hanson, *ibid.*, **70**, 816 (1948); S. Winstein and E. Grunwald, *ibid.*, **68**, 536 (1946); S. Winstein, E. Grunwald and L. L. Ingraham, *ibid.*, **70**, 812 (1948); H. J. Lucas and H. K. Garner, *ibid.*, **72**, 2145 (1950).

[6] P. D. Bartlett and D. S. Tarbell, *ibid.*, **58**, 466 (1936); **59**, 407 (1937).

action between bromine and stilbene and in the reaction between chlorine and dimethylmaleic acid. It was the purpose of this work to determine if it was possible to prepare cyclic halonium compounds which do not contain iodine as part of the ring system. As a result the present authors have found that diazotized 2-amino-2′-iodobiphenyl is converted into iodonium salts. Similarly it has been found that 2-amino-2′-bromobiphenyl and 2-amino-2′-chlorobiphenyl are converted into bromonium and chloronium compounds, respectively.

All the compounds needed for the investigation were known, but only the acetyl derivative of 2-amino-2′-iodobiphenyl has been characterized.[7]

Experimental[8]

2-Amino-2′-iodobiphenyl (V) was prepared according to Mascarelli and Gatti[9] who used 2,2′-dinitrobiphenyl as the starting material. The over-all yield of crude 2-amino-2′-iodobiphenyl from 59 g. of the dinitro compound was 20 g. The amine failed to crystallize on long standing and was fractionally distilled; b.p. 197° at 8 mm. The distillate solidified on cooling and after several recrystallizations from ethanol yielded 12 g. of almost white, granular 2-amino-2′-iodobiphenyl; m.p. 81–82°.

Anal. Calcd. for $C_{12}H_{10}NI$: I, 43.0. Found: I, 42.8, 43.2.

An equally satisfactory starting material for preparing V was 2-amino-2′-acetamidobiphenyl (VI)[10] which was diazotized, treated with potassium iodide, hydrolyzed with hydrochloric acid in ethanol and finally made alkaline and steam distilled. The over-all yield of crude V from VI was about 25%. Compound VI was also used for the preparation of 2-amino-2′-bromobiphenyl (VII) and 2-amino-2′-chlorobiphenyl (VIII) which were known compounds. The over-all yield of crude VII from 41 g. of VI was 22 g. We were unsuccessful in making this compound solidify. The reported m.p. is 46–50°.[9] For that reason VII was purified as the hydrochloride, m.p. 184–185°, and used as such in subsequent work.

Anal. Calcd. for $C_{12}H_{11}NClBr$: Cl, 12.5. Found: Cl, 12.5, 12.5.

The over-all yield of crude VIII from 33 g. of VI was 11 g. It was crystallized from ethanol, m.p. 54°. The reported m.p. is 56–57°.[9]

Preparation of Diphenyleneiodonium Salts.—Three grams of 2-amino-2′-iodobiphenyl was dissolved in boiling 10% hydrochloric acid (180 ml.). On cooling the hydrochloride separated. The mixture was treated at 0–5° with sodium nitrite (1.5 g.) in water (60 ml.). The diazotized solution was allowed to stand at 0–5° for 30 minutes and then treated with urea (1.5 g.). After standing for another 30 minutes potassium iodide (5 g.) in water (20 ml.) was added and the mixture was heated on the steam-bath until the evolution of gas had ceased. During the heating diphenyleneiodonium iodide separated as a brown solid. The mixture was cooled, filtered and the crude salt converted into the nitrate[11] which was crystallized from water. The yield was 1.5 g.; decomposition temperature 241–242°.

Anal. Calcd. for $C_{12}H_8O_3NI$: I, 37.3. Found (Carius): I, 37.5, 37.4.

Sodium chloride was added to some of the nitrate in water. This afforded diphenyleneiodonium chloride which crystallized from water as white needles, decomposing at 292–294°.

Anal. Calcd. for $C_{12}H_8ClI$: Cl, 11.3. Found (silver nitrate and nitric acid): Cl, 11.3, 11.2.

Diphenyleneiodonium chloride was also made directly from V by diazotization in hydrochloric acid followed by heating on the steam-bath.

Preparation of Diphenylenebromonium Salts.—The hydrochloride of 2-amino-2′-bromobiphenyl (1.0 g.) was dissolved in boiling 10% hydrochloric acid (40 ml.). The cooled (0–5°) solution was treated with sodium nitrite (0.5 g.) in water (10 ml.). After standing at 0–5° for 30 minutes, urea (0.5 g.) was added. After another 30 minutes, the solution was heated on the steam-bath until the evolution of gas had ceased. The hot reaction mixture was clarified with charcoal, filtered hot, and the filtrate cooled in ice-water. Diphenylenebromonium chloride separated as white needles. After several crystallizations from water the yield was 0.4 g. and it decomposed at 205–207°.

Anal. Calcd. for $C_{12}H_8ClBr$: Cl and Br, 43.1. Found: Cl and Br (Carius), 42.7.

A small amount of the salt was decomposed by heat. The reaction product was crystallized from ethanol, which afforded white crystals, m.p. 58°. The reported m.p. for 2-bromo-2′-chlorobiphenyl is 58°.[9] A solution of the salt was treated with potassium iodide. The solid diphenylenebromonium iodide which separated was filtered, and recrystallized from water to give fine yellow crystals, decomposing at 165–170° with the evolution of iodine.

Anal. Calcd. for $C_{12}H_8BrI$: I, 35.4. Found (silver nitrate and nitric acid): I, 35.3, 35.4.

Preparation of Diphenylenechloronium Iodide.—The preparation of this compound from 2-amino-2′-chlorobiphenyl was the same as described for diphenylenebromonium chloride. However instead of standing for 30 minutes after the urea treatment, the solution was allowed to stand overnight at 5–10°. It was then heated *gently* on the steam-bath until gas evolution had ceased, cooled to 5–10° and the chloronium iodide precipitated as a brown solid by the addition of solid potassium iodide. The salt was filtered and redissolved in water using a *steam-bath* as a source of heat, clarified with charcoal and filtered hot. The cold filtrate was treated with solid potassium iodide which afforded the chloronium iodide as a solid which this time was much lighter in color. Three crystallizations from water (*steam-bath*), afforded diphenylenechloronium iodide as pale yellow needles (darkened in light) which decomposed with some violence at 125–130°. The yield from 1 g. of 2-amino-2′-chlorobiphenyl was 0.4 g.

Anal. Calcd. for $C_{12}H_8ClI$: I, 40.35, Cl and I, 51.6. Found: I (silver nitrate and nitric acid), 39.9, 40.5; Cl and I (Carius), 51.4.

A small amount of the salt was decomposed by heat. The residue was crystallized from ethanol which yielded white crystals, m.p. 63–64°. The reported m.p. for 2-chloro-2′-iodobiphenyl is 63–64°.[9]

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[7] *C. A.*, **26**, 1272 (1932), lists the 2-amino-2′-iodobiphenyl as melting at 129–130°. Evidently this is not the m.p. of the amine but of the acylated derivative.

[8] All melting points and decomposition temperatures are uncorrected.

[9] L. Mascarelli and D. Gatti, *Atti accad. Lincei*, **13**, 887 (1931).

[10] S. Sako, *Mem. Coll. Eng. Kyushu Imp. Univ.*, **6**, 263 (1932).

[11] A. Wasylewsky, R. K. Brown and R. B. Sandin, THIS JOURNAL, **72**, 1038 (1950).

Factors Involved in the Sharpening of the Ultraviolet Absorption Spectrum of Guanine at Reduced Temperatures[1]

BY J. F. SCOTT, R. L. SINSHEIMER AND J. R. LOOFBOUROW[2]

During the course of studies on the effect of low temperatures upon the ultraviolet absorption spectra of various compounds of biological importance, we have noted[3,4] that the spectra of thin films of sublimate of most of the pyrimidines examined show a considerable degree of sharpening

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[1] The work was supported in part by a grant from the American Cancer Society, recommended by the Committee on Growth of the National Research Council, and in part by a grant from the U. S. Public Health Service.

[2] Deceased, January 22, 1951.

[3] J. F. Scott, R. L. Sinsheimer and J. R. Loofbourow, *Science*, **107**, 302 (1948).

[4] (a) R. L. Sinsheimer, J. F. Scott, J. R. Loofbourow, *J. Biol. Chem.*, **187**, 299 (1950); (b) **187**, 313 (1950).

while the spectra of similar preparations of the purines show little or no fine structure even when the temperature of the sample was reduced to that of liquid H_2. Some of the pyrimidines show an increase in fine structure in the low-temperature spectra upon exposure of the film of sublimate to an atmosphere containing water vapor.[5]

By exposure of sublimed films of purines to high water vapor concentrations we have been able to produce certain spectral changes and to detect a simultaneous change in the order of the molecules comprising the film. Figure 1 demonstrates the changes in the low-temperature ultraviolet absorption spectrum of a thin film of sublimate of guanine (2-amino-6-purinone) upon exposure to high water vapor concentration for increasing periods of time.

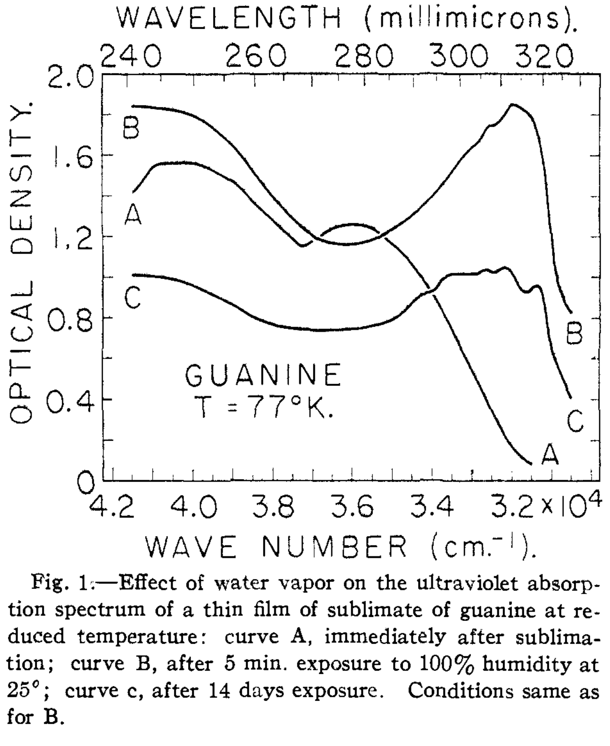

Fig. 1.—Effect of water vapor on the ultraviolet absorption spectrum of a thin film of sublimate of guanine at reduced temperature: curve A, immediately after sublimation; curve B, after 5 min. exposure to 100% humidity at 25°; curve c, after 14 days exposure. Conditions same as for B.

Corresponding changes in the infrared absorption spectrum of a similar but thicker film of the same compound are shown in Fig. 2. The two infrared spectra were obtained with identical conditions of resolution. The sample in this case was at room temperature.

Figure 3 shows the changes produced in the X-ray diffraction pattern of a film of sublimed guanine upon exposure of the film to water vapor. Heating the sublimed films to 60° for four days in a vacuum oven failed to reverse the alteration in the spectra produced by the exposure to water vapor.

Experimental

The details of the method for the preparation of the films of sublimate and for the absorption spectrophotometry have been published elsewhere.[4,5]

X-Ray Diffraction.—The sublimed material was scraped from the glass slide upon which it had been deposited and the resulting powder placed in a glass capillary tube for X-ray diffraction. A camera with a flat film cassette was used; specimen-to-film distance, 5 cm.; radiation, nickel filtered CuKα (λ 1.54 Å).

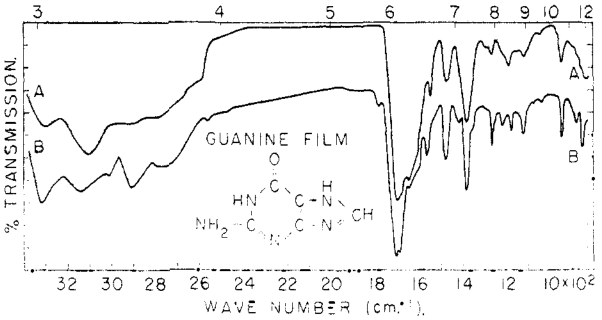

Fig. 2.—Effect of water vapor on the infrared absorption spectrum of a thin film of sublimate of guanine: curve A, immediately after sublimation; curve B, after 5 min. at 100% humidity at 25°. For clarity of presentation curve B has been displaced downward by subtracting 20% from each observed transmission value.

Discussion of Results

The appearance of fine structure in the low-temperature ultraviolet spectrum can be correlated with the changes in the infrared spectra. The latter show a sharpening and splitting of certain absorption bands upon exposure of the film of sublimate to high humidity. In the region of 2900–3300 cm.$^{-1}$ new bands appear while there is some splitting of the band in the 1700 cm.$^{-1}$ region indicating an alteration in the charge distribution about the double bonds in the molecule. One of the more interesting changes is the splitting of the band in the region of 800–900 cm.$^{-1}$. Blout, *et al.*,[6] noted that the major difference between the infrared spectrum of a film of sublimate of guanine and of a Nujol mull of the original material was primarily this difference in the band at 800–900 cm.$^{-1}$. The X-ray diffraction pattern shows clearly that exposure of the film to water vapor produces transition from a largely amorphous material to a largely crystalline material. The diffraction maxima of the latter correspond very closely to those reported by Clark.[7]

This evidence suggests that of the factors influencing the degree of sharpening of the ultraviolet absorption spectrum resulting from the reduction of the temperature of the sample,[4b] the degree of order in the spatial distribution of the fields acting on each absorber is of prime importance. Such spatial order may result when the molecules are arrayed in a crystal lattice. Reduction of the temperature reduces random fluctuations in the fields acting on each absorbing molecule during the period of observation. When conditions of order with respect to both space and time have been produced in the sample then fine structure may appear in the low-temperature ultraviolet absorption spectrum. Hainer and King[8] have demonstrated the effect of crystallization on the low temperature infrared absorption spectrum.

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[5] R. L. Sinsheimer, J. F. Scott and J. R. Loofbourow, *Nature*, **164**, 796 (1949).

[6] E. R. Blout, M. Field and R. Karplus, THIS JOURNAL, **70**, 194 (1948).

[7] C. Clark, Ph.D. thesis, Dept. of Zoology, Columbia Univ., New York, N. Y., 1950.

[8] R. M. Hainer and G. W. King, *Nature*, **166**, 1029 (1950).

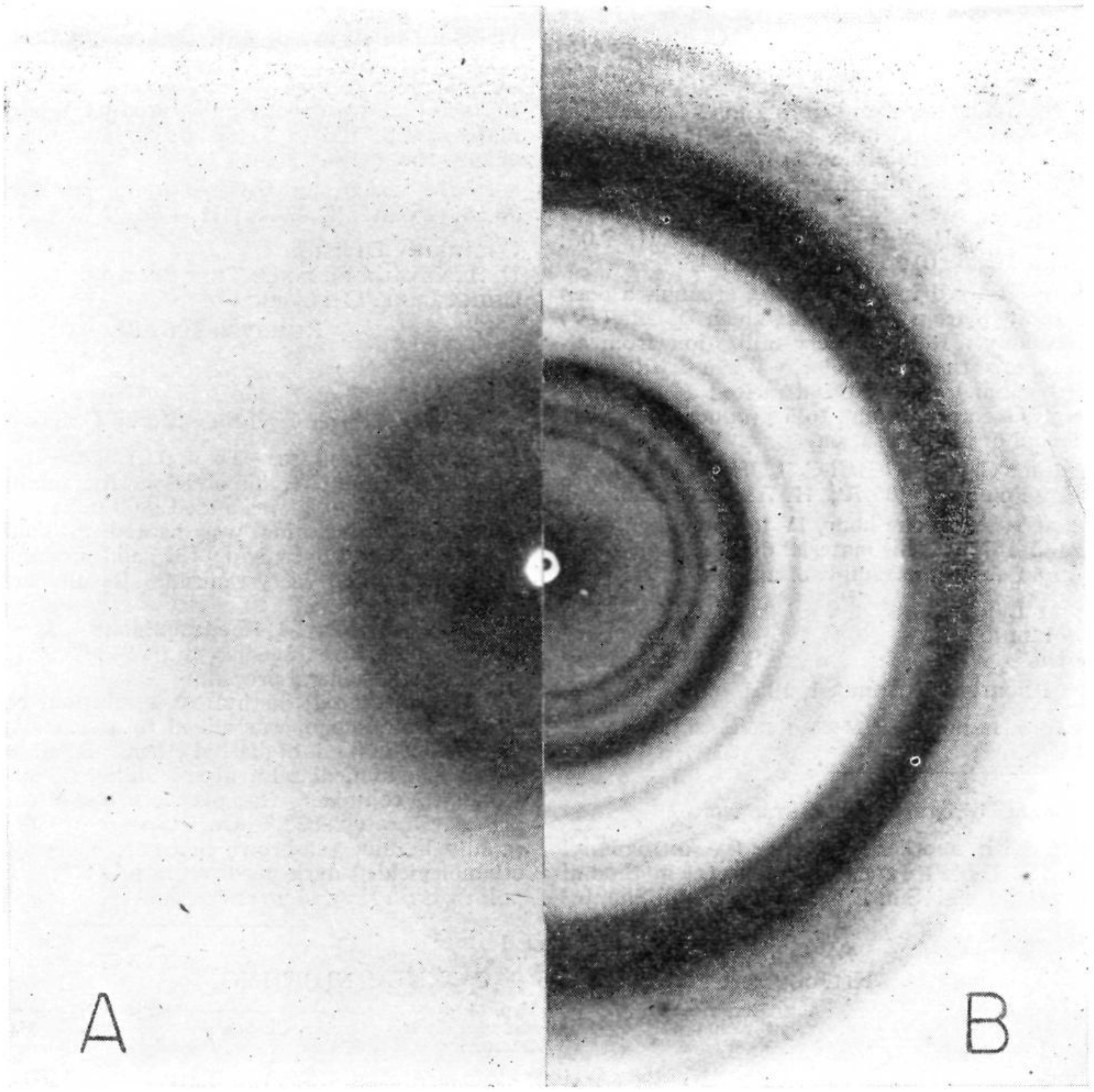

Fig. 3.—Effect of water vapor upon the X-ray diffraction pattern of a film of sublimate of guanine: A, immediately after sublimation; B, after 2 days at 100% humidity at 25°.

From our results the influence of spatial order on the infrared absorption band width is also evident at room temperature.

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NEW COMPOUNDS

1,5-Diphenyl-3-(β-morpholinoethyl)-2-pyrazoline Hydrochloride

1,5-Diphenyl-3-(β-morpholinoethyl)-2-pyrazoline hydrochloride was prepared by an acid-catalyzed isomerization of the phenylhydrazone of 1-phenyl-5-morpholino-1-penten-3-one hydrochloride. The method employed was a modification of that described by Nisbet.[1]

1-Phenyl-5-morpholino-1-penten-3-one Hydrochloride (I).—A mixture of 36.5 g. (0.25 mole) of benzalacetophenone, 31 g. (0.25 mole) of morpholine hydrochloride and 10 g. (0.3 mole) of paraformaldehyde in 25 ml. of absolute ethanol was heated quickly to the boiling temperature with frequent stirring. One milliliter of concentrated hydrochloric acid was then added and the mixture boiled under reflux 30 minutes. Three more grams of paraformaldehyde was added gradually through the reflux condenser and the boiling continued another 30 minutes. After the contents had cooled to room temperature, 150 ml. of acetone was added and the mixture was allowed to stand overnight in the refrigerator. Thirty grams (44%) of pale yellow crystals, m.p. 175.5–176.6° dec.[2] was collected. The crude hydrochloride was dissolved in 200 ml. of boiling absolute ethanol, the solution treated with Norite and allowed to cool slowly. Twenty-seven grams of white crystals, m.p. 175.5–177° dec., was collected. Repeated crystallization furnished feathery white needles melting at 177–179° dec.

Anal.[3] Calcd. for $C_{15}H_{19}NO_2 \cdot HCl$: C, 63.93; H, 7.15; N, 4.97. Found: C, 64.34, 64.40; H, 7.30, 7.22; N, 5.08, 5.17.

Phenylhydrazone (II).—When prepared in the usual manner (yield 89%) and recrystallized from absolute ethanol, this derivative melts at 175–179°, depending on the rate of heating.

Anal. Calcd. for $C_{21}H_{25}N_3O \cdot HCl$: C, 67.81; H, 7.05; N, 11.30. Found: C, 68.59, 68.61; H, 7.16, 7.24; N, 11.16, 11.07.

1,5-Diphenyl-3-(β-morpholinoethyl)-2-pyrazoline Hydrochloride (III).—A suspension of 10.3 g. (0.027 mole) of crude II in 150 ml. of 1 *N* hydrochloric acid was heated to boiling. While heating, the mixture gradually became thin and changed from yellow to chartreuse. At the boiling

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[1] H. B. Nisbet, *J. Chem. Soc.*, 1237 (1938).

[2] All melting points are corrected.

[3] Analyses by Emily Davis, Jean Fortney and K. Pih.