NOTES

The Solid Solution Series, Boron–Boron Carbide[1]

By Robert D. Allen

Received March 7, 1953

Boron carbide has been produced whose B/C ratio is considerably greater than four; only part of the excess boron can be removed by nitric acid or aqua regia. This observation led to the notion that a degree of solid solution can exist between boron and B_4C. Early difficulties experienced in ascertaining the combining proportions of boron and carbon were probably caused by inconstancy of the B/C ratio.

Three samples of boron carbide were employed in this investigation. Normal Hot-Molded Boron Carbide (B_4C) was designated Sample No. 1. Sample No. 2 ($B_{5.66}C$) consisted of boron carbide fragments obtained as by-product during the manufacture of boron by the "hot wire" method. The boron carbide formed on the surface of the graphite rod prior to deposition of high purity boron. Sample No. 3 (B_7C) was prepared by ball milling a composite of high-boron boron carbide crudes. These crudes were produced in three separate runs in a small closed-shell resistor furnace; the charge in each case consisted of B_4C and B_2O_3 glass. Experimental work encompassed the following chemical and physical properties: B/C ratio, unit cell dimensions, specific gravity, Knoop hardness and lapping characteristics.

The object of this endeavor was threefold: (1) to establish the limit of solid solution of boron in boron carbide; (2) to determine the mechanism of solid solution; (3) to correlate changes in physical properties with change in the B/C ratio.

Historical Review.—The only allusion in the literature to solution of boron in B_4C was made by Clark and Hoard.[2] They suggested that excess boron might be interstitially accommodated in the boron carbide structure.

The following hexagonal unit cell dimensions have been determined on B_4C:

Source	a_0	c_0
Laves[3]	5.62kX. (5.63 Å.)	12.12kX. (12.14 Å.)
Zhdanov and Sevast'yanov[4]	5.60kX. (5.61 Å.)	12.10kX. (12.12 Å.)
Clark and Hoard[2]	5.60kX. (5.61 Å.)	12.12kX. (12.14 Å.)

Experimental Work

Specimens were X-rayed on a North American Philips Geiger Counter X-Ray Spectrometer over the range $2\theta = 4 - 90°$ with nickel-filtered copper radiation. The appropriate *hk.l* indices were assigned. It was then possible to determine the hexagonal unit cell dimensions a_0 and c_0. As a check on the accuracy of these measurements d/n values were calculated for the various reflecting planes and compared with observed d/n values.

The principal X-ray constants are presented in Table I. Detailed X-ray data appear in Table II.

Table I

X-Ray Constants of B_4C, $B_{5.66}C$ and B_7C

Specimen	1. (B_4C)	2. ($B_{5.66}C$)	3. (B_7C)
c_0, Å.	12.07	12.15	12.19
a_0, Å.	5.61	5.65	5.67
c_0/a_0	2.151	2.150	2.150
Hexagonal unit cell vol. Å.^{3}	328.94	335.86	339.38
Unit cell vol. expansion (over normal B_4C), %	...	2.10	3.17

Samples no. 2 and 3 were subjected to chemical analysis and density measurement after the following treatment. They were reduced to 240 mesh and boiled in concentrated HNO_3 for three hours to dissolve free boron. After acid treatment samples were copiously washed with hot water and dried in an oven. Chemical and specific gravity data are contrasted with ideal data for normal B_4C in Table III.

Decreased bonding strength in high-boron boron carbide was demonstrated by physical tests of Knoop hardness and lapping effectiveness. The following values for Knoop hardness were obtained: B_4C—2810; $B_{5.66}C$—2580. B_7C was too fine grained to permit hardness measurement. As a lapping abrasive the high-boron modification was less effective than B_4C with respect to the following criteria: (1) weight of stock removed and (2) rate of break-down of abrasive grain.

In short, increase in the B/C ratio is reflected by changes in physical properties as follows: (1) dimensions of the unit cell increase; (2) specific gravity, hardness and "strength" decrease.

Mechanism of Solid Solution.—Theoretical densities have been calculated assuming alternate hypothetical solid solution mechanisms. Use was made of the equation

$$\text{S. G.} = \frac{(10.82x + 12.01y)(1.66)}{V}$$

where S. G. is the specific gravity, V is the volume and x and y are the respective numbers of boron and carbon atoms in the unit volume selected. $B_{5.66}C$ was employed in the calculations assuming successively: (1) extra boron atoms are accommodated interstitially, (2) extra boron atoms replace carbon atoms, (3) carbon atoms have been omitted from the structure.

(1) Interstitial Solid Solution

$B_{12}C_3$ plus 5B equals $B_{17}C_3$ in one rhombohedral cell.

$$\text{S. G.} = \frac{[(17)(10.82) + (3)(12.01)]\,[1.66]}{(0.33)(335.86)} = 3.29$$

(2) Substitutional Solid Solution

3 B's replace 3 C's in four rhombohedral cells to give $B_{51}C_9$

$$\text{S. G.} = \frac{[(51)(10.82) + (9)(12.01)]\,[1.66]}{(1.33)(335.86)} = 2.45$$

(3) Omission Solid Solution

$B_{5.66}C$ equals *ca.* $B_{12}C_2$ in one rhombohedral cell.

$$\text{S. G.} = \frac{[(12)(10.82) + (2)(12.01)]\,[1.66]}{(0.33)(335.86)} = 2.28$$

The experimental density of 2.484 is best ex-

---

[1] Contribution from the Research and Development Department, Norton Company, Worcester, Massachusetts.

[2] H. K. Clark and J. L. Hoard, This Journal, **65**, 2113 (1943).

[3] F. Laves, *Z. Ges. Wiss. Göttingen, Mathem.-Physik Kl., Neue Folge*, 1, 57 (1934).

[4] (a) G. S. Zhdanov and N. G. Sevast'yanov, *Compt. Rend. Acad. Sci. URSS*, **32**, 432 (1941); (b) G. S. Zhdanov and N. G. Sevast'yanov, *J. Phys. Chem. URSS*, **42**, 326 (1943).

TABLE II

X-RAY DATA ON B_4C, $B_{5.66}C$ AND B_7C ($d_{hk.l}$ (Å.))

hk.l (hexagonal)	Intensity	1. B_4C Obsd.	1. B_4C Calcd. (from a_0 = 5.61 Å., c_0 = 12.07 Å.)	2. $B_{5.66}C$ Obsd.	2. $B_{5.66}C$ Calcd. (from a_0 = 5.65 Å., c_0 = 12.15 Å.)	3. B_7C Obsd.	3. B_7C Calcd. (from a_0 = 5.67 Å., c_0 = 12.19. Å)
10.1	3	4.49	4.51	4.52	4.54	4.53	4.55
00.3	4	4.02	4.03	4.04	4.05	4.06	4.06
01.2	7	3.78	3.79	3.81	3.81	3.81	3.82
11.0	3	2.81	2.81	2.82	2.82	2.83	2.83
10.4	8	2.57	2.57	2.59	2.58	2.58	2.59
02.1	10	2.38	2.38	2.40	2.40	2.41	2.41
11.3	1	2.30	2.30	2.32	2.32	2.32	2.32
00.6	1	2.02	2.01	2.04	2.02	...	...
21.1	1	1.82	1.82	1.83	1.83	...	...
20.5	3	1.714	1.713	1.725	1.724	1.730	1.730
11.6	1	1.637	1.635	1.645	1.645	1.651	1.652
10.7	1	1.628	1.625	1.634	1.635	...	...
30.3	2	1.505	1.503	1.516	1.513	1.519	1.518
12.5	3	1.463	1.462	1.474	1.474	1.477	1.477
01.8	3	1.446	1.442	1.455	1.451	1.455	1.455
02.7	3	1.407	1.407	1.416	1.416	...	...
22.0	3	1.403	1.403	1.412	1.412	1.419	1.418
00.9	2	1.345	1.342	1.350	1.350	1.354	1.354
13.1	2	1.342	1.340	1.347	1.348	...	...
22.3	2	1.326	1.325	1.333	1.334	1.339	1.339
20.8	1	1.286	1.283	1.293	1.290	1.296	1.295
30.6	2	1.261	1.263	1.270	1.270	1.273	1.274
04.2	1	1.191	1.191	...	...	1.204	1.204

TABLE III

CHEMICAL AND SPECIFIC GRAVITY DATA ON B_4C, $B_{5.66}C$ AND B_7C

	1. B_4C	2. $B_{5.66}C$	3. B_7C
C, %	21.71	16.18	13.27
B, %	78.29	82.48	83.69
SiO_2, %	...	...	0.42
B_2O_3 (uncombined), %	...	...	0.42
N_2, %	...	...	0.14
Total, %	100.00	98.66	97.94
B/C	4.00	5.66	7.00
Sp. gr. (29/4°)	2.51	2.484	2.47

plained by the substitutional solid solution mechanism.

Assuming substitution of boron atoms for carbon, the theoretical density of B_7C was calculated.

9 B's replace 9 C's in eight rhombohedral cells to give $B_{105}C_{15}$.

$$\text{S. G.} = \frac{[(105)(10.82) + (15)(12.01)][1.66]}{(2.66)(339.38)} = 2.42$$

The experimental density was 2.47.

Clark and Hoard have shown that the B_4C structure is an approximate NaCl type referred to rhombohedral axes, with a compact group of 12 boron atoms substituting for Na^+ and a linear group of 3 carbon atoms for Cl^-. The central carbon atom has as immediate neighbors only the two end carbon atoms. Each end carbon atom has, on the other hand, four immediate neighbors, *i.e.*, three boron atoms and one carbon atom. The central position would seem more favorable for trivalent boron than either end position. Whatever the mechanics of the substitution, it would appear that the bonding strength between boron groups and carbon groups is diminished. This would be the normal accompaniment of increase in size of the unit cell and decreased specific gravity. Decreased Knoop hardness and inferior lapping characteristics attest to diminution of bonding strength within the high-boron boron carbide structure.

Acknowledgments.—The writer was greatly assisted by members of the Norton Company Research Laboratories. Contributions to the experimental work were made by N. W. Thibault, L. J. Beaudin and G. R. Finlay. W. M. Hazel supplied the chemical and specific gravity data. The manuscript was reviewed by S. S. Kistler and A. A. Klein.

332 VILLANOVA DRIVE
CLAREMONT, CALIFORNIA

The Solubility and Absorption Spectrum of Iodine in Sulfuric Acid Solutions

BY J. G. BOWER AND R. L. SCOTT

RECEIVED DECEMBER 24, 1952

The colors exhibited by iodine in different solvents have been the subject of extensive interest for more than fifty years. Substances in which iodine dissolves may be put in two general classes; "violet" or "inert" solvents in which iodine has the color of its vapor and "brown" solvents in which the color ranges from brown to dark red. The "brown" solvents have attracted the attention of many investigators since spectroscopic data have been obtained indicating the formation of 1:1 molecular complexes in some of these media. Detailed work on iodine in benzene, substituted benzenes, naphthalene and other aromatic hydrocarbons[1-7] has resulted in the determination of equilibrium constants and in some cases[8] heats of formation for these molecular complexes. A theory of their structure has been expounded in some detail by Mulliken.[9-11]

This interest in iodine and its interaction with various solvents led us to examine its behavior in sulfuric acid solutions. In 1925, Carter[12] measured the solubility of iodine in various concentrations of sulfuric acid and water, and found that the solubility decreased as the acid concentration was increased, and observed that at the same time, the solutions changed from a brown color to a light pink. The present study was undertaken in order to obtain a more quantitative elucidation of the colors by means of the spectrophotometer and to redetermine the solubilities.

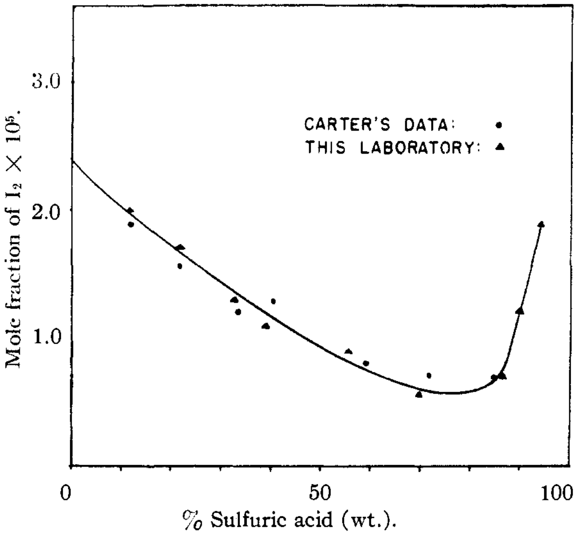


Fig. 1.—Solubility of iodine (expressed as the mole fraction) as a function of the sulfuric acid concentration: ●, Carter's data; ▲, this Laboratory.

Experimental

The iodine used in these determinations was Baker Reagent Grade further purified by resublimation. The sulfuric acid was du Pont C.P., which proved on analysis to be 94.9% H_2SO_4.

Saturated solutions of iodine were prepared by adding an excess of solid iodine to sulfuric acid solutions of varying concentrations heating them to bring about supersaturation and then after partial cooling, immersing in a constant temperature bath at 25.00 ± 0.02°. While in the bath the solutions were agitated to assure complete saturation. The undissolved iodine was filtered off in a sintered glass filter, which was also immersed in the 25° bath.

Immediately following the filtration, part of each solution was sealed into ampules and reserved for spectrophotometric study, while the remainder was analyzed for the iodine content.

Four samples of about 50 g. each were weighed out and the iodine extracted with carbon tetrachloride. The carbon tetrachloride extract was washed with dilute sodium acetate solution to eliminate any residual sulfuric acid, and then titrated with approximately 0.002 *N* sodium thiosulfate, using the color of the carbon tetrachloride layer as indicator.

The spectra of the various solutions were run on a Cary Model 11S recording spectrophotometer, and the optical density of the solutions (relative to distilled water in the reference cell) determined from 210 to 775 mμ. The cell was surrounded by two aluminum blocks through which water at 30.0 ± 0.1° was circulated, after the method of McCullough and Barsh.[13]

Results.—The solubilities determined here and those obtained by Carter are plotted together in Fig. 1. The agreement is rather good over the entire range where there are measurements to be compared. Carter did not determine the solubility in solutions stronger than 87% H_2SO_4 and consequently did not observe the minimum in the solubility. Therefore, to check the enhanced solubility in the 94.9% acid, we made two completely independent determinations, which agreed within 1.5%. The minimum solubility expressed as mole fraction occurs between 75 and 80% acid, but a graph (not shown) of solubility in moles per liter looks quite different. The solubility, which is 1.32 m*M*/l. in pure water falls gradually to a minimum of 0.207 m*M*/l. in 86.5% H_2SO_4 and then rises steeply to 0.423 m*M*/l. at 94.9%.

Spectra of some of the solutions are shown in Fig. 2. The spectra omitted (11.5, 22.0 and 33.4%) are unexceptional, except for the appearance of high peaks at 288 and 350 mμ at concentrations of acid between 5 and 20%. We have evidence to support the belief that these are due to triiodide ion[14] formed in some process greatly accelerated by the high temperatures used in getting the iodine into solution.

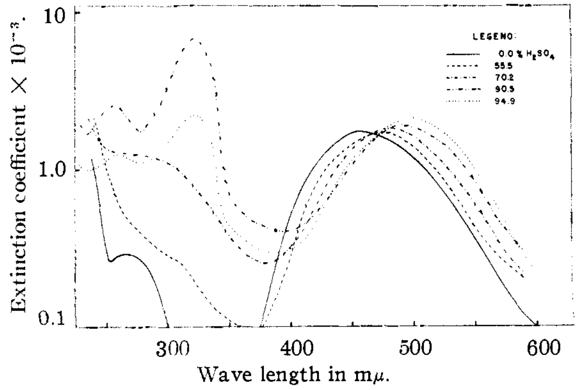


Fig. 2.—Spectra of iodine in solutions of 0.0 to 94.9% sulfuric acid (note that the extinction coefficient is plotted on a logarithmic scale, rather than in the usual manner): —, 0.0% H_2SO_4; ---, 55.5% H_2SO_4; ....., 70.2% H_2SO_4; —·—·—, 90.5% H_2SO_4; ......, 94.9% H_2SO_4.

---

[1] H. A. Benesi and J. H. Hildebrand, This Journal, **70**, 2382 (1948).

[2] H. A. Benesi and J. H. Hildebrand, *ibid.*, **71**, 2703 (1949).

[3] R. M. Keefer and L. J. Andrews, *ibid.*, **72**, 5170 (1950).

[4] N. W. Blake, H. Winston and J. A. Patterson, *ibid.*, **73**, 4437 (1951).

[5] G. Pimental, G. Jura and L. Grotz, *J. Chem. Phys.*, **19**, 513 (1951).

[6] S. Ham, A. Rees and A. Walsh, *ibid.*, **20**, 1336 (1952).

[7] R. M. Keefer and L. J. Andrews, This Journal, **74**, 4500 (1952).

[8] T. M. Cromwell and R. L. Scott, *ibid.*, **72**, 3825 (1950).

[9] R. S. Mulliken, *ibid.*, **72**, 600 (1950).

[10] R. S. Mulliken, *J. Chem. Phys.*, **19**, 514 (1951).

[11] R. S. Mulliken, This Journal, **74**, 811 (1952).

[12] J. S. Carter, *J. Chem. Soc.*, 2861 (1925).

[13] J. D. McCullough and M. K. Barsh, This Journal, **71**, 3029 (1949).

[14] Compare the spectrum of I_3^- reported by A. D. Awtrey and R. E. Connick, *ibid.*, **73**, 1842 (1951). Added in proof.—L. I. Katzin, *J. Chem. Phys.*, **21**, 490 (1942), has recently discussed the appearance of the triiodide spectrum in solutions of iodine in water and the alcohols.

As the acid content is increased, the visible peak begins to shift toward that of iodine vapor (520 mμ), a shift which becomes more marked in the region of concentrated acid (see Table I). Note that the molar extinction coefficient is fairly constant, varying by no more than 30% over the entire range.

TABLE I

Concn. of acid, wt. %	$\lambda_{max.}$	$\epsilon_{max.}$
0	460	1.73
11.5	453	1.95
21.9	460	1.56
33.4	465	1.49
38.9	468	1.73
55.5	474	1.43
70.2	481	1.80
79.6	482	1.88
86.5	483	1.78
90.5	493	1.88
94.9	500	2.11

Discussion

The color changes corresponding to the shift of $\lambda_{max.}$ in the visible region may be considered, in terms of the Lewis theory, as arising from two related effects. In the first place, iodine and sulfuric acid are both Lewis acids; consequently, one would expect no electron exchange interaction to occur when these are mixed. In addition, since H_2SO_4 is a stronger acid than I_2 it may displace the halogen from its complex with water. Thus as the acid concentration increases, the color of the solution shifts toward the violet color which one would expect to find in an inert solvent. In the most concentrated sulfuric acid, the visible peak appears at 500 mμ[15] while in typical inert solvents the maximum usually occurs between 510 and 520 mμ. Table II gives values of $\lambda_{max.}$ and molar extinction coefficients, $\epsilon_{max.}$, for iodine in various solvents.

TABLE II

	$\lambda_{max.}$	$\epsilon_{max.}$
Iodine vapor[16]	520	820
n-Heptane[2]	520	910
Carbon disulfide[2]	518	1120
Carbon tetrachloride[2]	517	930
Benzene[2]	500	1040
Mesitylene[2]	490	1185
Diethyl ether[2]	462	880
Water	460	700
Acetone[2]	363	610

Thus the absorption of iodine in concentrated sulfuric acid would lead one to believe that if a complex does exist between iodine and sulfuric acid, it is a relatively weak one.

In general, one might expect sulfuric acid to be an even poorer solvent for non-polar non-electrolytes than water, but any difference is magnified by the fact that the solubility of iodine in water is enhanced by the acid–base interaction which is absent in sulfuric acid. Such an interpretation would account for the steady decrease in solubility from that found in water to that in 80% sulfuric acid; however, the sharp increase in solubility and the high absorption peaks in the ultraviolet observed beyond 90% sulfuric acid do not fit into this picture, and must be due to some as yet unexplained special effect.

NOTE ADDED IN PROOF.—Professor T. F. Young has pointed out to us that our minimum solubility occurs just short of 50 mole per cent. sulfuric acid (84.2% by weight) where he has found the species in solution to be almost exclusively H_3O^+ ond HSO_4^- [*Record Chem. Progress* (*Kresge-Hooker Sci. Lib.*), 12, 81 (1951)]. At higher concentrations, the amount of undissociated sulfuric acid becomes appreciable, which may account for the increased solubility.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF CALIFORNIA
LOS ANGELES, CALIF.

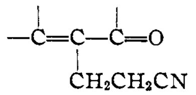
Cyanoethylation of Isophorone

BY HERMAN A. BRUSON AND THOMAS W. RIENER

RECEIVED FEBRUARY 25, 1953

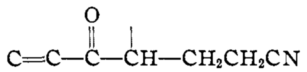
Some time ago it was reported that isophorone resisted cyanoethylation with acrylonitrile.[1] Upon repeating this work with isophorone which had been freed from acidic impurities that poison the alkaline catalyst used for cyanoethylation, namely, benzyltrimethylammonium hydroxide ("Triton B"), it was found possible to obtain mono-, di- and tricyanoethylation products of isophorone.

Infrared analyses were made of these three compounds (1% in chloroform) with a Beckman IR-2T infrared spectrophotometer. Using sodium chloride cells of 16 mil thickness, and maximum gain, spectrograms were obtained covering the range 5.5 to 8.0 μ. A strong absorption peak was observed for all three compounds as well as for isophorone itself, in the neighborhood of 6 μ, ascribed to the conjugated C=C–C=O grouping. For monocyanoethyl isophorone as well as isophorone, this peak occurs at 6.05 μ; whereas for the dicyanoethyl- and tricyanoethyl isophorones the peak occurs at 5.9 μ. Since the grouping



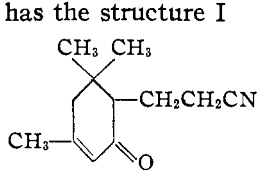
$$-\overset{|}{C}=\underset{\underset{CH_2CH_2CN}{|}}{C}-\overset{|}{C}=O$$

would be expected to show a greater displacement of the isophorone peak than the grouping



$$C=C-\overset{\overset{O}{\|}}{C}-\overset{|}{C}H-CH_2CH_2CN$$

it appears most probable that the monocyanoethylation product has the structure I



I

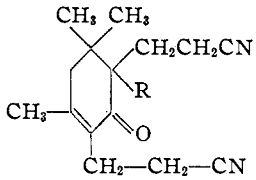
the dicyanoethylation product the structure II, and the tricyanoethylation product the structure III.

---

[15] At the American Chemical Society meeting in Atlantic City, New Jersey, on Sept. 15, 1952, R. E. Buckles and J. F. Mills, THIS JOURNAL, **75**, 552 (1953) reported similar observations on the spectrum of iodine in 96% sulfuric acid and drew essentially the same conclusions which we had drawn from our own research, which was then largely complete.

[16] E. Rabinowitch and W. C. Wood, *Trans. Faraday Soc.*, **32**, 540 (1936).

[1] H. A. Bruson and T. W. Riener, THIS JOURNAL, **64**, 2853 (1942).



II, R = H
III, R = —CH_2CH_2CN

We were unable to obtain a benzylidene derivative from I and benzaldehyde.

Upon alkaline hydrolysis I and II gave the corresponding mono- and dicarboxylic acids IV and V, in crystalline form. However, the tricyanoethylation product III gave a non-crystallizable acidic material under the same hydrolysis conditions.

Experimental

The isophorone used was the commercial product available from Carbide and Carbon Chemicals Corporation. If the material has stood in a partly filled bottle in the sunlight for more than a few months, it often fails to react with acrylonitrile even after redistillation. Apparently, peroxidic or acidic bodies are formed by autoxidation, which poison the catalyst. A similar phenomenon is shown by mesityl oxide[2] and other unsaturated ketones.

In order to purify the isophorone it was thoroughly washed with a 5% solution of sodium carbonate and then distilled under reduced pressure, immediately before use.

Cyanoethyl-isophorone (I).—To a stirred mixture of 276 g. of isophorone (2 moles), 200 g. of *t*-butyl alcohol and 3 cc. of "Triton B" (40% aqueous solution of benzyltrimethylammonium hydroxide) there was added dropwise during the course of one hour, 106 g. of acrylonitrile (2 moles) while maintaining the reaction temperature at 26–28° with water cooling. The mixture was stirred at 26–30° for 4 hours longer, then rendered slightly acidic with dilute hydrochloric acid, washed with water, the oil layer separated and distilled in vacuum.

After a forerun of 146 g. of material boiling up to 135° (1 mm.) had been removed, three separate fractions were collected as follows: (a) 52 g., b.p. 135–190° (1 mm.); (b) 95 g., b.p. 190–240° (1 mm.); (c) 27 g., b.p. 240–290° (1 mm.).

Fraction (a) upon redistillation gave 46 g. of a pale yellow oil, b.p. 115–120° (0.3 mm.). Upon redistillation through an 8-inch column, this yielded 35 g. of monocyanoethylation product, b.p. 109–111° (0.3 mm.), as a colorless oil, m.p. 23–24°.

Anal. Calcd. for $C_{12}H_{17}NO$: N, 7.32. Found: N, 7.39.

Fraction (b) contains dicyanoethylated isophorone which, however, is obtained in better yield by using 2 moles of acrylonitrile for 1 mole of isophorone as given below.

Di-(cyanoethyl)-isophorone (II).—To a stirred mixture of 138 g. of isophorone (1 mole), 200 g. of *t*-butyl alcohol and 4 g. of "Triton B" there was added dropwise 106 g. of acrylonitrile during the course of one hour at 28–32° with cooling. After stirring 4 hours longer at 30° and working up as described above, the following fractions were collected: (a) 50 g., boiling up to 155° (1 mm.) (discarded); (b) 20 g., b.p. 155–210° (1 mm.) (mostly I); (c) 75 g., b.p. 210–220° (1 mm.); (d) 48 g., b.p. 220–295° (1 mm.). Fraction (c) crystallized on standing. Upon recrystallization from ethanol colorless crystals, m.p. 83°, were obtained; yield 53 g.

Anal. Calcd. for $C_{15}H_{20}N_2O$: N, 11.47. Found: N, 11.38.

Tri-(cyanoethyl)-isophorone (III).—Upon redistilling fraction (d), b.p. 220-295° (1 mm.), from the preceding preparation, there was obtained 24 g. of viscous reddish oil, b.p. 265–280° (1 mm.), which became partly crystalline when allowed to stand for several weeks with a small amount of ethanol in a refrigerator at 0–7°. The filtered solid material upon recrystallization from ethanol yielded 4 g. of colorless crystals, m.p. 120–121°.

Anal. Calcd. for $C_{18}H_{23}N_3O$: N, 14.13. Found: N, 14.23.

Carboxyethyl-isophorone (IV).—A mixture of 19.1 g. of cyanoethyl-isophorone (I), 11.2 g. of potassium hydroxide and 100 g. of water was boiled under reflux for eight hours. The clear solution was cooled and acidified with hydrochloric acid. The soft mass which precipitated became solid after stirring for a short time; yield 90%. After several recrystallizations from petroleum ether, the compound was obtained as colorless crystals, m.p. 76–77°.

Anal. Calcd. for $C_{12}H_{18}O_3$: neut. equiv., 210. Found: neut. equiv., 209.

Di-(carboxyethyl)-isophorone (V).—A mixture of 12.2 g. of di-(cyanoethyl)-isophorone (II), 11.2 g. of potassium hydroxide and 90 g. of water was boiled under reflux for 18 hours. The clear solution was cooled and acidified with hydrochloric acid; crude product yield 9 g. After recrystallization from nitromethane, it formed colorless crystals, m.p. 181°.

Anal. Calcd. for $C_{15}H_{22}O_5$: neut. equiv., 141. Found: neut. equiv., 140.2.

INDUSTRIAL RAYON CORPORATION
CLEVELAND, OHIO

---

[2] R. L. Frank and J. B. McPherson, *ibid.*, **71**, 1387 (1949).

Bis-cyclopentadienyl Compounds of Rhodium(III) and Iridium(III)

BY F. A. COTTON, R. O. WHIPPLE AND G. WILKINSON

RECEIVED FEBRUARY 5, 1953

The great stability of the unipositive bis-cyclopentadienylcobalt(III) (cobalticinium) ion[1] led us to attempt the preparation of the analogous bis-cyclopentadienylrhodium(III) and bis-cyclopentadienyliridium(III) cations. These ions, hereafter referred to as the rhodicinium and iridicinium ions, respectively, have been prepared and some of their properties determined.

Experimental

A benzene solution of the metal acetylacetonate[2] was added to a benzene solution of cyclopentadienylmagnesium bromide, the proportion being 10 moles of the Grignard reagent per mole of the acetylacetonate. Although the reaction appeared to take place immediately, as evidenced by the formation of a red-brown precipitate, the mixture was held at about 70° for 24 hours. It was then decomposed using an equal volume of ice slush. The mixture was filtered, and the yellow aqueous layer was separated. The aqueous solutions so obtained were extracted several times with ether and were made essentially free of magnesium by adding barium hydroxide to precipitate magnesium hydroxide, the barium being removed by adding an equivalent amount of dilute sulfuric acid. The organometallic ions were then precipitated with a solution of iodine in potassium iodide; after thorough washing, the precipitates were dissolved in 6 *N* nitric acid, the solutions were then boiled to remove iodine, and evaporated nearly to dryness to remove excess nitric acid. Solutions of salts of other anions such as chloride and perchlorate were obtained by passing the nitrate solutions through columns of anion-exchange resin (Dowex A2) in the appropriate form.

The rhodicinium and iridicinium ions and salts show chemical stability comparable to that of the cobalticinium analogs. Solutions of these salts can be evaporated almost to dryness with concentrated nitric acid without decomposition. In neutral or acid solution they seem quite stable toward light. They are, however, rather unstable in basic solution; a basic solution of rhodicinium ion becomes cloudy after a few hours at room temperature and develops a fluffy white precipitate after a few seconds of boiling. In order to analyze for the metal, the compounds can be decomposed by fuming with perchloric acid.

The rhodicinium and iridicinium ions in aqueous solution behave similarly to other large unipositive ions. Their salts with anions of common mineral acids are all very soluble in water and cannot be crystallized; on evaporation of such

---

[1] (a) G. Wilkinson, THIS JOURNAL, **74**, 6148 (1952); (b) E. O. Fischer and W. Pfab, *Z. Naturforschung*, **7B**, 377 (1952); E. O. Fischer and R. Jira, *ibid.*, **8B**, 1 (1953).

[2] Made and reported independently by F. P. Dwyer and A. M. Sargeson, THIS JOURNAL, **75**, 984 (1953).

solutions yellow, glassy melts result, and some decomposition occurs. These ions differ somewhat from the cobalticinium ion in being more difficult to precipitate from aqueous solution, even with very large anions. The following reagents, many of which precipitate the cobalticinium ion,[1] failed to precipitate the rhodicinium or iridicinium ions from solutions 1.0 to 10.0 m*M* in concentration: H_2PtCl_6, $K_3Co(NO_2)_6$, $KMnO_4$, $KClO_4$, picric acid, salicylic acid, potassium phthalimide, and various substituted naphthol sulfonic acids.

Polyiodides of both ions are obtained upon adding to solutions of at least 0.1 m*M* concentration a solution of iodide in sodium iodide. However, in contrast to the behavior of the cobalticinium ion with this reagent, no simple triiodides are obtained. Analyses on various samples indicated between five and seven iodine atoms per metal atom.

The addition of bromine water to solutions of at least one m*M* concentration produces flocculent orange precipitates. If these precipitates are then alternately washed with water and dried in a vacuum desiccator at room temperature, two or three times, pure salts of the tribromide ion Br_3^- result. *Anal.* Calcd. for $(C_5H_5)_2RhBr_3$: C, 25.40; H, 2.18; Br, 51.79. Found: C, 25.46; H, 2.18; Br, 50.68.

Reinecke's salt, $NH_4[Cr(CNS)_4(NH_3)_2]\cdot H_2O$, precipitates the rhodicinium and iridicinium ions from solutions of concentration 0.1 m*M* or higher. The resulting salts cannot be recrystallized from water because of the instability of the anion. They can be obtained in a quite pure state, however, by digesting them with water below 60° for several hours. *Anal.* Calcd. for $[(C_5H_5)_2Rh][Cr(CNS)_4(NH_3)_2]\cdot H_2O$: C, 29.52; H, 3.19; N, 14.76; S, 22.52; Rh, 18.1; Cr, 9.13. Found: C, 30.19; H, 3.23; N, 14.14; S, 22.81; Rh, 18.9; Cr, 9.16. Calcd. for $[(C_5H_5)_2Ir][Cr(CNS)_4(NH_3)_2]\cdot H_2O$: Cr, 7.74. Found: Cr, 7.93.

With a freshly prepared solution of dipicrylamine, the rhodicinium and iridicinium ions give scarlet precipitates which were recrystallized from acetone.

Anal. Calcd. for $[(C_5H_5)_2Rh][N(C_6H_2N_3O_6)_2]$: C, 39.35; H, 2.10; N, 14.61; Rh, 15.32. Found: C, 39.36; H, 2.06; N, 14.36; Rh, 15.87. Calcd. for $[(C_5H_5)_2Ir][N(C_6H_2N_3O_6)_2]$: C, 34.70; H, 1.85; N, 12.88. Found: C, 33.98; H, 1.94; N, 12.70.

Silicotungstic acid gives precipitates with acid solutions one m*M* or more in rhodicinium or iridicinium ions.

Solutions of the rhodicinium and iridicinium ions were treated with various oxidizing agents and in no case was there any evidence that they could be oxidized to cations of higher charge. The conclusion that no such higher oxidation states exist is corroborated by the absence of any polarographic oxidation waves in the region 0.0 to +0.5 v. *versus* S.C.E. The polarograms were made using neutral perchlorate solutions of the ions, concentration about millimolar, with 0.1 *M* sodium perchlorate as supporting electrolyte.

Polarographic study of a rhodicinium perchlorate solution in a 0.1 *M* sodium perchlorate supporting electrolyte at *p*H about 7 (also containing 0.05% gelatin to suppress a maximum which otherwise appeared) shows a cathodic wave at the dropping mercury electrode with a half-wave potential of −1.53 v. *versus* the S.C.E. Using the polarographic constant for the cobalticinium ion,[3] calculation shows that this wave represents a one-electron change, thus corresponding to the reduction of the rhodicinium ion to the neutral bis-cyclopentadienylrhodium(II) compound $(C_5H_5)_2Rh$. Like the neutral compound of cobalt(II), evidence for the existence of which has been obtained in the form of unstable easily oxidized solutions in organic solvents from the reaction of cobalt(II) acetylacetonate with cyclopentadienylmagnesium bromide,[4] the neutral compound $(C_5H_5)_2Rh$ cannot be isolated from aqueous solutions.

No reduction wave could be obtained for the iridicinium ion since even at a *p*H of 11 it is masked by a catalytic hydrogen wave. Solutions of Ir^{+3} and Ir^{+4} compounds are known to catalyze the reduction of hydrogen ion at the dropping mercury electrode, and in the present case the effect is probably due to similar action of the reduction or decomposition products formed from the iridicinium ion at the dropping mercury electrode.

Rhodicinium hydroxide was made in aqueous solution by the action of freshly prepared silver oxide on a solution of rhodicinium chloride. This solution was then titrated potentiometrically with 0.03 *N* hydrochloric acid using a Beckman Model G *p*H meter with glass and saturated calomel electrodes. From titration curves so obtained, the value of the dissociation constant of rhodicinium hydroxide was calculated to be 1.1×10^{-3}. Iridicinium hydroxide is a base of comparable magnitude.

The ultraviolet absorption spectra of the rhodicinium and iridicinium ions are shown in Fig. 1 together with the spectrum of the cobalticinium ion. Measurements at several wave lengths indicated that Beer's law is obeyed by solutions of both ions over a concentration range of 0.01 to 1.0 m*M*.

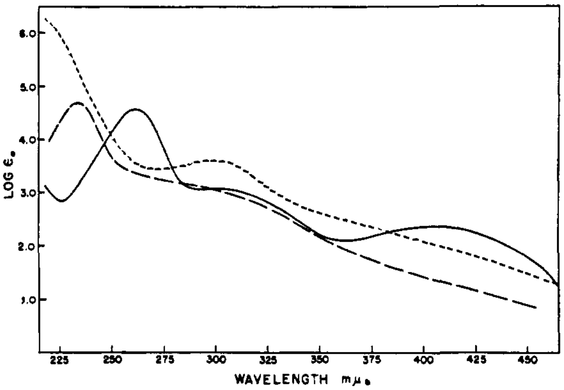


Fig. 1.—Ultraviolet absorption spectra of cobalticinium (—), rhodicinium (— —) and iridicinium (----) perchlorates in water; Beckman spectrophotometer, silica cells, 25°.

The magnetic susceptibility of rhodicinium tribromide was measured by the Gouy split tube method, using air ($\kappa = +0.029 \times 10^{-6}$ c.g.s.u.) and water (-0.72×10^{-6} c.g.s.u.) as references. The values obtained were independent of field strength. The averaged value of the molar susceptibility, χ^{25}_{mol}, is $-165 \pm 10 \times 10^{-6}$ c.g.s.u.

We are indebted to the Allied Chemical and Dye Company (Barrett Division) for financial support (F.A.C.), and to the Mallinckrodt Chemical Company (F.A.C., R.O.W.) and the Atomic Energy Commission (G.W.) for the support of research expenses.

MALLINCKRODT CHEMICAL LABORATORY
HARVARD UNIVERSITY
CAMBRIDGE, MASS.

---

[3] J. A. Page and G. Wilkinson, THIS JOURNAL, **74**, 6149 (1952).

[4] P. L. Pauson, private communication.

Acetic Oxalic Anhydride[1]

BY W. R. EDWARDS, JR., AND WALTER M. HENLEY[2]

RECEIVED JANUARY 20, 1953

The moderate stabilities of the mixed anhydrides of oxalic acid and certain nitrobenzoic acids,[3] and of formic acetic anhydride,[4] together with the chemical behavior of the last-named, suggested that acetic oxalic anhydride (I) might be prepared and might prove useful for the synthesis of oxalic acid derivatives. Furthermore, we wished to ascertain whether it would form amides and esters of acetic acid or of oxalic acid. As its structure is in some ways unique, such preference would be of theoretical interest.

---

[1] Presented before the 8th Southwest Regional Meeting of the American Chemical Society, Little Rock, Arkansas, December 4–6, 1952.

[2] From Part 1 of the Ph.D. thesis of Walter M. Henley, Louisiana State University, August, 1952.

[3] R. Adams, W. V. Wirth and H. E. French, THIS JOURNAL, **40**, 424 (1918); R. Adams and L. H. Ulich, *ibid.*, **42**, 599 (1920).

[4] A. Behal, *Compt. rend.*, **128**, 1460 (1899).

The closest approach to a successful preparation was achieved by treating silver oxalate with acetyl chloride, in ether, at temperatures of −5° or lower; separating the ethereal solution and removing its relatively volatile components by application of reduced pressure at the same low temperature. A colorless crystalline solid was obtained. Because of its method of preparation, its hydrolysis products, its thermal decomposition products, and its reaction with aniline, this was believed to be crude (I).

When not used immediately, it was stored at −19°. In ethereal solution, it decomposed with visible evolution of gases at −3.5°, and with increasing rapidity at higher temperatures; free from solvent, it was even less stable. Feasible purification and analytical techniques were therefore limited. Even in a low-temperature room, samples of the solid material could not be weighed accurately. It was more satisfactory to employ it in ether and to estimate its concentration by treating samples with standard alkali at temperatures low enough to discourage thermal decomposition, subsequently determining the quantities of acetate and oxalate thus formed. Its reagent use appears to be confined to those few reactions which occur readily in cold systems.

Attempts to prepare (I) from sodium oxalate and acetyl chloride were unsuccessful. Action of ketene on anhydrous oxalic acid gave what appeared to be a slightly higher yield of (I), but this method was slow and contamination of the product was probably greater. Direct action of acetic anhydride on anhydrous oxalic acid over a wide temperature range was uniformly unsuccessful; at low temperatures, little or no reaction resulted, while at higher temperatures the familiar decomposition of oxalic acid to oxides of carbon was complete.

Hydrolysis of ethereal solutions of (I) by gradual addition of water at low temperatures yielded oxalic and acetic acids. The acetyl:oxalyl ratio, determined by low-temperature alkaline hydrolysis, averaged 2.27, compared to the theoretical value of 2. A high value for this ratio was to be expected, since partial disproportionation of (I) before or during hydrolysis would be followed by immediate decomposition of the hypothetical oxalic anhydride.

When a cold ethereal solution of (I) was treated with aniline in 1:2 molar proportions, oxanilide was formed exclusively and almost quantitatively in one instance; in another, it was the principal product, accompanied by a small amount of an oily by-product which may have contained a little acetanilide. With an excess of aniline, good yields of both oxanilide and acetanilide were obtained.

Such priority of formation of oxanilide over acetanilide is in accord with theory. Three possible influences may affect anilide formation by this anhydride: (a) the hyperconjugative effect of the methyl groups, diminishing the electrophilic character of the acetocarbonyl carbons; (b) the inductive effect of the methyl groups, exerting a similar influence; and (c) the inductive effect (electron-withdrawing in this case) of each oxalo carbonyl group on the other one, increasing the electrophilic character of the oxalocarbonyl carbons. All three effects work in the same direction, enhancing the relative electrophilic character of the oxalo carbonyl carbons as compared to the aceto ones. Oxanilide should be formed, therefore, in preference to acetanilide.

Attempts to form oxalates from (I) by treating it with various alcohols at temperatures ranging from −30 to 25° were unsuccessful, probably because of an inescapable dilemma. At very low temperatures, (I) may have formed oxalates more rapidly than acetates, but both esterification rates were negligibly low. At higher temperatures (possibly at lower ones also) disproportionation of (I) with subsequent destruction of the oxalic fragment appeared to be faster than esterification, making acetic anhydride, rather than (I), the available esterifying agent. Unless a set of conditions can be discovered in which rate of esterification exceeds rate of disproportionation by a substantial margin, it seems impossible to determine the relative priorities of oxalate and acetate formation from (I).

A mixture obtained by treating (I) with furfuryl alcohol exploded when distilled at reduced pressure.[5]

Whitford[6] explained the decomposition of anhydrous oxalic acid by acetic anhydride by proposing and offering evidence of the formation of an intermediate which decomposed readily to liberate acetic acid, carbon dioxide and carbon monoxide. He believed this intermediate to be a molecular compound, $(COOH)_2 \cdot (CH_3CO)_2O$. Since the present work indicates that (I) can exist, and that it decomposes rapidly at temperatures at which acetic anhydride causes oxalic acid decomposition, it appears possible that the actual intermediate is acetic oxalic anhydride.

Experimental

Acetic Oxalic Anhydride.—A three-neck flask was fitted with stirrer, dropping funnel and drying tubes, shielded from light, and immersed in an ice–salt mixture in a dewar flask, maintaining a temperature of −7 to −3° during the preparation. Powdered silver oxalate (39 g. or 0.13 mole) and 200 ml. of dry ether were placed in the flask, stirring was begun, and a solution of 19 ml. (0.26 mole) of acetyl chloride in 50 ml. of dry ether was added gradually over a two-hour period. The mixture was allowed to stand overnight at a temperature of −5°. The ethereal layer was siphoned into a distilling flask maintained at −10 to −5° and subjected to a pressure of 3 to 5 mm. until apparent distillation ceased and for one additional hour. The residue, a colorless crystalline solid was stored at −19° or lower when not used immediately. Assuming it to be (I), the yield approximated 9%.

Variations of reaction and distillation temperatures between −5 and −25°, and small variations in the proportions of the reagents, using similar or longer times for the distillation of volatile matter, led to no conspicuous differences in the results.

A sharp explosion resulted when 2 ml. of acetyl chloride was added to 5 g. of powdered silver oxalate at room temperature, in the absence of any solvent.

As an alternative method, powdered anhydrous oxalic acid was suspended by stirring in ether, and treated with ketene at −17°. The ethereal solution was siphoned off and subjected to distillation at low temperature and pressure, leaving a residue similar in appearance and in chemical behavior to the product obtained from silver oxalate and acetyl chloride.

---

(5) *cf.* W. R. Edwards, Jr., and L. H. Reeves, THIS JOURNAL, **64**, 1584 (1942), describing similar behavior, upon heating, of a mixture of oxalic acid and furfuryl acetate.

(6) E. L. Whitford, *ibid.*, **47**, 2934 (1925).

A sample of solid (I), allowed to come gradually to room temperature, decomposed completely, emitting a colorless gas and leaving a residue of acetic anhydride (anilide, m.p. 112.6–114°). The gas appeared to be a mixture of carbon dioxide and carbon monoxide. When it was passed through aqueous barium hydroxide, a portion of it was absorbed, forming a white precipitate which dissolved with effervescence when treated with hydrochloric acid; the remainder, unaffected by the barium hydroxide solution, burned with a blue flame.

Hydrolysis of (I).—Hydrolysis was accomplished by adding water dropwise, with stirring, to an ethereal solution of (I) at −10°, maintaining this temperature for two hours, and then allowing a slow rise to room temperature. Products were identified as acetic and oxalic acids.

Determination of Acetyl–Oxalyl Ratio.—A measured quantity of a 0.17 N solution of potassium hydroxide in 1:1 ethanol–water was cooled to −19° and added at the rate of one drop every five seconds, with stirring, to an ethereal solution of (I) at the same temperature. The mixture was allowed to stand for 18 hours at −19° and then for 2 hours at 3°. Total acid was determined by acidimetric titration of the excess base, oxalyl content by oxidimetric titration, and acetyl content by difference. Theoretical ratio of acetyl to oxalyl, 2.00; found, 2.23, 2.31.

Reaction with Aniline.—The concentration of (I) in an ethereal solution was estimated by the procedure just described. To a measured sample of this solution at −19° was added an ethereal solution of aniline at the same temperature, in the ratio of two moles of aniline to one mole of (I), at a rate of one drop per 10–15 seconds. The reactants then stood for 12 hours at −19°, followed by six hours at 3°. The precipitate was filtered, washed successively with ether and water, and dried under vacuum. It melted at 247.5–249°; its mixed melting point with a known sample of oxanilide was the same. It was further identified by nitrogen determination.[7]

Anal. Calcd. for $C_{14}H_{12}O_2N_2$: N, 11.66. Found: N, 11.47, 11.41.

Yield of oxanilide was theoretical in one run, 81% in another. No acetanilide was isolated, but in the second run there was a small amount of an unidentified oily by-product.

---

[7] Method of I. M. Kolthoff and V. A. Stenger, "Volumetric Analysis," Vol. II, Interscience Publishers, Inc., New York, N. Y., 1947, p. 173.

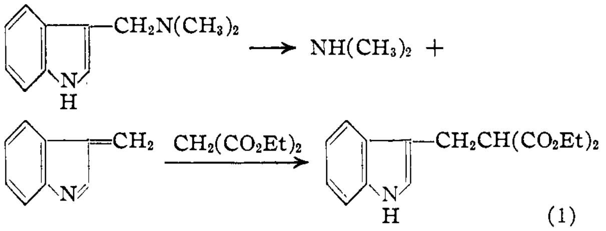
Coates Laboratory
Department of Chemistry
Louisiana State University
Baton Rouge, La.

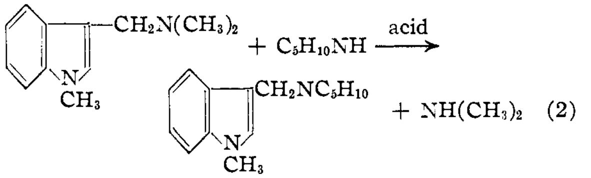
Cyanomethylation of Indole with Diethylaminoacetonitrile

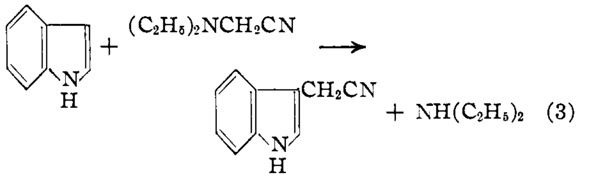
By Ernest L. Eliel and Neal J. Murphy

Received February 7, 1953

The extensive use of tertiary amines as alkylating agents[1] has prompted speculation on the mechanism of the alkylation reaction. It was at first assumed that alkylation proceeded by an elimination–addition mechanism[2] as illustrated for gramine in equation (1). Later, instances were found, however, where alkylations could not readily be explained by an elimination–addition mechanism, such as in the reaction of piperidine with 1-methylgramine[3] (equation 2) and with N-(2-nitroisobutyl)-dimethylamine,[4] and of indole[5] and diethyl malonate[6] with the Mannich base of formamidomalonic ester.







To these interesting examples of direct alkylation with tertiary amines should now be added the alkylation of indole with diethylaminoacetonitrile (equation 3). This alkylation proceeds at *ca.* 170° in the absence of a solvent to produce indole-3-acetonitrile in moderate (33–44%) yield. The nitrile was identified by comparison of its infrared spectrum with that of an authentic sample,[7] by the melting point of its picrate[7] and by hydrolysis to the acid in excellent yield. This identification incidentally indicates that the nitrile obtained by the "cyanomethylation" reaction was a very pure sample, and that the method here developed is a convenient one for the preparation of indole-3-acetonitrile on a small scale. Unfortunately attempts to scale up the preparation resulted in diminishing yields; this is probably due to the great sensitivity of the cyanomethylation reaction to temperature fluctuations. At temperatures below 160° very little reaction ensues at all, while around 180° tar formation supervenes.

While this work was in progress, a publication appeared[6] describing unsuccessful attempts at alkylating diethyl formamidomalonate with diethylaminoacetonitrile and piperidinoacetonitrile. We were likewise unable to alkylate acetophenone, 2-naphthyl methyl ether or 2-naphthol with diethylaminoacetonitrile; in the former two cases the starting materials were recovered while in the latter case phenolic polymers constituted the bulk of the reaction product.

Experimental

Indole-3-acetonitrile.—A mixture of 11.8 g. (0.1 mole) of indole[8] and 22.4 g. (0.2 mole) of diethylaminoacetonitrile[9]

---

[1] For a review, see J. H. Brewster and E. L. Eliel in R. Adams "Organic Reactions," Vol. 7, John Wiley and Sons, Inc., New York, N. Y., 1953, chapter 3.

[2] K. Auwers, *Ber.*, **36**, 1878 (1903); *Ann.*, **344**, 131 (1906); K. von Auwers and Ph. Bullmann, *Ber.*, **59**, 2719 (1926); C. Mannich, W. Koch and F. Borkowsky, *ibid.*, **70**, 355 (1937); H. R. Snyder and E. L. Eliel, This Journal, **70**, 1703 (1948); H. R. Snyder and J. H. Brewster, *ibid.*, **70**, 4230 (1948); C. E. Dalgliesh, *ibid.*, **71**, 1697 (1949).

[3] H. R. Snyder and E. L. Eliel, *ibid.*, **70**, 4233 (1948).

[4] H. R. Snyder and W. E. Hamlin, *ibid.*, **72**, 5082 (1950).

[5] A. Butenandt, H. Hellmann and E. Renz, *Z. physiol. Chem.*, **284**, 175 (1949).

[6] H. Hellmann and E. Brendle, *ibid.*, **287**, 235 (1951).

[7] J. Thesing and F. Schülde, *Ber.*, **85**, 324 (1952).

[8] We are indebted to E. I. du Pont de Nemours and Co., Inc., for a generous gift of indole.

[9] C. F. H. Allen and J. A. VanAllan, *Org. Syntheses*, **27**, 20 (1947).

was maintained at an internal temperature close to 170° under nitrogen for six hours in a flask equipped with a reflux condenser. The excess diethylaminoacetonitrile was then removed at water pump pressure and the residue was submitted to distillation at the oil pump. After a small forerun of indole, indoleacetonitrile was collected at 144–152° (0.03 mm.) or 160–165° (0.2 mm.) (lit.[7] 157° (0.2 mm.)) as a viscous, slightly cloudy liquid weighing 5.2–6.9 g. (33–44%). The picrate[7] melted at 128–129° without recrystallization (lit.[7] 127–128°) and hydrolysis of the nitrile with 20% aqueous potassium hydroxide[7] yielded the acid, m.p. 162–164° (dec.) in 85% yield (lit.[7] m.p. 164–165° (dec.), yield 86%). We were unable to find a solvent for the reaction, aromatic hydrocarbons or aliphatic alcohols having been proved unsuitable. Attempts to scale up the preparation led to a drop in yield.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF NOTRE DAME
NOTRE DAME, INDIANA

The Estimation of the Relative Activities of a Series of Specific Substrates[1]

BY ROBERT J. FOSTER AND CARL NIEMANN[2]

RECEIVED MARCH 6, 1953

It is generally recognized that when the rate of disappearance of the specific substrate S_f in the system

$$E_f + S_f \underset{k_2}{\overset{k_1}{\rightleftarrows}} ES \xrightarrow{k_3} E_f + P_{1f} + P_{2f} \ldots \quad (1)$$

is given by equation (2), where $K_S = (k_2 + k_3)/k_1$, a plot of $\ln [S]_0/[S]_t$ *versus* t will at particularly

$$-d[S]/dt = k_3[E][S]/(K_S + [S]) \quad (2)$$

low concentrations of $[S]_0$ when K_S is large relative to $[S]_0$ approximate that of a first-rrder reaction, that a plot of $([S]_0 - [S]_t)$ *versus* t will at particularly high concentrations of $[S]_0$ when K_S is small relative to $[S]_0$ approximate that of a zero-order reaction.

Despite the apparent success in relating the activities of several series of specific substrates on the basis of their respective approximate first-order constants determined at a single and arbitrary initial specific substrate concentration, *i.e.*, on the basis of so-called first-order proteolytic coefficients,[3-6] it is clear from the investigations of Neurath and his co-workers[7-9] that this practice is basically unsound and should be abandoned.

In an attempt to devise a more rational procedure for the comparison of the activities of a series of specific substrates Neurath, *et al.*,[7-9] suggested that the approximate first-order constants be extrapolated to zero initial specific substrate concentrations, *i.e.*, where the so-called maximum first-order proteolytic coefficient $C^1_{\max}$ is defined by equation (3).

$$2.3\, C^1_{\max} \doteq k_3/K_S \quad (3)$$

There are two limiting cases for equation (3): I, where $k_3 \gg k_2$, $K_S \doteq k_3/k_1$ and $C^1_{\max} \doteq k_1$; and II, where $k_3 \ll k_2$, $K_S \doteq k_2/k_1$ and $C^1_{\max} = k_1k_3/k_2$. It is obvious that in case I $C^1_{\max}$ is in no way related to the susceptibility of ES to subsequent reaction being clearly the constant for the reaction depicted in equation (4). Thus, if

$$E_f + S_f \xrightarrow{k_1} ES \quad (4)$$

it can be shown that for all specific substrates being compared $k_3 \gg k_2$ then values of $C^1_{\max}$ can be used to compare the rates with which these specific substrates will combine with a given enzyme present in a particular reaction system recognizing of course that independent evidence must be provided to show that all of the specific substrates are reacting with the same catalytically active site if the results are to be interpreted in this manner.

For case II $C^1_{\max}$ is directly proportional to k_3, which in many instances, but not in all, can be taken as an index of the suceptibility of ES to subsequent reaction, and inversely proportional to the dissociation constant k_2/k_1 of ES. Thus, in this case $C^1_{\max}$ can only lead to a somewhat ambiguous estimate of the relative activity of a series of specific substrates and cannot be used to estimate on one hand the affinity of the enzyme for a particular specific substrate, or set of specific substrates, and on the other the susceptibility to subsequent reaction of the corresponding enzyme–substrate complexes. An example of the confusion that can arise through the use of $C^1_{\max}$ values to estimate the relative activity of a series of specific substrates where $k_3 \ll k_2$ is given immediately below.

If it is assumed with some justification[10,11] that the molecular weight of α-chymotrypsin is *ca.* 22,000 and its nitrogen content is *ca.* 16%, then for acetyl-L-tryptophanamide[12] $k_3 = 0.029$ sec.$^{-1}$, $K_S = 0.0053\ M$ and $C^1_{\max} = 5.5\ M^{-1}$ sec.$^{-1}$, and for acetyl-L-phenylalaninamide[13] $k_3 = 0.047$ sec.$^{-1}$, $K_S = 0.034\ M$ and $C^1_{\max} = 1.4\ M^{-1}$ sec.$^{-1}$ For these two specific substrates it is probable that in both instances $K_S \doteq k_2/k_1$[13,14] and consequently $C^1_{\max}$ is to be interpreted in terms of case II above. The fact that $C^1_{\max}$ for acetyl-L-phenylalaninamide is but *ca.* 1/4 of that for acetyl-L-tryptophanamide is not due to a greater susceptibility to hydrolysis of the enzyme–substrate complex arising from acetyl-L-tryptophanamide than that arising from acetyl-L-phenylalaninamide since the respective k_3 values, *i.e.*, 0.029 and 0.047 sec.$^{-1}$ actually predict the reverse situation, but rather to the far greater affinity of the enzyme for acetyl-L-tryptophanamide than for acetyl-L-phenylalaninamide as indicated by the K_S values of 0.0053 and 0.034 M, respectively. Thus in the absence of any knowl-

---

[1] Supported in part by a grant from Eli Lilly and Company.

[2] To whom inquiries regarding this article should be sent.

[3] G. W. Irving, Jr., J. S. Fruton and M. Bergmann, *J. Biol. Chem.*, **138**, 231 (1941).

[4] M. Bergmann and J. S. Fruton, *ibid.*, **146**, 247 (1942).

[5] E. L. Smith, *ibid.*, **175**, 39 (1948).

[6] E. L. Smith in J. B. Sumner and K. Myrbäck, "The Enzymes," Academic Press, Inc., New York, N. Y., 1951, p. 793 *et seq.*

[7] E. Elkins-Kaufman and H. Neurath, *J. Biol. Chem.*, **175**, 893 (1948).

[8] S. Kaufman, H. Neurath and G. Schwert, *ibid.*, **177**, 793 (1949).

[9] H. Neurath and G. Schwert, *Chem. Revs.*, **46**, 69 (1950).

[10] G. W. Schwert and S. Kaufmann, *J. Biol. Chem.*, **190**, 807 (1951).

[11] M. Kunitz, *J. Gen. Physiol.*, **22**, 207 (1938).

[12] H. T. Huang and C. Niemann, THIS JOURNAL, **73**, 1541 (1951).

[13] H. T. Huang, R. J. Foster and C. Niemann, *ibid.*, **74**, 105 (1952).

[14] H. T. Huang and C. Niemann, *ibid.*, **73**, 3223 (1951).

edge of the pertinent K_S and k_3 values it is clear that values of $C^1_{\max}$ for case II provide no more than an ambiguous estimate of relative activity in which the contributions due to K_S and those due to k_3 can not be separately evaluated. It should be noted that past experience has shown that there is no basis for the assumption that in an extended series K_S is approximately constant and k_3 is the important variable or *vice versa*.[13]

While it is true that in the system depicted in equation (1) there is no ambiguity arising in the interpretation of C°, *i.e.*, the true zero-order coefficient, since it is directly proportional to k_3, it is obvious that valid comparisons cannot be made between C° values on one hand and $C^1_{\max}$ values on the other.

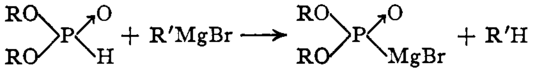
CONTRIBUTION NO. 1787 FROM THE
GATES AND CRELLIN LABORATORIES OF CHEMISTRY
CALIFORNIA INSTITUTE OF TECHNOLOGY
PASADENA 4, CALIFORNIA

Bromomagnesium Salts of Dialkyl Phosphites as Intermediates in the Synthesis of Substituted Hydroxymethyl Phosphonic Acid Esters

BY OSCAR GAWRON, CHESTER GRELECKI, WILLIAM REILLY AND JAMES SANDS

RECEIVED JANUARY 10, 1953

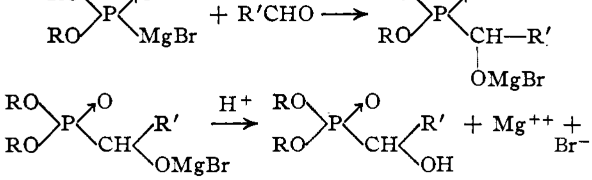
Recent reports[1-4] on the base-catalyzed condensation of dialkyl phosphites with carbonyl compounds to yield α-hydroxy phosphonates prompt us to report preliminary work on their synthesis by the use of bromomagnesium derivatives of dialkyl phosphites prepared *in situ*. These derivatives may be prepared by the addition of an ether solution of a Grignard reagent to an ether solution of a dialkyl phosphite according to the equation



$$(RO)_2P(\rightarrow O)H + R'MgBr \longrightarrow (RO)_2P(\rightarrow O)MgBr + R'H$$

Refluxing the bromomagnesium derivative with an aldehyde or ketone and decomposing the reaction mixture with saturated ammonium chloride solution or dilute acid yields after drying and vacuum distillation the α-hydroxyphosphonate.

The reactions leading to the formation of the α-hydroxyphosphonates may be written in a manner analogous to the reaction of Grignard reagents with carbonyl compounds.



$$(RO)_2P(\rightarrow O)MgBr + R'CHO \longrightarrow (RO)_2P(\rightarrow O)CH(OMgBr)-R'$$

$$(RO)_2P(\rightarrow O)CH(R')(OMgBr) \xrightarrow{H^+} (RO)_2P(\rightarrow O)CH(R')(OH) + Mg^{++} + Br^-$$

The acidity of dialkyl phosphites is well known,[5] magnesium salts,[6] in addition to others, having been prepared and while cognizance of this is taken in the replacement of alkoxy groups of dialkyl phosphites by alkyl groups from Grignard reagents,[7] apparently no previous attempt has been made to prepare and utilize halomagnesium derivatives for synthetic purposes.[8]

The *in situ* prepared bromomagnesium salts are stable on refluxing in diethyl ether, do not react with alkyl halides (n-butyl bromide and methyl iodide) on refluxing in diethyl ether and react with oxides and acyl halides in addition to ketones and aldehydes. These and other reactions are under investigation.

Experimental

Ethane Evolution from Ethylmagnesium Bromide and Diethyl Phosphite.—A solution of 1.38 g. (0.010 mole) of diethyl phosphite in 6 ml. of anhydrous ether was placed in a 3-necked flask of 20-ml. capacity. The flask was connected *via* a small cold-water condenser to two gas burets arranged in series. After displacement of air by ether vapors, 6.65 ml. (0.010 mole) of a 1.50 *M* solution of ethylmagnesium bromide in anhydrous ether was added dropwise with shaking over a period of 20 minutes at room temperature. The evolved gas was collected in the first buret and then transferred to the second buret where its volume was measured at room temperature and atmospheric pressure. The confining liquid in both burets was 85% phosphoric acid. Blank determinations indicated essentially complete absorption of ether vapors. The volume of gas collected, reduced to standard conditions, was 218 ml. (97.4% of theory).[9]

***In situ* Preparation of the Bromomagnesium Salt of Dibutyl Phosphite.**—Into a 3-necked flask, equipped with sealed stirrer, dropping funnel, reflux condenser and calcium chloride drying tubes, a solution of 38.8 g. (0.2 mole) of dibutyl phosphite in 50 ml. of anhydrous ether was placed. A solution of 0.2 mole of ethylmagnesium bromide in 100 ml. of anhydrous ether was then added dropwise with stirring and cooling in an ice–salt mixture. Toward the end of the addition, the reaction mixture separated into two layers, the lower a thick oil. In the case of diethyl phosphite a pasty mass separated which on continued stirring dispersed and two layers formed. The intact reaction mixture or that prepared by reverse addition under the same conditions was used as a source of the bromomagnesium salt in subsequent experiments.

Attempts to isolate the bromomagnesium derivative of diethyl phosphite by separation of the lower layer, washing with ether and drying in high vacuum yielded a white, hygroscopic powder whose analysis consistently failed to agree with the calculated values and from which no empirical formula could be calculated.

Anal. Calcd. for $C_4H_{10}O_3BrMgP$: C, 19.82; H, 4.11; Br, 33.12; Mg, 9.95; P, 12.83. Found: C, 13.65; H, 5.61; Br, 26.56; Mg, 18.90; P, 11.50.

Stability of the Bromomagnesium Salt of Dibutyl Phosphite to Reflux in Ether.—After preparation of the bromomagnesium salt, using the quantities and conditions indicated above, the cooling bath was removed and the reaction mixture was refluxed for three hours. After standing overnight at room temperature decomposition of the salt was effected by shaking the reaction mixture with 100 ml. of cold

---

(1) A. E. Arbuzov and M. M. Azanovskaya, *Doklady Akad. Nauk S. S. R.*, **58**, 1961 (1947); *C. A.*, **46**, 8606 (1952).

(2) V. S. Abramov, *Doklady Akad. Nauk. S. S. R.*, **73**, 487 (1950); *C. A.*, **45**, 2855 (1951).

(3) A. N. Pudovik, *Doklady Akad. Nauk. S. S. R.*, **73**, 499 (1950); *C. A.* **45**, 2856 (1951).

(4) E. K. Fields, U. S. 2,579,810 (Dec. 25, 1951).

(5) G. M. Kosolapoff, "Organophosphorus Compounds," John Wiley and Sons, Inc., New York, N. Y., 1950, p. 193.

(6) T. Milobendzki and T. Knoll, *Chem. Polsk.*, **15**, 79 (1917); *C. A.*, **13**, 2867 (1919).

(7) G. M. Kosolapoff and R. M. Watson, THIS JOURNAL, **73**, 4101 (1951), use a Grignard to dialkyl phosphite ratio of 3.3:1 for the preparation of phosphinous acids intermediate in a synthesis of phosphinic acids.

(8) During the preparation of this manuscript, A. N. Pudovik, *Zhur. Obschchei Khim.*, **22**, 109 (1952); *C. A.*, **46**, 11099 (1952), prepared, *in situ*, the bromomagnesium salts of diethyl and dibutyl phosphite and treated these with 1-alkoxy-5-chloro-3-pentenes and 1-alkoxy-3-chloro-4-pentenes to give the corresponding 1-alkoxy-5-(dialkylphosphono)-3-pentenes.

(9) Pudovik, footnote 8, using almost identical quantities as described above, on addition of diethyl phosphite to ethylmagnesium bromide found the evolution of ethane to be 32.4%.

saturated ammonium chloride solution. The ether layer was then separated, dried over anhydrous sodium sulfate and vacuum distilled to yield 31.0 g. (79%) of dibutyl phosphite, b.p. 89–91° (3 mm.), $n^{19.5}{}_{\mathrm{D}}$ 1.4246.

Diethyl 2-Hydroxypropane-2-phosphonate.—To 0.1 mole of the bromomagnesium derivative of diethyl phosphite, 5.8 g. (0.1 mole) of acetone in 25 ml. of anhydrous ether was added. The reaction mixture was then refluxed for three hours and after standing overnight at room temperature was decomposed in the manner previously indicated. After separation of the ether layer and drying over anhydrous sodium sulfate, vacuum distillation yielded 8.0 g. (41%) of product, b.p. 145–148° (20 mm.), m.p. 14–16°, literature[10] b.p. 145° (20 mm.), m.p. 14–15°.

Diethyl Ester of α-Hydroxybenzylphosphonic Acid.—To 0.1 mole of the bromomagnesium derivative of diethyl phosphite, 10.6 g. (0.1 mole) of benzaldehyde in 25 ml. of anhydrous ether was added. The reaction mixture was refluxed for three hours and then worked up as previously indicated. After removal of some unreacted phosphite and benzaldehyde by vacuum distillation, the residue in the still flask was recrystallized from benzene–petroleum ether to give 15 g. (61.5%) of crude product. After several recrystallizations, pure product, m.p. 83–84°, was obtained; lit.[11] m.p. 83–84°.

Acknowledgment.—This investigation was supported in part by a research grant (C-1347) from the National Cancer Institute of the National Institutes of Health, Public Health Service.

---

[10] C. Marie, *Ann. Phys. Chem.*, [8] **3**, 335 (1904).

[11] M. I. Kabachnik and P. A. Rossiskaya, *Bull. acad. sci. U. R. S. S., Classe sci. Chim.*, 364 (1945); *C. A.*, **40**, 4688 (1946).

DEPARTMENT OF CHEMISTRY
DUQUESNE UNIVERSITY
PITTSBURGH, PA.

Reaction of Triphenyltin Hydride with Methyllithium

BY HENRY GILMAN AND SANDERS D. ROSENBERG

RECEIVED MARCH 23, 1953

Triethylsilane has been treated with methyllithium,[1] *n*-propyllithium, *n*-butyllithium, phenyllithium and lithium ethoxide.[2] In each reaction the products were lithium hydride and the corresponding substituted triethylsilane. This type

$$(C_2H_5)_3SiH + RLi \longrightarrow (C_2H_5)_3SiR + LiH$$

$$(C_2H_5)_3SiH + C_2H_5OLi \longrightarrow (C_2H_5)_3SiOC_2H_5 + LiH$$

of reaction was extended to the aromatic series when triphenylsilane was treated with methyllithium and phenyllithium to form lithium hydride and triphenylmethylsilane and tetraphenylsilane, respectively,[3] and appeared to be general for hydrides of Group IV-B elements when it was shown that triphenyltin hydride[3] and triphenylgermane[4] yielded lithium hydride and tetraphenyltin and tetraphenylgermanium, respectively, when reacting with phenyllithium. Benkeser and Riel[5] treated four substituted triarylsilanes with methyllithium to form, in each case, the triarylmethylsilane and lithium hydride.

Recently it was reported that when triphenyltin hydride reacts with methyllithium the products are triphenyltin-lithium and methane.[6] The re-

$$(C_6H_5)_3SnH + CH_3Li \longrightarrow (C_6H_5)_3SnLi + CH_4$$

active intermediate, triphenyltin-lithium, was identified by reaction with triphenyltin bromide to form hexaphenylditin in 49% yield.

It may not be valid to generalize that the reaction of trisubstituted tin hydrides with methyllithium will be the same as that of trisubstituted silanes. The latter when treated with methyllithium form trisubstituted methylsilanes.[1,3,5] But because of this apparent anomalous result[6] and our interest in the organometallic complex, triphenyltin-lithium,[7] the reaction was repeated in this Laboratory.

It was found that triphenyltin hydride and methyllithium react to form triphenylmethyltin (18%), tetraphenyltin (25%) and lithium hydride in accordance with results cited previously.[1–5] In a check run the yield of triphenylmethyltin was 15% and of tetraphenyltin, 25%. No gas evolution was noted in either run and the characteristic yellow-tan color, denoting triphenyltin-lithium, was not evident. It is interesting to note the formation of tetraphenyltin, possibly as a con-

$$(C_6H_5)_3SnH + CH_3Li \longrightarrow (C_6H_5)_3SnCH_3 + (C_6H_5)_4Sn + LiH$$

sequence of disproportionation, even under these mild conditions.[3]

We are also presenting at this time a method for the quantitative analysis of tin in organotin compounds.[8]

Experimental

Triphenyltin Hydride.—This preparation was carried out as described by Wittig and co-workers[6] except that triphenyltin iodide was used in place of triphenyltin bromide. Two runs were made and in both the yield of triphenyltin hydride, distilling at 151° (0.05 mm.), was 1.8 g. (51.6%). It was found that if triphenyltin chloride was substituted for triphenyltin iodide no reaction took place under corresponding conditions.

Reaction of Triphenyltin Hydride with Methyllithium.—The methyllithium used in this reaction was prepared[9] by refluxing for one hour, 1.42 g. (0.01 mole) of freshly opened methyl iodide (Eastman Kodak Co., white label) with 0.08 g. (0.01 g. atom plus 10%) of lithium metal in 100 ml. of ether. The lithium iodide thus formed was allowed to settle out and the clear methyllithium solution was used.

A 250-ml. flask was equipped with a magnetic stirrer, a 100-ml. graduated dropping funnel, a nitrogen inlet tube and a gas outlet tube. The gas outlet tube was attached to a gas bubble counter filled with concentrated sulfuric acid; the counter was, in turn attached to a Dumas tube filled with fine cupric oxide; this tube was attached to water- and carbon dioxide-absorption tubes used in micro carbon and hydrogen quantitative analysis.[10]

About 50 ml. of ether was placed in the flask, gentle stirring was begun, and a very slow stream (*ca.* one bubble every three seconds) of nitrogen gas was passed through the entire system for one hour. The long burner under the Dumas tube was turned on during the sweep-through of the gas. The absorption tubes were then weighed.

After the absorption tubes were returned to their positions 1.6 g. (0.0046 mole) of triphenyltin hydride was added to the reaction flask and 0.0046 mole of methyllithium in 35 ml. of ether was placed in the dropping funnel. The same rate of nitrogen sweep-through and stirring as before were

---

[1] H. Gilman and S. P. Massie, THIS JOURNAL, **68**, 1128 (1946).

[2] R. N. Meals, *ibid.*, **68**, 1880 (1946).

[3] H. Gilman and H. W. Melvin, *ibid.*, **71**, 4050 (1949).

[4] O. H. Johnson and D. M. Harris, *ibid.*, **72**, 5566 (1950).

[5] R. A. Benkeser and F. J. Riel, *ibid.*, **73**, 3472 (1951).

[6] G. Wittig, F. J. Meyer and G. Lange, *Ann.*, **571**, 12 (1951).

[7] H. Gilman and S. D. Rosenberg, THIS JOURNAL, **74**, 531 (1952).

[8] A qualitative test for tin in organotin compounds has been described recently by H. Gilman and T. N. Goreau, *J. Org. Chem.*, **17**, 1470 (1952).

[9] H. Gilman, E. A. Zoellner and W. M. Selby, THIS JOURNAL, **55**, 1252 (1933).

[10] J. B. Niederl and V. Niederl, "Micromethods of Quantitative Organic Analysis," 2nd Edition, John Wiley and Sons, Inc., New York, N. Y., 1942, p. 111.

maintained while the methyllithium solution was added dropwise. There was no discernible increase in the bubble rate during the addition of the methyllithium solution and a white solid precipitated. No yellow-tan colored precipitate or yellow solution indicative of triphenyltin-lithium formed. The system was swept with nitrogen for 0.5 hour after the addition was completed. The absorption tubes were then reweighed and, within limits of allowable error, there was no change in weight for either tube. A Color Test I,[11] made one hour after the addition was completed, was negative.

The ethereal solution was filtered from the white solid, extracted with 50 ml. of water, and dried over sodium sulfate. This white solid was analyzed as lithium hydride by the method outlined previously.[3] The ether layer yielded an oil which was digested with 50 ml. of methanol, and the mixture was allowed to cool slowly. On cooling, 0.4 g. of solid melting over the range 170–225° was recovered. This solid was recrystallized from 25 ml. of petroleum ether (b.p. 77–120°) to yield 0.35 g. (25.0% calculated on the number of phenyl groups available) of tetraphenyltin melting at 222–225°. A mixed melting point with an authentic specimen showed no depression. The methanol was removed by distillation leaving an oil. Thorough cooling in a Dry Ice-bath yielded an oily solid. This mass was extracted twice with 5-ml. portions of cold ethanol to yield 0.5 g. of crude triphenylmethyltin melting over the range 48–54°. This crude solid was recrystallized from 5 ml. of ethanol to yield 0.3 g. (18.1%) of triphenylmethyltin melting at 59–61°.[12] A mixed melting point determination with an authentic specimen prepared in essential accordance with the procedure of Bullard and Robinson[12] showed no depression.

Run 2.—This run was carried out precisely as was the first. Once again no gas evolution was noted, the characteristic yellow-tan color of triphenyltin-lithium was not observed and the weight of the gas absorption tubes remained constant. In this experiment 0.35 g. (25%) of tetraphenyltin melting at 224–225° and 0.25 g. (15.0%) of triphenylmethyltin melting at 60–61° was obtained. Both compounds were identified by the method of mixed melting points.

A Method for the Quantitative Analysis for Tin in Organotin Compounds.—Tin in organotin compounds usually is determined as stannic oxide. Pfeiffer[13] introduced a method which involves decomposition of the sample by the use of fuming nitric acid in a sealed tube, followed by evaporation of the product with concd. sulfuric acid and ignition to stannic oxide. A more convenient method[14] uses fuming nitric plus fuming sulfuric acid in a covered porcelain crucible to decompose the sample, followed by ignition to stannic oxide. Concentrated sulfuric acid plus 30% hydrogen peroxide has been used in place of fuming nitric plus fuming sulfuric acid.[15] Volatile organotin compounds usually give low results by the fuming acid procedure. A method has been introduced whereby the volatile organotin compound is first decomposed with bromine in carbon tetrachloride, followed by treatment with concd. nitric plus sulfuric acid and finally ignition to stannic oxide.[16]

It has been found that organotin compounds can be completely decomposed simply by treatment with concd. sulfuric acid followed by ignition to stannic oxide. This method can be applied to volatile as well as non-volatile compounds. Vycor crucibles have been used in place of porcelain crucibles because of the greater visibility afforded by the former.

In a 30-ml. Vycor crucible (Corning Glass Works, Corning, N. Y., code word GIKYN) was weighed approximately 0.2 g. of the organotin compound to be analyzed. To this was added, with caution, 20 drops (1.0 ml.) of concd. sulfuric acid (sp. gr. 1.84), and the crucible was placed on a Rogers ring burner. The sample usually turned jet black almost immediately. The excess acid was then cautiously removed by heating the uncovered crucible at its top. The ring was then raised at intervals, thereby gradually lowering the position of the flame on the sides of the crucible until the flame was directed to the bottom, and the carbonaceous material formed by the action of the acid was completely ignited leaving a white solid. The uncovered crucible was then ignited on a Bunsen burner for 0.5 hour to insure complete conversion to stannic oxide, cooled and weighed in the usual manner. A complete analysis requires about two hours to run. Some representative results follow.

(1) Triphenyl-*o*-methoxyphenyltin, a solid; calcd. for $C_{25}H_{22}OSn$: Sn, 25.97. Found: Sn, 26.10, 26.21.

(2) Tri-*n*-butylphenyltin, a liquid; calcd. for $C_{16}H_{32}Sn$: Sn, 32.33. Found: Sn, 32.37, 32.47.[17]

(3) Triphenyl-*m*-dimethylaminophenyltin, a solid; calcd. for $C_{26}H_{25}NSn$: Sn, 25.24. Found: Sn, 25.28, 25.41.

(4) Triphenyl-3-dimethylamino-6-(4′-bromophenylazo)-phenyltin, a solid; calcd. for $C_{32}H_{28}N_3BrSn$: Sn, 18.01. Found: Sn, 18.10, 18.17.

---

[11] H. Gilman and F. Schulze, THIS JOURNAL, **47**, 2002 (1925).

[12] R. H. Bullard and W. R. Robinson, *ibid.*, **49**, 1369 (1927).

[13] P. Pfeiffer, *Z. anorg. allgem. Chem.*, **68**, 102 (1910).

[14] E. Krause and R. Becker, *Ber.*, **53**, 173 (1920).

[15] N. Strafford, *Mikrochim. Acta*, **2**, 306 (1937).

[16] H. Gilman and W. B. King, THIS JOURNAL, **51**, 1213 (1929).

[17] For extremely volatile organotin compounds it may be advisable to wet the sample with acetic acid before adding the sulfuric acid; H. Gilman, B. Hofferth, H. W. Melvin and G. E. Dunn, *ibid.*, **72**, 5767 (1950).

DEPARTMENT OF CHEMISTRY
THE IOWA STATE COLLEGE
AMES, IOWA

Some Glyoxylic Steroids

BY DAVID GOULD AND E. B. HERSHBERG

RECEIVED FEBRUARY 27, 1953

The acid-catalyzed rearrangement of cortisone acetate has been shown to lead to a glyoxal side chain.[1] Some related results on glyoxylic steroids stem from our attempt to hydrolyze cortisone acetate by the Freudenberg[2] conditions. This reaction failed to give cortisone, but instead gave the product of Mattox and Kendall,[3] 21,21-dimethoxy-4-pregnene-3,11,20-trione (I). We obtained the same product from free cortisone, using the same procedure. These hydrolytic conditions were then applied to pregnane-17α,21-diol-3,11,20-trione 21-acetate which, according to infrared analysis, also gave a product with a saturated ether bond but without acetate or hydroxyl groups. This is presumably 21,21-dimethoxypregnane-3,11,20-trione (II), in analogy with the structure of the product obtained from cortisone acetate.

These structures were not then known, and we felt that possible formulations of I and II were those also considered by Mattox to be 16,21-dimethoxypregnantriones.[1] Since we had successfully cleaved methanol from 16α-methoxy-5-pregnen-3β-ol-20-one to give 5,16-pregnadien-3β-ol-20-one acetate,[4] we similarly treated the dimethoxy trione I obtained from cortisone, with acetic anhydride and *p*-toluenesulfonic acid, expecting to obtain the corresponding Δ^{16}-20-ketone. The isolated product, however, did not contain hydroxyl, methoxyl or conjugated carbonyl, according to infrared spectra. It did show infrared bands corresponding to acetate and enol acetate, conjugated diene, carbonyl (*e.g.*, at C_{11}), and interacting 21-acetate and 20-carbonyl. This evidence applied to the correct formulation of I[1] and combined with the negative rotatory shift and the analysis, indicates that the material is 3,5-pregnadiene-3,21,21-triol-11,20-dione triacetate (III).

---

[1] V. R. Mattox, THIS JOURNAL, **74**, 4340 (1952).

[2] K. Freudenberg and W. Jakob, *Ber.*, **74**, 1001 (1941).

[3] V. R. Mattox and E. C. Kendall, *J. Biol. Chem.*, **188**, 287 (1951).

[4] D. Gould, F. Gruen and E. B. Hershberg, THIS JOURNAL, **75**, 2510 (1953).

Thus the 3-ketone has been enol-acetylated as expected, while the dimethylacetal at C-21 has been cleaved and replaced by a diacetate,[5] under the strongly acidic acetylating conditions.

Experimental[6]

21,21-Dimethoxy-4-pregnen-3,11,20-trione (I) **from Cortisone.**—One hundred milligrams of cortisone was dissolved in 10 ml. of methanol and treated with 0.25 ml. of acetyl chloride (equiv. to 1% HCl in the solution). The mixture was allowed to stand at room temperature for 18 hours and then was neutralized by the addition of aqueous potassium acetate solution. The mixture was concentrated to give a precipitate which was collected and dried *in vacuo*, weight 0.07 g., m.p. 145–150°. Recrystallization from isopropyl alcohol gave 30 mg. of 21,21-dimethoxy-4-pregnen-3,11,20-trione, m.p. 160–162°, $\epsilon_{\max}$ 15,600 at 236 mμ (EtOH), $[\alpha]_D$ +211.4° (acetone). The infrared spectrum (Nujol mull) showed peaks at 5.85 μ (C_{11} and C_{20} carbonyl), 5.96 μ (C_3 carbonyl), 6.16 μ (Δ^4) and 9.04 μ (C–O–C), and was identical with that of material obtained by the same procedure from cortisone acetate.

21,21-Dimethoxypregnan-3,11,20-trione (II).—Two grams of pregnan-17α,21-diol-3,11,20-trione 21-acetate was suspended in 100 ml. of absolute methanol. To this was cautiously added 2.5 ml. of acetyl chloride. The mixture was warmed to dissolve the solid and allowed to stand 20 hours. Thereupon the clear solution was treated with 4 g. of potassium acetate in water and evaporated to dryness *in vacuo*. Upon crystallization from isopropyl alcohol and heptane, the residue gave 21,21-dimethoxy-pregnan-3,11,20-trione, m.p. 131–132.4°, $[\alpha]_D$ +107.8° (dioxane). *Anal.* Calcd. for $C_{23}H_{34}O_5$: C, 70.74; H, 8.78. Found: C, 70.90; H, 8.84. The infrared absorption spectrum (Nujol mull) showed carbonyl peaks at 5.78 and 5.88 μ and a strong C–O–C peak at 9.15 μ.

3,5-Pregnadiene-3,21,21-triol-11,20-dione Triacetate (III).—One gram of 21,21-dimethoxy-4-pregnene-3,11,20-trione (I) was dissolved in 4 ml. of acetic anhydride and treated with 5 mg. of *p*-toluenesulfonic acid. The mixture was refluxed for 30 minutes and chilled to give crystals which were collected and washed with cold methanol, weight 0.28 g., m.p. 170–176°, $E_{\max}$ 385 at 231 mμ (EtOH). Crystallization from isopropyl alcohol gave the triacetate, m.p. 176.5–179°, $[\alpha]_D$ +3.4° (dioxane).

The infrared spectrum (Nujol mull) showed the following bands: 5.67 and 5.75 μ (21-acetate-20-carbonyl interaction), 5.88 (11-carbonyl), 5.98 and 6.09 ($\Delta^{3,5}$-diene), 8.21 (C–O–C of acetate and enol acetate). *Anal.* Calcd. for $C_{27}H_{34}O_8$: C, 66.65; H, 7.04. Found: C, 66.89; H, 7.11.

Dilution of the mother liquor with aqueous methanol gave 0.55 g. of crude enol acetate, m.p. 160–172°, showing the same ultraviolet spectrum as above.

---

(5) *Cf.* W. Schulz, *Ber.*, **85**, 249 (1952).

(6) All melting points are corrected. $E^{1\%}_{1\,\text{cm.}} = (1/cd) \log I_0/I$; $\epsilon = E \times$ M.W./10. Analyses and optical data were obtained by the Microanalytical and Physical Chemical Departments of this Laboratory.

CHEMICAL RESEARCH LABORATORIES
SCHERING CORPORATION
BLOOMFIELD, NEW JERSEY

The Heat of Combustion of Lanthanum[1]

BY ELMER J. HUBER, JR., AND CHARLES E. HOLLEY, JR.

RECEIVED FEBRUARY 20, 1953

Introduction.—The literature[2-6] values for the heat of formation of lanthanum oxide, like most of the rare earths, show wide variations. The discrepancies are probably due to the use of impure lanthanum metal. This paper reports the results of burning very pure lanthanum in oxygen to determine the heat of formation of the oxide.

Method.—The method involves the determination of the heat evolved from burning a weighed sample of the metal in an oxygen bomb calorimeter at 25 atmospheres pressure. The energy equivalent of the calorimeter was determined from the heat of combustion of standard benzoic acid and also was determined electrically. The completeness of combustion was determined by treating the combustion products with 6 *N* hydrochloric acid and measuring the amount of hydrogen evolved from any unburned metal present.

The uncertainties given are twice the corresponding standard deviations.

Results are expressed both in absolute joules and in defined calories; 1 defined calorie = 4.1840 absolute joules.

Apparatus.—Details of the construction and calibration of the calorimeter have been described.[7] The energy equivalent of the calorimeter was 10,096 ± 3.1 joules/degree.

Lanthanum Metal.—The lanthanum metal was supplied by Dr. F. H. Spedding of the Ames Laboratory of the A. E. C. This metal was analyzed with the following results: Na, 0.005%; Mg, 0.005%; Ca, 0.005%; C, 0.006%; N, 0.0075%; H, 0.001%; O, 0.061%. Any other metallic impurities were present in amounts too small to be detected by the spectroscopic method used. A Debye X-ray pattern showed lines only of α-lanthanum.

Combustion of Lanthanum.—The lanthanum was burned as chunks on sintered discs of 98% pure La_2O_3 supported on a platinum platform weighing 103.8 g. Two new discs were used for each run. They were formed by pressing the lanthanum oxide with an added 2.5% beeswax in a steel die. Ignition was carried out at 1200° for eight hours in air after which the discs were removed at 100° to a desiccator to prevent absorption of water. No lanthanum carbide is believed to be formed during this process since the discs when treated with 6 *N* HCl, evolve no gas and dissolution is complete. Pure magnesium fuse wire was used. The heat of combustion was taken as 24,667 joules/g.[7] The amount varied from 0.0053 to 0.0056 g. The formation of a double oxide $MgO \cdot La_2O_3$ from the two oxides is possible. The heat of formation of such an oxide is probably not great, and since only a small fraction of the total magnesium is close to the lanthanum metal and because the amount of magnesium is not large, a correction would probably be very small. Correction was made for the electrical energy used in igniting the wire. The total energy equivalent of the calorimeter and contents was used, taking into account the discs, the platinum, and the difference between the La_2O_3 formed and the oxygen used. The completeness of combustion of the lanthanum varied from 99.97 to 100.00%. The initial temperature was 24.6° and the average final temperature was 25.9°. The results are summarized in Table I.

TABLE I

COMBUSTION OF LANTHANUM

Mass La, g.	ΔT, °C.	Total energy, abs. joules	Energy from La, abs. joules/g.	Deviation, abs. joules/g.
2.1274	1.3626	13801.0	6414.7	2.5
2.0694	1.3247	13415.2	6413.8	1.6
2.0351	1.3035	13199.8	6413.2	1.0
1.9492_5	1.2477	12640.1	6410.0	2.2
2.0533	1.3143	13312.8	6409.5	2.7
		Av.	6412.2	2.0

2 × standard deviation = 2.1

---

(1) This work was performed under the auspices of the A. E. C.

(2) W. Muthmann and L. Weiss, *Ann.*, **331**, 1 (1904).

(3) W. A. Roth, U. Wolf and O. Fritz, *Z. Elektrochem.*, **46**, 42 (1940).

(4) J. E. Moose and S. W. Parr, THIS JOURNAL, **46**, 2656 (1924).

(5) F. R. Bichowsky and F. D. Rossini, "The Thermochemistry of the Chemical Substances," 1936, p. 337.

(6) L. Brewer, "The Thermodynamics of the Rare Earth Oxides," UCRL-1931, September, 1952.

(7) C. E. Holley, Jr., and E. J. Huber, Jr., THIS JOURNAL, **73**, 5577 (1951).

The value in the table for the heat of combustion of lanthanum metal as used must be corrected for the impurities present. If it is assumed that the oxygen is present as La_2O_3, that the nitrogen is present as LaN which burns to $N_2O_5(s)$ and La_2O_3, that the carbon exists as free graphite which burns to CO_2, and that the other impurities are negligible, the corrected value for the heat of combustion of lanthanum is found to be 6439.2 joules/g. Actually the carbon probably exists as lanthanum carbide, but the heat of formation of this compound is not available. Essentially we are taking its heat of formation as zero. For the small amount of carbon present this does not introduce an error of any consequence.

The uncertainty to be attached to this value must include the uncertainty in the energy equivalent. When this is included the value becomes 6439.2 ± 2.9 joules/g. There are small additional unknown uncertainties due to the corrections for the impurities.

Composition of the Lanthanum Oxide.—The La_2O_3 formed was tan in color. A Debye X-ray pattern showed only lines of hexagonal La_2O_3. Analysis by the "active oxygen" method of Barthauer and Pearce[8] gave a formula of $La_2O_{3.001}$. This analysis was made on run No. 2 in which the combustion was assumed to be complete.

Heat of Formation of La_2O_3.—The heat of combustion reported above gives, for the reaction in the bomb, a value of $\Delta E_{24.6}° = -1789.1 \pm 0.8$ kjoules/mole. The correction of this value to 25° is less than the uncertainty in the result. To obtain the heat of formation it is necessary to correct for the deviation of oxygen from the perfect gas law and to convert from ΔE to ΔH. Using Rossini and Frandsen's[9] value of $(\partial \Delta E/\partial P)_{301° \mathrm{K}} = -6.51$ joules/atm./mole for oxygen and taking $\Delta H = \Delta E + \Delta(PV)$, we have for the heat of formation of La_2O_3, $\Delta H_{25}° = -1793.1 \pm 0.8$ kjoules/mole. In defined calories this is -428.57 ± 0.19 kcal./mole. This value differs by about 6.4% from the value of -458 kcal./mole selected by the National Bureau of Standards.[10]

Acknowledgments.—The authors are appreciative of the courtesy of Dr. F. H. Spedding of the Ames Laboratory, A. E. C., through whom the lanthanum metal was obtained. They also wish to express their appreciation of the valuable assistance of F. H. Ellinger, R. D. Gardner, O. R. Simi, E. Cramer and W. G. Smiley in performing most of the analytical work.

[8] G. L. Barthauer and D. W. Pearce, *Ind. Eng. Chem.*, **18**, 479 (1946).

[9] F. D. Rossini and M. Frandsen, *J. Research Natl. Bur. Standards*, **9**, 733 (1932).

[10] Selected Values of Chemical Thermodynamic Properties, N. B. S. Circular 500, 1952, p. 351.

UNIVERSITY OF CALIFORNIA
LOS ALAMOS SCIENTIFIC LABORATORY
LOS ALAMOS, N. M.

The Isolation of Desacetylneoprotoveratrine from *Veratrum Viride* Ait.

BY M. W. KLOHS, M. D. DRAPER, F. KELLER, W. MALESH AND F. J. PETRACEK

RECEIVED MARCH 13, 1953

A further investigation of the more hydrophilic ester alkaloids of *Veratrum viride* Ait. has resulted in the isolation of a new hypotensively active triester, desacetylneoprotoveratrine; m.p. 182–183°, $[\alpha]^{24}_{D} -9.6 \pm 2$ (*c* 1.0 in py.). Mild alkaline hydrolysis afforded protoverine, acetic acid, (levo) α-methylbutyric acid and α-methyl-α,β-dihydroxybutyric acid. On the basis of the hydrolysis products and analytical data, the empirical formula $C_{39}H_{61}O_{14}N$ was established.

Except for the absence of an acetyl group, it seemed probable that the new ester was structurally identical with neoprotoveratrine.[1] A similar relationship has been demonstrated in the germine ester series (germitrine → germerine,[2] neogermitrine → germidine,[3] germanitrine → germanidine[4]) where in each case a labile acetyl group is lost upon subjecting the triester to methanolysis. For this reason, neoprotoveratrine was treated with methanol and a compound was obtained which proved to be identical with the triester, desacetylneoprotoveratrine, isolated directly. The ease with which the acetyl group was removed from neoprotoveratrine suggests the possibility that desacetylneoprotoveratrine may be of secondary rather than primary origin.

Pharmacology.[5]—The hypotensive activity of desacetylneoprotoveratrine was found to be 1.0 µg. [0.72 – 1.64].[6]

Experimental[8]

Countercurrent Separation of the "Amorphous Bases" of *Veratrum Viride* Ait.—The amorphous bases (30 g.) remaining after the removal of protoveratrine and neoprotoveratrine as described in our previous publication[4] were subjected to an 8-plate Craig countercurrent distribution using benzene–2 *M* acetate buffer *p*H 5.5 (1500 ml. per phase, lower phase moving). The material recovered from tube 8 (6.4 g.) was then distributed on a 24-plate countercurrent machine using benzene–2 *M* acetate buffer *p*H 6.9 (450 ml. per phase, lower phase moving).

Desacetylneoprotoveratrine.—The material recovered from tubes 22–24 (2.25 g.) was dissolved in benzene with heating. On standing, desacetylneoprotoveratrine separated as clusters of needles (0.7 g.); m.p. 182–183° (vac.), $[\alpha]^{24}_{D} -9.6 \pm 2$ (*c* 1.0 in py.), $+9.8 \pm 2$ (*c* 0.89 in $CHCl_3$). For analysis the sample was dried at 120° (2 mm.) to constant weight.

Anal. Calcd. for $C_{39}H_{61}O_{14}N$: C, 61.00; H, 8.01; N, 1.83; equiv. wt., 767.89. Found: C, 60.47; H, 8.40; N, 1.76; equiv. wt., 777.

In a volatile acid determination 8.185 mg. required 2.01 ml. of 0.01 *N* $Na_2S_2O_3$ or 1.87 equivalents.[9]

Hydrolytic Cleavage of Desacetylneoprotoveratrine to Protoverine, Acetic Acid, (levo)α-Methylbutyric Acid[10] and α-Methyl-α,β-dihydroxybutyric Acid.—Desacetylneoprotoveratrine (0.48 g.) was hydrolyzed in the same manner as that reported for neoprotoveratrine,[4] yielding protoverine,[11] m.p. 193°; $[\alpha]^{24}_{D} -16.2 \pm 2$ (*c* 1.03 py.). On admixture with an authentic sample of protoverine, no melting point depression was observed.

The acid fraction when treated in the same manner as re-

---

[1] M. W. Klohs, R. Arons, M. D. Draper, F. Keller, S. Koster, W. Malesh and F. J. Petracek, THIS JOURNAL, **74**, 5107 (1952).

[2] Josef Fried, Howard L. White and O. Wintersteiner, *ibid.*, **72**, 4621 (1950).

[3] J. Fried, P. Numerof and N. H. Coy, *ibid.*, **74**, 3041 (1952).

[4] M. W. Klohs, M. D. Draper, F. Keller, S. Koster, W. Malesh and F. J. Petracek, *ibid.*, **74**, 4473 (1952).

[5] The pharmacological tests were carried out under the supervision of Dr. R. O. Bauer of the Riker pharmacology section.

[6] Expressed as micrograms per kilogram of anesthetized dog per minute required for a 10-minute intravenous infusion to lower the mean arterial blood pressure 30% when administered according to a previously described assay procedure.[7] The bracketed numbers express the 95% confidence limits.

[7] George L. Maison and J. W. Stutzman, *Arch. Intern. pharmacodynamie*, **86**, 357 (1951).

[8] All melting points are corrected. We are indebted to Dr. Adalbert Elek for the micro analyses and to C. H. Stimmel for equivalent weight determinations.

[9] It has previously been shown[4] that α-methyl-α,β-dihydroxybutyric acid is non-volatile under the conditions of the volatile acid determination.

[10] The specific rotation of the volatile acids from desacetylneoprotoveratrine indicated the presence of one mole of (levo) α-methylbutyric acid.

[11] By hydrolyzing for longer periods of time, isoprotoverine rather than protoverine was obtained.

ported for neoprotoveratrine,[4] yielded *p*-phenylphenacyl acetate, m.p. 110–111°, *p*-phenylphenacyl α-methylbutyrate, m.p. 69–70°, and α-methyl-α,β-dihydroxybutyric acid, m.p. 97–98.5°. The above compounds were further identified by mixed melting points with authentic samples and by their infrared spectra.

Conversion of Neoprotoveratrine to Desacetylneoprotoveratrine by Methanolysis.—Neoprotoveratrine (0.78 g.) was allowed to stand for 15 hours in methanol (100 ml.). At the end of this time, the methanol was evaporated to dryness *in vacuo* and the residue was subjected to a 24-plate countercurrent distribution using the same solvent system employed in the isolation of desacetylneoprotoveratrine. The material recovered from tubes 22–24 (0.262 g.) was crystallized from benzene, yielding clusters of needles (0.12 g.), m.p. 182–183.5°, $[\alpha]^{24}D$ −9.6 ± 2 (*c* 0.99 in py.). A mixed melting point with desacetylneoprotoveratrine isolated directly gave no depression. The infrared spectra of the two compounds were identical. For analysis the sample was dried at 120° (2 mm.) to constant weight.

Anal. Calcd. for $C_{39}H_{61}O_{14}N$: C, 61.00; H, 8.01. Found: C, 60.99; H, 8.02.

In a volatile acid determination 16.31 mg. required 3.654 ml. of 0.01 *N* $Na_2S_2O_3$ or 1.72 equivalents.

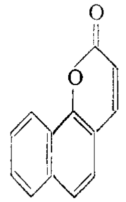
RIKER LABORATORIES, INC.
LOS ANGELES, CALIFORNIA

Preparation of 7,8-Benzocoumarin and 1-Methoxynaphthalene-2-propionic Acid[1]

BY C. F. KOELSCH AND P. T. MASLEY

RECEIVED APRIL 2, 1953

α-Naphthol reacts with malic acid in presence of sulfuric acid to form 7,8-benzocoumarin (I)[2] but the best yields so far reported[3] were only 25–30%. Through systematic experiments it has now been found that nearly double the previous yield can be obtained by using acetic acid as a diluent for the reaction mixture and by using an excess of malic acid.


I

Experimental

A well ground mixture of 170 g. of technical α-naphthol and 226 g. of technical malic acid was added in portions during 20 minutes to a hot solution of 360 ml. of concd. sulfuric acid in 240 ml. of acetic acid. Gas evolution and some refluxing took place. During the addition and for 90 minutes afterwards, the mixture was stirred and kept at 135–141°. The solution was then stirred into one liter of crushed ice. The resulting mixture was boiled and then cooled while it was being stirred. The crude tarry product was separated, suspended in one liter of boiling water, and treated with enough sodium carbonate to cause the aqueous liquor to turn from dark brown to a reddish color. The mixture was cooled, and the solid was removed and washed with water. The product could be crystallized from acetic acid at this point, but it was usually easier to obtain a colorless product if it was distilled first, b.p. 235–240° at 6 mm., m.p. 141–142°, yield 110–127 g., 45–55%.

Anal. Calcd. for $C_{13}H_8O_2$: C, 79.6; H, 4.1. Found: C, 79.9; H, 4.1.

Reduction of 35 g. of the coumarin dissolved in 200 ml. of 10% sodium hydroxide by treatment with 360 g. of 3% sodium amalgam gave a little dimeric product and mainly **3,4-dihydro-7,8-benzocoumarin**. The product was precipitated with hydrochloric acid, distilled (b.p. 210–220° at 15 mm.) and then crystallized from alcohol, yielding 29 g. of needles, m.p. 76–77°.

Anal. Calcd. for $C_{13}H_{10}O_2$: C, 78.7; H, 5.6. Found: C, 78.7; H, 5.1.

The dihydrocoumarin reacted rapidly with phenylhydrazine in alcohol, forming **1-hydroxynaphthalene-2-propiophenylhydrazide**, colorless crystals from alcohol, m.p. 176–178° dec.

Anal. Calcd. for $C_{19}H_{18}N_2O_2$: C, 74.5; H, 5.9. Found: C, 74.9, 74.2; H, 5.7, 5.9.

The dihydrocoumarin (40 g.) was methylated with aqueous sodium hydroxide and methyl sulfate, giving 80–90% of **1-methoxynaphthalene-2-propionic acid**, colorless needles from ligroin containing 5% of chloroform, m.p. 94–96°, b.p. *ca.* 240° at 20 mm.

Anal. Calcd. for $C_{14}H_{14}O_3$: C, 73.1; H, 6.1. Found: C, 72.8, 73.2; H, 6.1, 5.7.

1-Methoxynaphthalene-2-propionamide, colorless needles from dilute alcohol, m.p. 103–105°, was obtained from the acid with thionyl chloride and ammonium hydroxide.

Anal. Calcd. for $C_{14}H_{15}NO_2$: C, 73.3; H, 6.0. Found: C, 73.5; H, 6.3.

SCHOOL OF CHEMISTRY
UNIVERSITY OF MINNESOTA
MINNEAPOLIS 14, MINNESOTA

---

[1] From the M.S. Thesis of Paul Thomas Masley, July, 1942.

[2] V. Pechmann, *Ber.*, **17**, 1651 (1884).

[3] K. Bartsch, *ibid.*, **36**, 1966 (1903).

Direct Halogenation of Some Aromatic Amines

BY GENNADY M. KOSOLAPOFF

RECEIVED MARCH 18, 1953

The complexes between dioxane and halogens which were noted by Favorskii some years ago[1] afford an interesting method for mild direct halogenation of sensitive aromatic compounds. We have examined the bromination of several amines by means of the dioxane–bromine complex and found that monohalogenation can be carried out with moderately good yields without resorting to the customary blocking procedure.

Experimental Part

The complex, an orange-yellow solid, m.p. 64°, is readily prepared in quantity by mixing equimolar amounts of the components and quenching the hot product in ice-water. However, if the material is to be used in solution, it is merely necessary to add the desired amount of bromine to a cooled and stirred mass of dioxane. The bromination of amines can be carried out either by direct addition of the finely powdered complex to a solution of the amine, preferably in dioxane, or by addition of a dioxane solution of the complex to a cooled and stirred solution of the amine in dioxane in the presence of the requisite amount of concentration aqueous alkali. The latter procedure appears to be more economical of the amine.

Aniline.—The complex (25 g.) was added over 15 minutes in its original crystalline state (crystals 1–2 mm. diameter) to 9.3 g. of aniline in 20 g. of dioxane at 5–10° with stirring, in a beaker. The resulting precipitate was filtered off, washed with a little water and dilute sodium hydroxide, and again with water. The product (7 g.) was then dissolved in 75 ml. of hot ethanol and cooled, yielding 1.75 g. of 2,4,6-tribromoaniline. The solution was diluted with two volumes of water and on cooling yielded 4.5 g. (26%) of *p*-bromoaniline, m.p. 66.0–66.5°, characterized by mixed melting point with an authentic specimen and further by conversion to the acetyl derivative, which melted at 165°.

When the above experiment was repeated with finely ground complex which permitted more rapid solution and better distribution of the halogenating agent in the mixture, yields up to 50–57% were obtained and the amount of tribromoaniline declined to a small fraction of a gram.

---

[1] A. E. Favorskii, *J. Russ. Phys. Chem. Soc.*, **38**, 741 (1906).

Finally, a solution of 16 g. of bromine in 160 ml. of dioxane was added dropwise with good agitation (stirrer near the bottom of the flask) at 5° to a solution of 9.3 g. of aniline in 30 ml. of dioxane and 5.6 g. of potassium hydroxide in 20 ml. of water. The addition was made over two hours. The organic layer was washed with 15 ml. of 40% potassium hydroxide and distilled under reduced pressure to remove the solvent. The residue was recrystallized from dilute alcohol, yielding 68% of *p*-bromoaniline. This was the highest yield attained.

Dimethylaniline.—When 12.1 g. of dimethylaniline was brominated with 16 g. of bromine according to the technique outlined above (*cf.* aniline), there was obtained 80–85% *p*-bromodimethylaniline, m.p. 55°.

***p*-Nitroaniline.**—When 13.8 g. of *p*-nitroaniline was brominated with 16 g. of bromine according to the above technique, there was obtained, after three crystallizations from ethanol, 40–45% yield of 2-bromo-4-nitroaniline, m.p. 104°.

***p*-Toluidine.**—Reaction of 21.4 g. of *p*-toluidine with 32 g. of bromine, under the conditions described above (350 ml. of dioxane total volume; 11.2 g. of potassium hydroxide in 50 ml. of water; temperature, 5–8°) yielded, upon vacuum distillation of the washed reaction product, a fraction, b.p. 142–145° at 22 mm., weighing 22 g., which after crystallization from dilute alcohol gave 19.8 g. of 2-bromo-4-methylaniline, m.p. 25–26°, which yielded the acetyl derivative, m.p. 117–118°; the yield 53%.

Direct bromination of *p*-toluidine with the powdered complex, as described under aniline, gave considerable amounts of the 2,6-dibromo derivative, which melted at 78–79°, and very small amounts of isolated monobromo compound were obtained. This result is expected owing to the high order of aromatic reactivity of this amine.

ROSS CHEMICAL LABORATORY
ALABAMA POLYTECHNIC INSTITUTE
AUBURN, ALABAMA

8-Nitro-7-methoxyisoquinoline

BY MARSHALL KULKA

RECEIVED MARCH 18, 1953

In harmony with theoretical considerations 7-methoxyisoquinoline[1] undergoes nitration in the 8-position. The nitration product, which was obtained in 80% yield, was reduced and the resulting 7-methoxy-8-aminoisoquinoline converted to 7-methoxy-8-chloroisoquinoline. The identity of this was established by comparing with an authentic sample prepared by methylating 7-hydroxy-8-chloroisoquinoline. The latter compound[2] was previously obtained from 2-chloro-3-hydroxybenzaldehyde and aminoacetal.

Experimental

7-Methoxy-8-nitroisoquinoline.—To a stirred solution of 7-methoxyisoquinoline[1] (7.0 g.) in concentrated sulfuric acid (100 cc.) was added portionwise a solution of potassium nitrate (5.0 g.) in concentrated sulfuric acid (35 cc.) while the temperature was maintained at 0–5° by cooling. After stirring for an additional one-half hour at 0–5°, the reaction mixture was poured onto cracked ice. The resulting solution was basified and the yellow precipitate filtered, washed and dried. Crystallization from benzene yielded 7.0 g. (80%) of yellow prisms melting at 164–165°. *Anal.* Calcd. for $C_{10}H_8N_2O_3$: C, 58.83; H, 3.92; N, 13.73. Found: C, 58.66, 58.70; H, 3.97, 3.64; N, 13.53.

7-Methoxy-8-aminoisoquinoline.—To a stirred solution of 7-methoxy-8-nitroisoquinoline (6.0 g.) in concentrated hydrochloric acid (30 cc.) was added portionwise a solution of stannous chloride dihydrate (30 g.) in concentrated hydrochloric acid (50 cc.) while the temperature was maintained at 35–40° by cooling. Then the reaction mixture was allowed to stand at room temperature overnight with occasional cooling during the first hour in order to keep the temperature below 40°. The reaction mixture was diluted with an equal volume of water and then added to a mixture of 30% sodium hydroxide solution (300 cc.) and cracked ice (about 300 g.). The precipitated amine was extracted with three 400-cc. portions of ether and the ether was removed from the extract. Crystallization of the residue from benzene yielded 3.8 g. (74%) of yellow needles melting at 156–157°. *Anal.* Calcd. for $C_{10}H_{10}N_2O$: C, 68.97; H, 5.75; N, 16.10. Found: C, 69.12, 69.25; H, 5.83, 5.99; N, 15.90.

7-Methoxy-8-chloroisoquinoline.—A solution of 7-methoxy-8-aminoisoquinoline (0.6 g.) in concentrated hydrochloric acid (2 cc.) and water (10 cc.) was diazotized at 0° with sodium nitrite (0.25 g.) in water (5 cc.). The resulting diazonium chloride solution was added to a solution of cuprous chloride (2 g.) in concentrated hydrochloric acid (20 cc.) previously warmed to 70°. After standing overnight the reaction mixture was basified and steam distilled. The steam distillate was filtered and the white solid (0.32 g. or 50%) was crystallized from methanol, white needles, m.p. 124–125°. The methylation of 7-hydroxy-8-chloroisoquinoline[2] with diazomethane yielded a compound melting at 124–125° alone or in admixture with the compound above. *Anal.* Calcd. for $C_{10}H_8NOCl$: C, 62.02; H, 4.14; N, 7.23. Found: C, 62.43, 62.44; H, 4.26, 4.37; N, 7.20.

DOMINION RUBBER COMPANY, LIMITED
RESEARCH LABORATORY
GUELPH, ONTARIO

---

[1] von P. Fritsch, *Ann.*, **286**, 1 (1895).

[2] R. H. F. Manske and M. Kulka, *Can. J. Research*, **B27**, 161 (1949).

Quinoxaline Studies. V. Synthesis of 2-Hydroxy-3,5-dimethylquinoxaline and 2-Hydroxy-3,8-dimethylquinoxaline

BY GEORGE KYRYACOS[1] AND HARRY P. SCHULTZ

RECEIVED SEPTEMBER 3, 1952

Although a number of papers have discussed the synthesis of unsymmetrically substituted quinoxalines with substituents in the 6- and 7-position of the quinoxaline ring, no work has been reported with substituents in the 5- and 8-positions of the unsymmetrically substituted quinoxaline ring. The purpose of this investigation was to synthesize and determine the physical properties of 2-hydroxy-3,5-dimethylquinoxaline and 2-hydroxy-3,8-dimethylquinoxaline.

The starting material for the synthesis of 2-hydroxy-3,5-dimethylquinoxaline was 2-amino-3-nitrotoluene. *o*-Acetotoluidide was nitrated by the procedure used by Bacharach[2] to nitrate *p*-acetotoluidide. Hydrolysis of the 3-nitro-2-acetotoluidide, followed by steam distillation, gave 2-amino-3-nitrotoluene. Condensation of 2-amino-3-nitrotoluene with α-bromopropionic acid gave N-(2-nitro-6-methylphenyl)-*dl*-α-alanine.

The amino acid, N-(2-nitro-6-methylphenyl)-*dl*-α-alanine, was reduced catalytically to the dihydro derivative of 2-hydroxy-3,5-dimethylquinoxaline. The unisolated 3,4-dihydro-2-hydroxy-3,5-dimethylquinoxaline was oxidized by basic hydrogen peroxide solution to 2-hydroxy-3,5-dimethylquinoxaline.

The preparation of 2-hydroxy-3,8-dimethylquinoxaline utilized similar reactions, starting with 2-nitro-3-aminotoluene, which was prepared by the procedure of Hoogewerff and van Dorp.[3] Higher yields of substituted alanine derivative were ob-

---

[1] Abstracted from the M.S. thesis of George Kyryacos, The University of Miami, 1952.

[2] C. Bacharach, THIS JOURNAL, **49**, 1522 (1927).

[3] S. Hoogewerff and W. van Dorp, *Rec. trav. chim.*, **8**, 1921 (1889).

tained when α-bromopropionic acid was condensed with 2-nitro-3-aminotoluene than were obtained with the hindered 2-amino-3-nitrotoluene.

The melting point curve for mixtures of 2-hydroxy-3,5- and -3,8-dimethylquinoxalines showed an eutectic at 214–217° for a 1:1 mixture of the two substances. Data from the ultraviolet absorption spectra of the two compounds are recorded in Table I.

TABLE I

ULTRAVIOLET ABSORPTION SPECTRA FOR 2-HYDROXY-3,5- AND -3,8-DIMETHYLQUINOXALINES

		Absorption maxima	
Compound	Solvent	Mμ	$\epsilon \times 10^{-3}$
2-Hydroxy-3,5-dimethylquinoxaline	95% ethanol	250.0	7.47
		255.5	7.47
		292.0	7.02
	0.1 *N* HCl	230.0	15.7
		256.0	10.2
	0.1 *N* NaOH	241.0	20.7
		300.0 (infl.)	3.55
2-Hydroxy-3,8-dimethylquinoxaline	95% ethanol	256.5	8.00
		291.0	5.91
	0.1 *N* HCl	230.0	16.4
		257.0	11.0
	0.1 *N* NaOH	242.0	21.2

Experimental Procedures

2-Amino-3-nitrotoluene.—This material was prepared in 39% yield by the nitration, hydrolysis and steam distillation of *o*-acetotoluidide according to the procedure used by Bacharach[2] for the nitration of *p*-acetotoluidide.

N-(2-Nitro-6-methylphenyl)-*dl*-α-alanine.—Into an 8-inch test-tube were placed 5.8 g. of 2-amino-3-nitrotoluene and 2.9 g. of α-bromopropionic acid. The reaction mixture was heated in a bath of water and sulfuric acid at 110° for 96 hours, then cooled and extracted with three 40-ml. portions of 15% ammonium hydroxide solution. The combined basic extracts were treated with 1 g. of activated charcoal, filtered through a bed of filter-aid, then slowly brought to *p*H 4 with 10% hydrochloric acid solution. A yellow-orange, powdery precipitate formed and was filtered. This purification process was repeated to give 0.7 g. (16.5%) of yellow N-(2-nitro-6-methylphenyl)-*dl*-α-alanine melting at 122–123°.

Anal. Calcd. for $C_{10}H_{12}O_4N_2$: N, 12.5. Found: N, 12.4, 12.4.

2-Hydroxy-3,5-dimethylquinoxaline.—A solution of 1.0 g. of N-(2-nitro-6-methylphenyl)-*dl*-α-alanine in 16 ml. of 95% ethanol was reduced over 0.1 g. of 5% palladium-charcoal catalyst[4] and 2 atmospheres of hydrogen for four hours at room temperature. The catalyst was removed and the solvent evaporated. The residue was dissolved in 10 ml. of 8% hydrogen peroxide and 10 ml. of 8% sodium hydroxide solution and heated on a steam-bath for two hours. A white precipitate of 2-hydroxy-3,5-dimethylquinoxaline was obtained when the oxidation mixture was cooled and brought to *p*H 4 with acetic acid. This precipitate was filtered and recrystallized from ethanol–water (2:1) to give 0.41 g. (52.5%) of white 2-hydroxy-3,5-dimethylquinoxaline melting at 256.5–257.5°. The product was sublimed with no loss at 180° (1 mm.) to give white, powdery crystals melting at the same temperature.

Anal. Calcd. for $C_{10}H_{10}ON_2$: C, 68.97; H, 5.74; N, 16.1. Found: C, 69.37; H, 5.56; N, 16.0, 15.8.

2-Nitro-3-aminotoluene.—This material was prepared in 74% yield from 2-nitro-3-toluamide[5] according to the procedure of Hoogewerff and van Dorp.[3]

N-(2-Nitro-3-methylphenyl)-*dl*-α-alanine.—This material was prepared by heating together α-bromopropionic acid and 2-nitro-3-aminotoluene at 110° for 36 hours in a manner similar to that described for the preparation of N-(2-nitro-6-methylphenyl)-*dl*-α-alanine. A 36.5% yield of yellow N-(2-nitro-3-methylphenyl)-*dl*-α-alanine melting at 164–165° was obtained.

Anal. Calcd. for $C_{10}H_{12}O_4N_2$: N, 12.5. Found: N, 12.6, 12.4.

2-Hydroxy-3,8-dimethylquinoxaline.—The preparation and purification of this compound were executed in the same manner as that described for 2-hydroxy-3,5-dimethylquinoxaline. A 34% yield of white 2-hydroxy-3,5-dimethylquinoxaline melting at 256.5–257.5° was obtained.

Anal. Calcd. for $C_{10}H_{10}ON_2$: C, 68.97; H, 5.74; N, 16.1. Found: C, 69.20; H, 5.60; N, 16.1, 16.3.

Ultraviolet Absorption Spectra.—The ultraviolet absorption spectra data in Table I were obtained on a Beckman Model DU quartz spectrophotometer.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF MIAMI
CORAL GABLES, FLORIDA

Some Reactions of Tris-(*p*-nitrophenyl)-methyl Bromide

BY JOHN E. LEFFLER

RECEIVED JANUARY 26, 1953

In an attempt to prepare tris-(*p*-nitrophenyl)-methyl *p*-nitrobenzoate from the bromide by displacement with sodium *p*-nitrobenzoate in acetone it was found that the tris-(*p*-nitrophenyl)-methyl free radical was produced instead. It was then found that the radical is also produced by reaction in acetone with iodide ion, thiosulfate ion, bisulfite ion, thiocyanate ion, bicarbonate ion, pyridine and dimethylaniline. The radical is also formed by phenol in wet pyridine–dioxane and in benzene with phenol plus pyridine. The color produced by these reagents is due to radical rather than to methide ion, since it is not discharged by strong acids but is discharged by oxygen with the formation of the expected peroxide. The reaction with sodium iodide gives iodine in nearly quantitative yield. Radical formation by sodium iodide is not prevented by the carbanion traps alcohol, acetic acid and *p*-nitrobenzaldehyde. Neither the carbinol, the *p*-nitrobenzoate, nor the anisate dissociates appreciably into radicals.

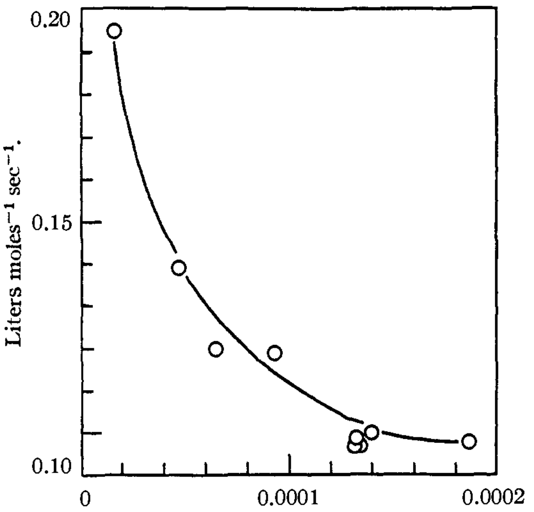
In contrast to its reactivity with negative ions and bases in acetone, tris-(*p*-nitrophenyl)-methyl bromide does not give any radical on treatment at room temperature with hydrazine sulfate, hydroxylamine hydrochloride, anisic hydrazide, sodium nitrite, or weak acids in acetone (acetone enol).

Kinetics of the Reaction with Sodium Iodide in Acetone.—The reaction is markedly slowed down by alcohol, does not take place with mercuric iodide, and is much slower with a mixture of mercuric and sodium iodides than with the latter alone. The reaction with sodium iodide in the presence of air can be followed by the light absorption due to the iodine for about one half-life. It is somewhat greater than first order with respect to sodium iodide and the deviation from first-order kinetics is not a general salt effect since it is only partially corrected by adding sodium perchlorate. The reaction is somewhat *less* than first order with respect to the bromide as is shown by the trend in second-order rate constants of Figs. 1–3. This effect is similar to that observed by Nixon and

---

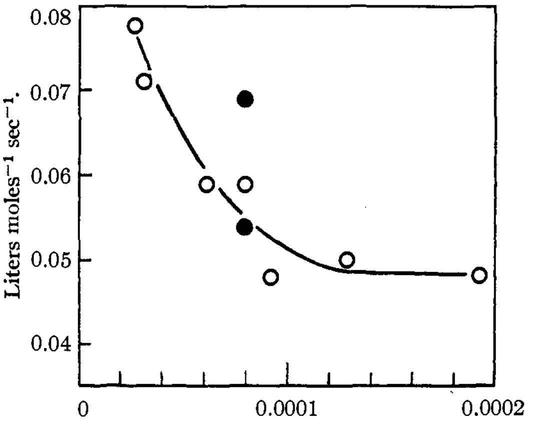
(4) R. Mozingo, *Org. Syntheses*, **26**, 78 (1946).

(5) M. Geerling and S. Wibaut, *Rec. trav. chim.*, **53**, 1015 (1934).



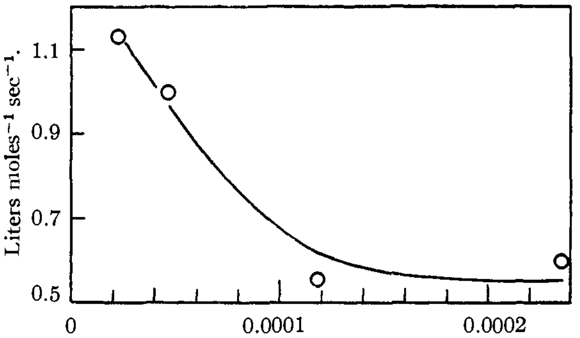
Initial concn. of tris-(*p*-nitrophenyl)-methyl bromide in moles per liter.

Fig. 1.—0.1 *N* sodium iodide at 3°.



Initial concn. of tris-(*p*-nitrophenyl)-methyl bromide in moles per liter.

Fig. 2.—0.02 *N* sodium iodide at 3°: ●, total salt concn. made up to 0.1 *N* with sodium perchlorate.



Initial concn. of tris-(*p*-nitrophenyl)-methyl bromide in moles per liter.

Fig. 3.—0.02 *N* sodium iodide at 26°.

Branch in the alcoholysis of triarylmethyl chlorides.[1] In both cases the dilution is so great as to make the usual kind of medium effect unlikely.

Comparison with Related Compounds.—Triphenylmethyl bromide itself reacts rapidly with an acetone solution of sodium iodide in air to give the peroxide plus iodine. In at least this case of the unsubstituted bromide the reaction is probably a simple displacement on carbon since the iodide is known to dissociate spontaneously into radicals and since the displacement should be fast.[2] Triphenylmethyl bromide reacts with potassium thiocyanate to give triphenylmethyl thiocyanate rather than the radical.[3] With sodium sulfite in aqueous acetone it gives only the carbinol. Bromonitromalonate with potassium iodide gives an ionic reaction in which iodide ion displaces carbanion from "positive" bromine.[4]

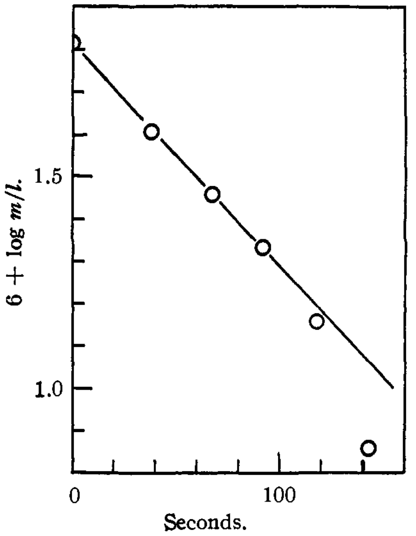


Fig. 4.—Rate of reaction of tris-(*p*-nitrophenyl)-methyl bromide with 0.1 *N* sodium iodide at 3°.

It is difficult to decide among the alternative mechanisms for the formation of radicals from tris-(*p*-nitrophenyl)-methyl bromide. In the case of the reaction with iodide there might be a nucleophilic displacement on carbon to form the iodide which would then dissociate into radicals. For the other reagents such a path is unavailable but two other possibilities remain. One of these is nucleophilic displacement on bromine to form a carbanion which is oxidized back to the radical in a subsequent step. Carbanion traps such as alcohol or acetic acid do not prevent the formation of radical in the reaction with sodium iodide, nor does water interfere with the thiosulfate reaction. The tris-(*p*-nitrophenyl)-methide ion might react so slowly with such substances that the oxidation reaction can compete. However, sodium tris-(*p*-nitrophenyl)-methide does not give the radical on reaction with the bromide in acetone plus water or acetic acid; this does not of course rule out a faster reaction with oxidizing agents other than tris-(*p*-nitrophenyl)-methyl bromide.

The other possibility is a radical decomposition of the bromide induced either by electron transfer from a reducing agent or by a displacement reaction of a new type in which the attacking negative ion accepts a bromine atom to become an ion-radical

---

[1] A. C. Nixon and G. E. K. Branch, This Journal, **58**, 492 (1936).

[2] S. T. Bowden, *J. Chem. Soc.*, 33 (1939); K. Ziegler, L. Ewald and P. Orth, *Ann.*, **479**, 277 (1930).

[3] W. H. Carothers, This Journal, **48**, 3193 (1926).

[4] R. Willstätter, *Ber.*, **37**, 1775 (1904).

and to displace tris-(*p*-nitrophenyl)-methyl radical. Although such negative-ion induced decompositions do not seem to have been observed in the past it is interesting to note the connection, in purely radical displacements, between the electron-donor ability of the attacking radical and the rate of the induced decomposition.[5] It is also to be expected that in the dissociation of a pair of radicals of unequal electronegativity, complexing one of them should reduce the electronegativity difference and accelerate the reaction.

Experimental

Tris-(*p*-nitrophenyl)-methyl Bromide.—This compound is more readily prepared by the method of Ziegler and Boye[6] than by the method of Lewis, Magel and Lipkin.[7] Previous workers report a melting point of 191°. The material used in these experiments was recrystallized many times at room temperature from acetone–petroleum ether until a constant active bromine titer was attained; it then melted at 200–200.5° with decomposition. *Anal.* Calcd. for $C_{19}H_{12}O_6N_3Br$: C, 49.8; H, 2.64; N, 9.2; Br, 17.4. Found: C, 49.93, 50.22; H, 2.72, 2.84; N, 8.35, 8.50, 8.55; Br, 17.2.[8,9]

Kinetic Experiments.—The acetone was dried over calcium chloride and distilled. The kinetic runs were made in a Beckman cell-holder jacketed with circulating water. Precooled sodium iodide solution was rapidly added to an equal volume of tris-(*p*-nitrophenyl)-methyl bromide by means of a hypodermic syringe and the timer started. Extinction coefficients for triiodide ion were determined for each sodium iodide concentration used.

Reactions of Tris-(*p*-nitrophenyl)-methyl Bromide.—With sodium iodide in acetone the free radical is formed very rapidly at room temperature or below. The intense blue color due to the radical is not discharged by acid but is discharged on swirling in air. The reaction with sodium iodide is very much slower in acetone–alcohol mixtures. The radical is still produced even in the presence of 1% acetic acid or excess *p*-nitrobenzaldehyde.

The radical is not produced by acids in acetone but is produced when a few drops of aqueous sodium bicarbonate are refluxed with the acetone solution, the color being discharged when the condenser is removed and air admitted. The color is not discharged by perchloric acid. Refluxing in acetone with sodium *p*-nitrobenzoate, with pyridine, or with dimethylaniline also gives the air-sensitive color.

The radical is also produced on refluxing in benzene with phenol plus pyridine but not with *p*-nitrobenzoic acid plus pyridine. In dioxane it was found that pyridine and pyridine plus phenol gave no color until water was added.

The radical is also produced by a rapid reaction with a mixture of sodium thiosulfate, water and acetone at room temperature. The product after exposure to air melts at 212.5–213° with decomposition. Binaghi reports 208–210° for the peroxide.[10]

Refluxing with a benzene solution of benzoyl peroxide also forms an air-sensitive colored radical.

Boiling with perchloric acid in aqueous acetic acid hydrolyzes the bromide to the carbinol, m.p. 190–191°.

The bromide reacts slowly with a suspension of silver *p*-nitrobenzoate in dry benzene at room temperature giving the ester in small yield. It melts at 191–191.5° and depresses the melting points of both the carbinol and the bromide. *Anal.* Calcd. for $C_{26}H_{16}O_{10}N_4 \cdot C_6H_6$: C, 61.7; H, 3.56. Found: C, 60.82, 61.10; H, 3.50, 3.51.[8] The anisate was made by refluxing the bromide and silver anisate in acetonitrile for about 1.5 hours, filtering, removing the solvent and crystallizing from benzene–petroleum ether. It melts at 264–269°, yield 50%. *Anal.* Calcd. for $C_{27}H_{19}O_9N_3$: C, 61.25; H, 3.62. Found: C, 61.95, 62.04; H, 3.59, 3.62.[11]

Acknowledgment.—This research was part of an investigation into reactions of variably radical or ionic mechanism. Its support by the Office of Naval Research is gratefully acknowledged.

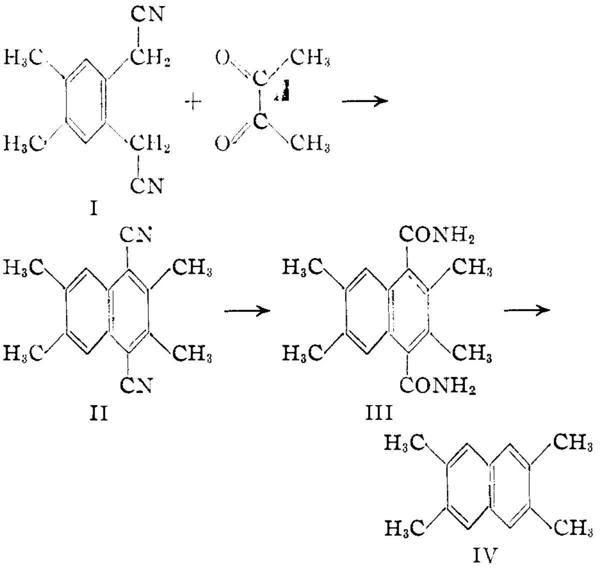
DEPARTMENT OF CHEMISTRY
FLORIDA STATE UNIVERSITY
TALLAHASSEE, FLORIDA

2,3,6,7-Tetramethylnaphthalene

BY WILLIAM L. MOSBY[1]

RECEIVED FEBRUARY 5, 1953

The hitherto unknown 2,3,6,7-tetramethylnaphthalene (IV) was obtained *via* the route



The dinitrile II was prepared by Dr. P. E. Hoch for another purpose, and advantage was taken of its availability to complete the rest of the sequence. The diamide III was obtained from the dinitrile II in excellent yield by refluxing II with potassium hydroxide in aqueous ethylene glycol. When heated at 200° with 100% phosphoric acid,[2] III readily afforded a 79% yield of IV.

The condensation of a substituted *o*-phenylenediacetonitrile with a 1,2-diketo compound is an extension of the synthesis employed by Moureu, Chovin and Rivoal[3] and by Orchin and Reggel.[4] The complete removal of two carboxamide groups from a benz[k]fluoranthene analog of III by hot 100% phosphoric acid was described by Orchin and Reggel.[4] This reagent had previously been recommended[2] for the saponification of hindered amides. Since it seemed probable that hot 100% phosphoric acid would act as a dehydrating agent, converting an amide to a nitrile, treatment of II directly was attempted. When II was heated to 200° with polyphosphoric acid, a good yield of IV was readily obtained. This procedure may offer a more convenient general method of removing such difficultly

---

(5) C. G. Swain, W. H. Stockmayer and J. T. Clarke, THIS JOURNAL, **72**, 5426 (1950).

(6) K. Ziegler and E. Boye, *Ann.*, **458**, 248 (1927).

(7) G. N. Lewis, D. Lipkin and T. T. Magel, THIS JOURNAL, **66**, 1579 (1944).

(8) Analysis by Clark Microanalytical Co., Urbana, Ill.

(9) Bromine by titration of iodine from reaction with sodium iodide.

(10) R. Binaghi, *Gazz. chim. ital.*, **53**, 879 (1923).

(11) Analysis by Weiler and Strauss, Inc., Oxford.

(1) Calco Chemical Division, American Cyanamid Company, Bound Brook, New Jersey.

(2) G. Berger and S. C. J. Olivier, *Rec. trav. chim.*, **46**, 600 (1927).

(3) H. Moureu, P. Chovin and G. Rivoal, *Bull. soc. chim. France*, [5] **13**, 106 (1946); *Compt. rend.*, **223**, 951 (1946); *ibid.*, **225**, 501 (1947).

(4) M. Orchin and L. Reggel, THIS JOURNAL, **73**, 436 (1951).

saponifiable nitrile groups in stable aromatic systems.

Experimental

2,3,6,7-Tetramethylnaphthalene-1,4-dinitrile (II).—The author is indebted to Dr. P. E. Hoch for a sample of this material which he prepared by a standard Knoevenagel reaction of biacetyl with 3,4-dimethyl-*o*-phenylenediacetonitrile. This product, when decolorized with charcoal and recrystallized from cyclohexane, formed felted yellow needles which appear greenish in reflected light as a result of a blue fluorescence. It decomposed at about 240° without melting.

Anal. Calcd. for $C_{16}H_{14}N_2$: C, 82.0; H, 5.98; N, 11.96. Found: C, 81.9; H, 5.88; N, 11.75.

2,3,6,7-Tetramethylnaphthalene-1,4-dicarboxamide (III).—A mixture of 250 mg. of the dinitrile II, 4.0 g. of potassium hydroxide, 40 ml. of ethylene glycol and 5 ml. of water was refluxed one hour. The solid II slowly dissolved to a clear yellow solution, which, when it was poured onto ice and filtered, gave 260 mg. (97% yield) of pale buff solid, m.p. above 320°.

2,3,6,7-Tetramethylnaphthalene (IV).—To a solution of 3.0 g. of phosphorus pentoxide in 7.0 g. of reagent 85% phosphoric acid was added 250 mg. of the diamide III. The mixture, contained in a small flask with reflux condenser, was heated at 200° for one hour with occasional shaking. White micro-platelets of product sublimed into the upper part of the flask and into the condenser. The mixture was cooled, diluted with water and extracted well with cyclohexane. The cyclohexane solution was dried and chromatographed on an 80 × 8 mm. column of alumina. The product, recovered from the effluent liquid by vacuum stripping, weighed 145 mg. (79% yield). One recrystallization from methanol gave shining, fluffy platelets, m.p. 191.2–191.8°.

Anal. Calcd. for $C_{14}H_{16}$: C, 91.25; H, 8.75. Found: C, 91.14; H, 8.80.

The **TNF derivative**, when recrystallized from benzene, gave scarlet microneedles, m.p. 176.0–176.6°.

Anal. Calcd. for $C_{27}H_{21}N_3O_7$: C, 65.0; H, 4.21; N, 8.42. Found: C, 65.5; H, 4.62; N, 8.32.

When 20 mg. of the dinitrile II and 2.0 g. of polyphosphoric acid were heated at 200° for a short time, white crystals sublimed into the upper part of the tube. The identity of these crystals with IV was confirmed by melting point and mixed melting point.

A comparison of the ultraviolet absorption spectrum and physical properties of this material with those of other tetramethylnaphthalenes has been made.[5]

---

[5] W. L. Mosby, This Journal, **75**, 3348 (1953).

CENTRAL RESEARCH LABORATORY
GENERAL ANILINE AND FILM CORPORATION
EASTON, PENNSYLVANIA

On the Starch–Iodine Complex

By Sôzaburo Ono, Shinpei Tsuchihashi and Takashi Kuge

Received February 4, 1953

This paper presents a quantitative study of the relationship between iodide concentration and wave length of maximum absorption of amylose–iodine complex. The authors attempt to explain the manner in which the iodide ion influences the starch–iodine complex formation.

Rundle and his co-workers[1] have found that the nature of the absorption spectra of the colored iodine in the starch–iodine complex is something quite different from that of iodine in any other medium. The structure of the amylose–iodine complex has been established as a helical amylose chain in which the iodine molecules are arranged in a linear array parallel to the helix axis, and resonance structures have been proposed for the polyiodine chains.[2] We may expect that this polyiodine chain has a structure similar to that of polyenes. The corresponding two p-electrons (those having the same symmetry) of each iodine atom may form a π-orbital along the polyiodine chain. The iodine chain may have two such π-orbitals, because each iodine atom possesses two pairs of such p-electrons, and these π-electrons may be responsible for the light absorption of the complex. We applied to our experimental results the relation which has been proposed by Kuhn[3] for polyenes. Kuhn's relation is expressed by

$$\lambda_{\max} = \left[\frac{V_0}{hc}\left(1 - \frac{1}{N}\right) + \frac{h}{8mc}\,\frac{N+1}{L^2}\right]^{-1} \qquad (1)$$

where $\lambda_{\max}$ is the wave length of maximum absorption, L, the resonating chain length, N, the number of π-electrons, h, Planck's universal constant, m, the mass of the electron, c, the velocity of light, V_0, the perturbation parameter.

The results obtained indicate that the $\lambda_{\max}$ shifts toward the shorter wave lengths and the resonating chain length becomes shorter with the increasing iodide concentrations. Our data are also in good agreement with those obtained by Rundle and co-workers[4] and Swanson,[5] concerning the relationship between starch chain length and $\lambda_{\max}$. Potentiometric[6] and spectrophotometric titrations[4] suggested that iodide enters the helix with iodine. Our suggested explanation for the shift of $\lambda_{\max}$ with the change of iodide concentration is that iodide ions enter into the polyiodine chains and break the resonating chains into shorter lengths.

Experimental

Amylose used was obtained from potato starch by hot water extraction (at 60°), and it had the following characteristics: intrinsic viscosity was $[\eta] = 0.80$. Using this value, the degree of polymerization was calculated to be D.P. = 480 glucose units.[7]

Absorption spectra were measured with a G. E. Recording Spectrophotometer at room temperature, using a cuvette 10 mm. thick. Amylose concentration used in this investigation was 0.01%. Iodide concentrations were varied from zero to 0.5 M at constant iodine concentration (13% of theoretical maximum complex formation). A parallel investigation was conducted using ethanol instead of iodide.

Results and Discussion

In our study, N is equal to twice the number of iodine atoms, n, and L is equal to $6.2(n/2 - 1)$ Å., based on the average I–I distance of 3.1 Å. in the polyiodine chain.[8] It was postulated that in the complex free of iodide, 80 iodine molecules form one polyiodine chain, since D.P. of the amylose used was 480 glucose units and 6 glucose units take up one iodine molecule.[4,9] At zero iodide concentration, all terms in equation (1) are known except V_0. V_0 is then calculated to be 3.09×10^{-12} erg (1.9 e.v.).

---

[1] R. E. Rundle, J. F. Foster and R. R. Baldwin, This Journal, **66**, 2116 (1944).

[2] R. S. Stein and R. E. Rundle, *J. Chem. Phys.*, **16**, 195 (1948).

[3] H. Kuhn, *ibid.*, **17**, 1198 (1949).

[4] R. R. Baldwin, R. S. Bear and R. E. Rundle, This Journal, **66**, 111 (1944).

[5] M. A. Swanson, *J. Biol. Chem.*, **172**, 825 (1948).

[6] F. L. Bate, D. French and R. E. Rundle, This Journal, **65**, 142 (1943).

[7] A. L. Potter and W. Z. Hassid, *ibid.*, **73**, 593 (1951).

[8] C. D. West, *J. Chem. Phys.*, **15**, 689 (1947).

[9] R. E. Rundle and D. French, This Journal, **65**, 1707 (1943).

Hach and Rundle[10] stated that it had not been determined experimentally whether polyiodine consists of chains with two different I–I distances, or whether all distances have become equal to 3.1 Å. From the V_0 value determined above, 1.9 e.v., it seems likely that polyiodine consists of chains with two I–I distances, due to unequal contributions of two limiting forms A and B.

$$\cdots \mathrm{I{-}I} \cdots\cdots \mathrm{I{-}I} \cdots\cdots \mathrm{I{-}I} \cdots \quad (A)$$

$$\mathrm{{-}I} \cdots\cdots \mathrm{I{-}I} \cdots\cdots \mathrm{I{-}I} \cdots\cdots \mathrm{I{-}} \quad (B)$$

TABLE I

No.	Concn. of KI, *M*	Concn. of EtOH, *M*	λ_{max}	*n* (chain length)
1	....	....	628	160
2	1.2×10^{-4}	....	625	134
3	6.1×10^{-4}	....	621	108
4	5.0×10^{-3}	....	613	77
5	3.0×10^{-2}	....	600	52
6	2.1×10^{-1}	....	572	30
7	5.0×10^{-1}	....	557	22
8	....	8.2×10^{-1}	594	45
9	....	1.6	588	40

Table I shows the values of λ_{max} observed and the corresponding chain lengths (n) which have been calculated with equation (1) and the V_0 value. Both the λ_{max} and the estimated chain length change in a regular fashion with the iodide concentration. Also, it appears that ethanol causes an effect similar to that of iodide.

Our data may not describe exactly the quantitative relation between the chain length and the λ_{max}, because the length of the polyiodine chain at zero iodide concentration is estimated. Nevertheless, our results indicated that Kuhn's theory is applicable to the polyiodine chain. They also account for the behavior of iodine in shifting the absorption spectrum of the complex.

Gilbert and Marriott[11] suggested that the amylose complex is composed mostly of groups of the type ($3I_2 \cdot 2I^-$), each probably a linear resonating group which develops the pure blue color in the complex. According to our model, it may be that iodide is chain terminating, even if it is in the resonating chain.

It is well known that the color of the complex disappears at higher temperature. The authors intend to investigate this phenomenon spectrophotometrically.

We are indebted to Mr. Tamotsu Fukuda of the Osaka Industrial Research Institute for the measurement of absorption spectra.

[10] R. J. Hach and R. E. Rundle, THIS JOURNAL, **73**, 4321 (1951).

[11] G. A. Gilbert and J. V. Marriott, *Trans. Faraday Soc.*, **44**, 84 (1948).

LABORATORY OF BIO-PHYSICAL CHEMISTRY
FACULTY OF AGRICULTURE
NANIWA UNIVERSITY
SAKAI CITY, JAPAN

Removal of Halogen from Aromatic Nitrohalo Compounds

BY WALTER T. SMITH, JR., AND LOUIS CAMPANARO

RECEIVED FEBRUARY 20, 1953

Earlier work has shown that the replacement of chlorine by hydrogen in aromatic compounds having a nitro group ortho to the chlorine can be accomplished by heating the compound with copper and benzoic acid.[1]

We wish to report a study of the application of this reaction to nitro compounds containing fluorine, bromine or iodine, and also the use of the reaction for the preparation of 3,5-dinitrotoluene.

In the earlier work it was found that a chlorine meta or para to a nitro group was not removed by the treatment with copper and benzoic acid. It has now been shown that a chlorine or bromine ortho to a nitro group can be removed without removal of a chlorine or bromine located meta to the same nitro group. Thus, the dehalogenation of 2,5-dichloro- and 2,5-dibromonitrobenzene leads to *m*-chloro- and *m*-bromonitrobenzene. The yields in these cases are 37–38%.

The monofluoronitrobenzenes did not dehalogenate under the conditions used. The *o*-, *m*- and *p*-isomers were all recovered without any formation of nitrobenzene.

The results observed with the monobromonitrobenzenes were comparable to those obtained with the chloronitrobenzenes. Only in the case of *o*-bromonitrobenzene did dehalogenation take place. While it might be expected that *p*-bromonitrobenzene might be sufficiently more reactive than the corresponding chlorine compound to permit dehalogenation, such was not the case. *p*-Bromonitrobenzene was recovered in 78% yield and there was no evidence that any nitrobenzene was formed.

The results with the iodonitrobenzenes are quite different than those obtained with the other halonitrobenzenes. As would be expected, the ortho isomer dehalogenated readily to give a 53% yield of nitrobenzene. It was not surprising to find that the presence of a nitro group para to the iodine was sufficient to activate the iodine, so that it was easily replaced by hydrogen upon treatment with copper and benzoic acid. The experiment with *m*-iodonitrobenzene indicates, however, that the location of the nitro group, and probably even its presence, is not an important factor in determining if iodine is replaced. The yield of nitrobenzene was 32% when *m*-iodonitrobenzene was used.

The dehalogenation of 2-chloro-3,5-dinitrotoluene provides a new synthesis of 3,5-dinitrotoluene. The presence of nitro groups located both ortho and para to the chlorine appears to enhance the ease of dehalogenation and 3,5-dinitrotoluene is obtained in 83% yield. This method of synthesis suffers from the low yield obtained in the preparation of the 2-chloro-3,5-dinitrotoluene. The usual "mixed acid" nitration of *o*-chlorotoluene was not successful, even at elevated temperatures. The use of concentrated sulfuric acid and sodium nitrate was also unsuccessful. By using a mixture of nitric, sulfuric and fuming nitric acids, *o*-chlorotoluene may be dinitrated to give a 9% yield of 2-chloro-3,5-dinitrotoluene.

Experimental

Dehalogenations.—The dehalogenations and attempted dehalogenations were carried out as illustrated below for *o*-fluoronitrobenzene. The results are summarized in Table I.

---

[1] W. T. Smith, Jr., THIS JOURNAL, **71**, 2855 (1949).

TABLE I

DEHALOGENATION OF SOME HALONITROBENZENES

Halonitrobenzene	Starting material recovered, %	Dehalogenation product yield, %
o-Fluoro-	53	0
m-Fluoro-	65	0
p-Fluoro-	59	0
o-Bromo-	0	52[a]
m-Bromo-	70	0
p-Bromo-	78	0
o-Iodo-	0	53[a]
m-Iodo-	10	32[a]
p-Iodo-	22	32[a]
2,5-Dichloro-	0	37[b]
2,5-Dibromo-	0	38[c]

[a] Product is nitrobenzene. [b] Product is *m*-chloronitrobenzene. [c] Product is *m*-bromonitrobenzene.

o-**Fluoronitrobenzene.**—To a molten mixture of 14 g. (0.11 mole) of benzoic acid and 5 g. (0.035 mole) of *o*-fluoronitrobenzene at 150–200° was added 10 g. of copper powder in several portions over a period of five minutes. Heating was stopped and the solidified mixture was taken up in 50 ml. of 20% sodium carbonate solution. The alkaline mixture was steam distilled until the distillate was clear. The distillate was extracted with ether and dried over barium oxide. The ether solution was filtered and evaporated. There was recovered 2.6 g. (53% recovery) of *o*-fluoronitrobenzene, m.p. −7 to −6°.

2-Chloro-3,5-dinitrotoluene.—In a 600-ml. beaker was placed 60 g. of fuming nitric acid (sp. gr. 1.59–1.60), 60 g. of concentrated nitric acid (sp. gr. 1.42) and 360 g. of concentrated sulfuric acid. To this solution was added 40 g. (0.318 mole) of *o*-chlorotoluene and the mixture was heated on the steam-bath for 3 hours. The solution was cooled, poured over ice, and extracted with a total of 500 ml. of ether. Evaporation of the ether gave a heavy yellow oil, which partly crystallized on standing in the ice-box for several days. The light yellow crystalline material was separated by drying on a clay plate. The product thus obtained weighed 24 g. and melted at 55–60°. It was recrystallized from carbon tetrachloride to give 16 g., m.p. 58–60°. Recrystallization from alcohol gave 12 g. (8.8%) of 2-chloro-3,5-dinitrotoluene, m.p. 62–63° (lit. m.p. 62–63°[2]).

Synthesis of 3,5-Dinitrotoluene.—To a hand-stirred mixture of 14 g. (0.11 mole) of benzoic acid and 5 g. (0.023 mole) of 2-chloro-3,5-dinitrotoluene was added 10 g. of copper powder, in several portions over a period of 5 minutes (temperature at 150–200°). Heating was stopped and the solidified mixture was then taken up with 50 ml. of 20% sodium carbonate solution. The insoluble residue was removed by filtration, dried, and extracted with ether. Evaporation of the ether gave 3.8 g., m.p. 90–91°. Recrystallization from 50 ml. of alcohol gave 3.5 g. (83%) of 3,5-dinitrotoluene, m.p. 93°.

---

(2) G. R. Yohe, *Trans. Ill. State Acad. Sci.*, **33**, No. 2, 125 (1940).

DEPARTMENT OF CHEMISTRY
STATE UNIVERSITY OF IOWA
IOWA CITY, IOWA

Azeotropes of Bromine. III. Azeotropes of Bromine with 1,2,2-Trichloro-1,1-difluoroethane and 1,1-Dichloro-2,2-difluoroethane

BY WILLIAM M. SPICER AND HENRY D. R. PAGE

RECEIVED MARCH 23, 1953

As a continuation of an investigation to prepare binary azeotropes consisting of one colored and one colorless component,[1,2] it was decided to study further possibilities in systems of bromine with colorless bromine solvents. Azeotropes of this general type are valuable in the study of the methods employed to separate azeotropic mixtures, since separation can be observed visually.

It was decided to investigate $CHCl_2CHF_2$ and $CHCl_2CF_2Cl$ as bromine solvents since these liquids possess boiling points near that of bromine, a condition favorable for azeotrope formation. Besides it was anticipated that these liquids would be miscible with and inert toward bromine.

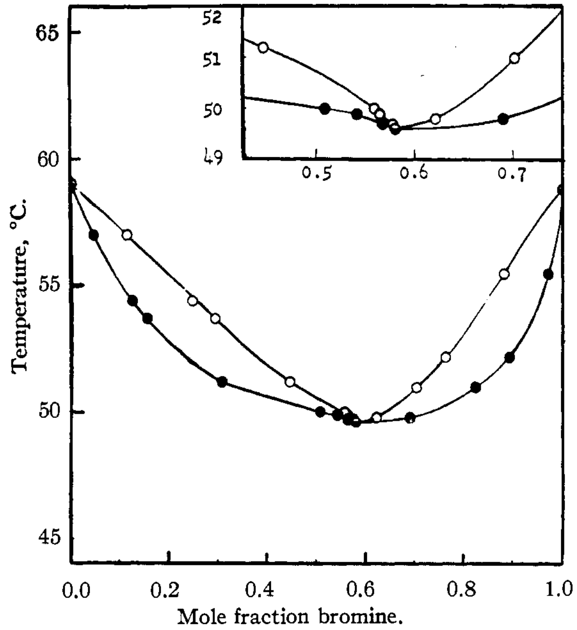


Fig. 1.—Temperature–composition diagram for the system Br_2–$CHCl_2CHF_2$ at 760 mm. pressure: ○, vapor; ●, liquid; ◒, vapor and liquid.

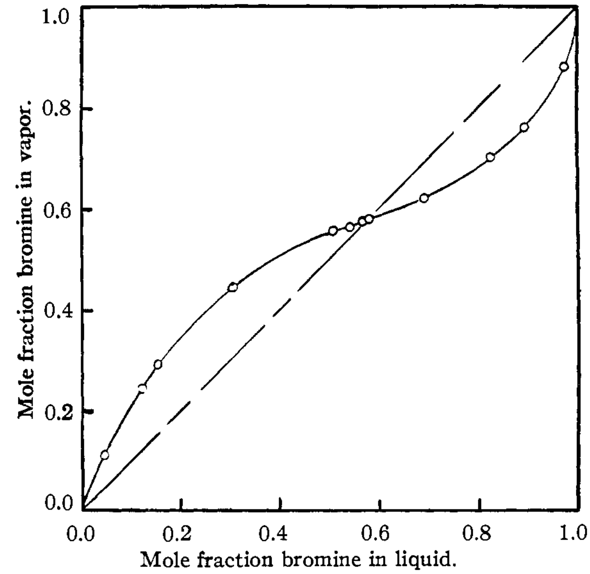


Fig. 2.—Vapor–liquid equilibrium diagram for the system Br_2–$CHCl_2CHF_2$ at 760 mm. pressure.

Experimental

Merck and Co., Inc., analyzed C.P. bromine was used without further purification. The $CHCl_2CHF_2$ and $CHCl_2CF_2Cl$ were obtained from Halogen Chemicals, Inc., and were listed as being better than 95% pure. These were

---

(1) W. M. Spicer and J. Kruger, THIS JOURNAL, **72**, 1855 (1950).

(2) W. M. Spicer and L. H. Myer, *ibid.*, **73**, 934 (1951).

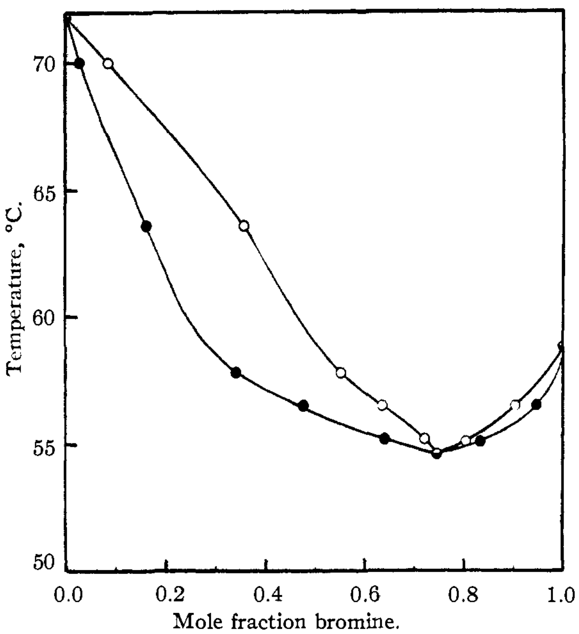


Fig. 3.—Temperature-composition diagram for the system Br_2-$CHCl_2CF_2Cl$ at 760 mm. pressure: ○, vapor; ●, liquid; ◒, vapor and liquid.

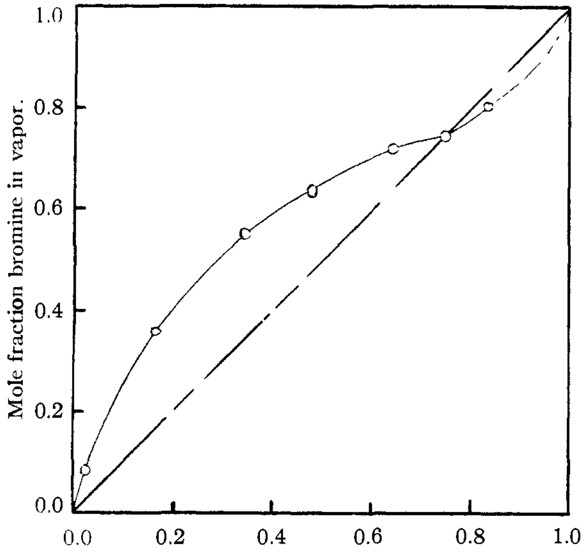


Fig. 4.—Vapor-liquid equilibrium diagram for the system Br_2-$CHCl_2CF_2Cl$ at 760 mm. pressure.

purified further by fractionation in a five-foot glass helix-packed column, taking a middle cut. The boiling point range of the $CHCl_2CHF_2$ was 58.4–59.5° at 735.2 mm. and that of the $CHCl_2CF_2Cl$ was 71.1–71.2° at 736.3 mm.

Vapor-liquid equilibrium data were obtained at 760 mm. as has been described previously.[1,2]

For each system exhibiting azeotrope formation, the azeotrope itself was prepared by fractionation at 760 mm. pressure of a liquid mixture of very nearly the azeotropic composition in a small glass helix-packed column (packed section 40 cm. in length and 2 cm. in diameter). After the column had reached equilibrium, the azeotropic temperature was read directly and the composition of the azeotrope determined by analyzing small samples of the condensed vapor.

To test the systems for evidence of reaction, although the likelihood of such was considered small, approximately 10% (by weight) bromine solutions were fractionated, the bromine being distilled off in the azeotrope. After removal of the bromine the refractive index of the residue in the still pot was determined and compared with that of the pure solvent at the same temperature. The index of the $CHCl_2CHF_2$ changed from 1.3769 to 1.3773 and that of the $CHCl_2CF_2Cl$ from 1.3900 to 1.3899. This slight change was felt to be due, not to reaction but to some slight fractionation of the solvents.

The azeotropic boiling points and compositions for these systems as obtained from the column mentioned above were found to be as follows: Br_2-$CHCl_2CHF_2$, 49.6°, 58.1 mole per cent. bromine and Br_2-$CHCl_2CF_2Cl$, 54.6°, 74.7 mole per cent. bromine.

The equilibrium data are plotted in the usual manners in the figures shown.

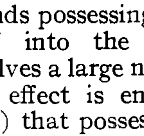
SCHOOL OF CHEMISTRY
GEORGIA INSTITUTE OF TECHNOLOGY
ATLANTA, GEORGIA

Molecular Rotation Differences for 17-Hydroxy-20-ketosteroids

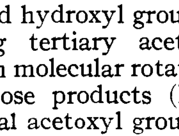
BY RICHARD B. TURNER

RECEIVED JANUARY 5, 1953

The method of molecular rotation differences[1] has been employed with outstanding success by Barton, Klyne and others in the elucidation of stereochemical and related structural problems encountered in investigations of a wide variety of steroids. An important application has been the correlation of configuration of hydroxyl substituents with the change in molecular rotation accompanying acetylation of these groups.[2] Recent development of procedures for acetylation of the hitherto refractory 17α-hydroxy-20-ketosteroids (I)[3] makes possible extension of the method to this important group of substances. Results of correlations in this series are summarized in Table I, which includes also available data for three epimeric 17β-hydroxy-20-keto derivatives (II).



I



II

It is at once apparent that conversion of compounds possessing an α-oriented hydroxyl group at C-17 into the corresponding tertiary acetates involves a large negative shift in molecular rotation. The effect is enhanced in those products (Nos. 7–11) that possess an additional acetoxyl group at C-21 and is particularly pronounced in S acetate (No. 10) and in cortisone acetate (No. 11), which contain an α,β-unsaturated ketonic grouping as well. A negative increment of intermediate magnitude is observed for the 17α-hydroxy ester (No. 6),

---

(1) A discussion of the method as developed by Barton, together with literature citations, is given in "Natural Products Related to Phenanthrene," 3rd ed., L. F. Fieser and M. Fieser, Reinhold Publ. Corp., New York, N. Y., 1949, p. 206. See also D. H. R. Barton, *Angew. Chem.*, **61**, 57 (1949), and D. H. R. Barton and W. Klyne, *Chemistry and Industry*, 755 (1948).

(2) D. H. R. Barton, *J. Chem. Soc.*, 813 (1945); W. Klyne and D. H. R. Barton, THIS JOURNAL, **71**, 1500 (1949).

(3) Huang-Minlon, E. Wilson, N. L. Wendler and M. Tishler, *ibid.*, **74**, 5394 (1952); R. B. Turner, *ibid.*, **74**, 4220 (1952); *ibid.*, **75**, 3484 (1953).

TABLE I[a]

MOLECULAR ROTATION DIFFERENCES (Δ^{Ac}) FOR 17-HYDROXY-20-KETOSTEROIDS

No.	Compound	M_D 17-Alcohol	M_D 17-Acetate	Δ^A
1	3β,17α-Dihydroxy-5-pregnen-20-one[b,c]	−114 Di	−254 Di	−140
2	3β,17α-Dihydroxy-5-pregnen-20-one 3-monoacetate[c,d]	− 94 Di	−271 Di	−177
3	17α-Hydroxy-4-pregnene-3,20-dione[c,d]	+354 Di	+208 Di	−146
4	3β,17α-Dihydroxyallopregnan-20-one 3-monoacetate[c,d]	+ 71 Di	− 39 Di	−110
5	3α,17α-Dihydroxypregnane-11,20-dione 3-monoacetate[e,f]	+327 An	+202 Chf	(−125)
6	Methyl 3α-acetoxy-17α-hydroxy-11-ketoetiocholane-17-carboxylate[f,g]	+289 Chf	+ 98 Chf	−191
7	3α,17α,21-Trihydroxypregnane-11,20-dione 3,21-diacetate[e,f]	+416 An	+201 Chf	(−215)
8	17α,21-Dihydroxypregnane-3,11,20-trione 21-monoacetate[e,f]	+333 An	+123 Chf	(−210)
9	17α,21-Dihydroxyallopregnane-3,11,20-trione 21-monoacetate[e,f]	+406 Chf	+197 Chf	−209
10	17α,21-Dihydroxy-4-pregnene-3,20-dione 21-monoacetate[c,d]	+512 Di	+213 Di	−299
11	17α,21-Dihydroxy-4-pregnene-3,11,20-trione 21-monoacetate[c,d]	+852 Di	+591 Di	−261
12	3β,17β-Dihydroxyallopregnan-20-one 3-monoacetate[d,h]	−120 Di	+ 6 Di	+126
13	3β,17β-Dihydroxy-5-pregnen-20-one[i,j]	−199 Chf	−198 Di	(+ 1)
14	3β,17β-Dihydroxy-5-pregnen-20-one 3-monoacetate[i,k]	−229 Chf	−225 Di	(+ 4)

[a] An = acetone, Chf = chloroform, Di = dioxane. Figures in the last column that are enclosed in parentheses indicate determinations made in different solvents. [b] P. L. Julian, E. W. Meyer and I. Ryden, THIS JOURNAL, **72**, 367 (1950). [c] R. B. Turner, *ibid.*, **75**, 3489 (1953). [d] R. B. Turner, this investigation. [e] L. H. Sarett, THIS JOURNAL, **70**, 1454 (1948). [f] Huang-Minlon, E. Wilson, N. L. Wendler and M. Tishler, *ibid.*, **74**, 5394 (1952). [g] E. Wilson and M. Tishler, *ibid.*, **74**, 1609 (1952). [h] C. W. Shoppee and D. A. Prins, *Helv. Chim. Acta*, **26**, 185 (1943). [i] C. W. Shoppee and D. A. Prins, *ibid.*, **26**, 201 (1943). [j] L. Ruzicka, M. W. Goldberg and F. Hunziker, *ibid.*, **22**, 707 (1939). [k] L. Ruzicka and H. F. Meldahl, *ibid.*, **21**, 1760 (1938).

which differs from other members of the series in the nature of the carbonyl function. The shift in molecular rotation occasioned by acetylation of 17β-hydroxy-20-keto derivatives (Nos. 12, 13 and 14), on the other hand, is either small or in a *positive* direction. The Δ values recorded for compounds 13 and 14, both of which possess 5,6-unsaturation, are zero, within the limits of the method. Although this result may be significant, it should be noted that the optical measurements in these cases were obtained in different solvents and hence are less reliable than those for which the same solvent was employed.

DEPARTMENT OF CHEMISTRY
THE RICE INSTITUTE
HOUSTON, TEXAS

Preparation of Crystalline Anhydrous β-Gentiobiose

BY A. THOMPSON[1] AND M. L. WOLFROM

RECEIVED MARCH 17, 1953

Crystalline anhydrous β-gentiobiose has heretofore been difficult to obtain because of crystallization difficulties. Consequently, the more easily crystallized but unstable bis-(methyl alcoholate), an α-D form, is usually prepared. We wish to report herein an improved procedure for the preparation of crystalline anhydrous β-gentiobiose based upon the finding that this crystalline phase forms quite readily at elevated temperatures. A similar temperature effect has been noted in the crystallization of the trisaccharide panose, 4-α-(isomaltopyranosyl)-D-glucose.[2]

Both of the above-mentioned crystalline forms of gentiobiose were first obtained by Bourquelot and Hérissey,[3] who reported for the crystalline anhydrous form, the constants: m.p. 190–195°, $[\alpha]_D$ $-6°$ (6 min.) → $+9.8°$ (final). Hudson[4,5] calculated that the initial specific rotation of β-gentiobiose should be $-11°$. Extrapolation of Bourquelot and Hérissey's data to zero time gives a value near $-11°$. For our preparation we find the constants: m.p. 188–190° (cor.), $[\alpha]^{25}_D$ $-3.0°$ (initial, extrapolated) → $+10.5°$ (final, *c* 4, water). This divergence of 8° between the calculated and determined rotations for β-gentiobiose appears to be real. It is interesting to compare it with the determined value of $+166°$ (calculated[4] $+175°$) found by Fletcher and Diehl[6] for the related (1 → 6)-linked disaccharide α-melibiose. That the crystalline form of gentiobiose herein described is a molecular compound containing a small amount of the α-anomer is possible but no evidence of this could be obtained.

It is convenient to isolate and purify gentiobiose, regardless of its source, in the form of its β-octaacetate because of the fine crystallizing properties of this substance. One of the better sources of this sugar is hydrol (the mother liquor or "molasses" from the commercial production of α-D-glucopyranose monohydrate) from which it can be isolated as the acetate by the method of Berlin.[7] We consider the presently described directions as the procedure of choice for preparing gentiobiose should the α-D form not be required.

Experimental

β-Gentiobiose.—β-Gentiobiose octaacetate[7] (15 g.) was suspended in 180 ml. of 0.05 *N* sodium methoxide in dry methanol and allowed to stand, with occasional shaking, at room temperature for 1 hr. It was then diluted with water to dissolve the suspended material and passed through columns of Amberlite IR-120[8] and Duolite A-4.[9] The re-

---

[1] Corn Industries Research Foundation Associate.

[2] S. C. Pan, L. W. Nicholson and P. Kolachov, THIS JOURNAL, **73**, 2549 (1951).

[3] E. Bourquelot and H. Hérissey, *Compt. rend.*, **135**, 290 (1902); *J. pharm. chim.*, [6] **16**, 417 (1902).

[4] C. S. Hudson, THIS JOURNAL, **38**, 1566 (1916).

[5] C. S. Hudson, *ibid.*, **46**, 483 (1924).

[6] H. G. Fletcher, Jr., and H. W. Diehl, *ibid.*, **74**, 5774 (1952).

[7] H. Berlin, *ibid.*, **48**, 2627 (1926); F. J. Bates and Associates, "Polarimetry, Saccharimetry and the Sugars," Circular of the Natl. Bur. Standards C440, 1942, p. 463.

[8] A product of Rohm and Haas Co., Philadelphia, Pa.

[9] A product of the Chemical Process Co., Redwood City, Calif.

sultant solution was evaporated to a sirup under reduced pressure and the residual water was removed by repeated distillation with 100% ethanol under reduced pressure. The sirup was then dissolved in 40 ml. of hot methyl cellosolve (ethylene glycol monomethyl ether), filtered, nucleated and placed in an oven at 80° overnight. The crystalline material was filtered and washed with 100% ethanol; yield 6.7 g. (89%), m.p. 187–189° (cor.), $[\alpha]^{28}\mathrm{D}$ $-1.5°$ (initial, extrapolated) → $+10.6°$ (final, *c* 4, water). The material was further purified by recrystallization from methyl cellosolve; yield 6.4 g. (95%), m.p. 190° (cor.), $[\alpha]^{25}\mathrm{D}$ $-3.0°$ (initial, extrapolated) → $+10.5°$ (final, *c* 4, water). These constants were unchanged on further crystallization from this solvent or from ethanol effected by solution in minimal water and addition of warm 100% ethanol followed by crystallization at 60° (an ethyl alcoholate was not formed). The constants were likewise unaltered on standing under 95% ethanol (twice changed) for 1 week.

DEPARTMENT OF CHEMISTRY
THE OHIO STATE UNIVERSITY
COLUMBUS 10, OHIO

Dibenzofuran-2-sulfonic and 3-Nitro-8-sulfonic Acids as Reagents for Amines and Amino Acids[1]

BY RAY WENDLAND, JOHN RODE AND ROGER MEINTZER

RECEIVED FEBRUARY 23, 1953

Dibenzofuran-2-sulfonic acid, recently prepared in this Laboratory[2] is a strong acid and reacts with most amines to give stable salts. Simple salt formation from aqueous solution is much more convenient for preparation of derivatives than reactions commonly employed to identify amines such as acylation, quaternary base formation, etc. We have found that dibenzofuran-2-sulfonic acid (I) precipitates a large variety of amines and amino acids and that the salts formed are crystallizable solids having good melting points. The saturated solution of I in water is 4 *N* at 111° (99 g. of acid per 35 g. of water) and 0.34 *N* at 25°.

Since 3-nitrodibenzofuran has long been known,[3,4] it was expected that the sulfonic acid obtained from it would be an interesting and useful variant of compound I, and might have value in identifying amino compounds for which I was not suited. However, our expectations were not confirmed. The new compound, presumably the 3-nitro-8-sulfonic acid of dibenzofuran (compound II), was successfully prepared[5] but with difficulty, and it has none of the favorable crystallization characteristics of compound I. The free acid, II, appears to be very soluble in water from which it cannot be separated by usual crystallization methods. Crystallization from acetic acid however was satisfactory and gave the desired product in suitable purity. Despite its water solubility, II precipitates rapidly by salt formation with various amines, particularly aromatics. However, many of these only decomposed at high temperatures without showing characteristic melting points, hence have much less promise as derivatives than the salts from I.

The amino acid derivatives of dibenzofuran-2-sulfonic acid had been previously prepared and reported by Wendland and Smith.[6] We wish to add to those results the present observation that the neutral equivalents determined in alcoholic solution by the Foreman method[7] are highly reliable, with variations mostly ±1 from calculated and at worst only ±3. Thus this analytical procedure is most valuable in amino acid identifications. The salt of a monoamino monocarboxy acid titrates as a dibasic acid, a diamine monocarboxy acid as a tribasic acid, etc. The same titration can probably be applied also to the simple amine salts.

Experimental Part

Amino Salts of Dibenzofuran-2-sulfonic Acid.—The acid was prepared according to the method described in (2). The purified amine (1 to 2 g.) was mixed with sufficient water to effect solution, or for those amines of very slight solubility, an equivalent of hydrochloric acid was added. To the resulting solution was added the equivalent amount of a saturated solution of the sulfonic acid (about 0.34 *N* at room temp.). Most of the salts precipitated shortly at room temperature; after filtration they were recrystallized from boiling water, or from aqueous alcohol if the water solubility was very small.

The solubility of the salts was determined by preparing a measured volume of a saturated water solution, chilling at 0° overnight, and sampling. The filtrates (or supernatant fluid) were evaporated in tared bottles over sulfuric acid; from the weights of the residues the water solubilities were calculated. The results are assembled in Table I.

Amino compounds which failed to give the desired sulfonate salts were *p*-bromoaniline, *o*-nitroaniline, 2,4-dinitroaniline, 2,4-dinitrophenylhydrazine, 1-amino-2-naphthol-4-sulfonic acid, diphenylamine and sulfanilic acid. This group of compounds is of extremely feeble basicity, and at the same time are quite insoluble in water and in dilute hydrochloric acid.

Another group of amines, most of which are soluble in water, failed to give precipitates when treated with the aqueous saturated sulfonic acid. This group includes: 2-amino-1-butanol, 2-amino-2-methyl-1,3-propanediol, bis-(hydroxyethyl)-*n*-butylamine, hydroxyethylbutylamine, hydroxyethyldi-*n*-butylamine, bis-(hydroxyethyl)-phenylamine, hydroxylamine (note the various hydroxylated amines) and in addition methyl and ethyl amines, dimethyl, diethyl and diisopropyl amines, morpholine, nicotine, nicotinic acid, pyridine and α- and β-picolines. Concentrated solutions of methyl- and ethylamines added to saturated solutions of the sulfonic acid gave the result of precipitation at −5°, but the precipitates proved to be largely the free sulfonic acid. In another trial the anhydrous vapors of ethyl- and methylamines were distilled directly into the saturated acid solution, but no precipitates were formed at room temperature.

It appears that the low molecular weight aliphatic amines form extremely soluble salts with dibenzofuran sulfonic acid which cannot be crystallized—the result being the hydrolysis of the salt to a sufficient degree to precipitate the acid component. This behavior contrasts sharply with that of ammonia which yields a quite insoluble salt, although it precipitates slowly. (It should be noted here that Mitchell and Bryant[8] encountered similar difficulties in preparing picrates of the lower aliphatic amines, several of which had to be added to a solution of picric acid in anhydrous ether before the salt could be recovered.

Notable is the easy precipitation of urea from dilute solutions. Of the compounds related to urea, thiourea precipitated very slowly, and was contaminated by I from which it

---

[1] Taken in part from the M.S. dissertations of Rode (1948) and Meintzer (1951).

[2] R. Wendland, C. H. Smith and R. Muraca, THIS JOURNAL, **71**, 1593 (1949).

[3] W. Borsche and R. Bothe, *Ber.*, **41**, 1941 (1908).

[4] H. Gilman, W. Bywater and P. Parker, THIS JOURNAL, **57**, 885 (1935).

[5] 3-Nitro-8-dibenzofuransulfonic acid had been formed by W. Borsche and B. Schacke, *Ber.*, **56**, 2501 (1923), but was isolated by them only as the sodium or potassium salt which is much less soluble.

[6] R. T. Wendland and C. H. Smith, *Proc. No. Dak. Acad. Science*, **III**, 31 (1949).

[7] F. W. Foreman, *Biochem. J.*, **14**, 451 (1920).

[8] J. Mitchell and W. M. D. Bryant, THIS JOURNAL, **65**, 123 (1943).

TABLE I

AMINE SALTS OF DIBENZOFURAN-2-SULFONIC ACID[a]

Compound	M.p., °C.	Solubility, g./100 g. H_2O	Analytical values, % Sulfur (Parr) Calcd.	Sulfur (Parr) Found	Nitrogen (Dumas) Calcd.	Nitrogen (Dumas) Found
N,N-Dimethylaniline[b]	61–62	0.52	8.70	8.67	...	...
Tri-*n*-butylamine[c]	117–118	.4	7.40	7.09	3.23	3.42
N-Ethylaniline[d]	128–129	.6	8.68	8.56	3.79	3.70
N-Methylaniline	148–149	.6	9.02	9.22	3.94	4.11
Hexamethylenetetramine (tetra)	158–159	.3	11.32	11.33	...	...
Di-*n*-butylamine	164	.24	8.49	8.17	3.71	3.81
Di-isobutylamine	168	.30	8.49	8.30	3.71	3.80
Phenylhydrazine	193–194 dec.	.1	9.00	8.80	7.86	7.69
Quinoline[d]	195–196	.2	8.50	8.53	3.71	4.01
Diphenylguanidine	195–196	.1	6.98	6.57	9.14	9.06
Urea	203 [h]dec.	1.9	10.40	10.39	9.09	8.93
m-Toluidine	205–206	0.24	9.02	9.13	3.94	3.81
n-Butylamine	207–208	.8	9.98	9.60	4.36	4.58
8-Hydroxyquinoline (yellow)	207–208	.05	8.15	8.05	3.56	3.57
o-Aminodicyclohexyl[d,e,j]	213–255	.04	7.46	7.28	3.26	3.33
Cyclohexylamine[e]	214–216	.04	9.23	9.02	4.03	3.98
o-Phenylenediamine	225 [f]dec.	.3	9.00	8.82	7.86	7.91
o-Chloroaniline[e]	228–230	.24	8.53	8.60	3.73	3.86
p-Toluidine	232–234	.2	9.02	9.01	3.94	3.53
Dicyclohexylamine[e]	239–240	.05	7.46	7.42	3.26	3.67
p-Nitroaniline	240 dec.	.1	8.30	8.11	7.25	7.00
o-Toluidine	242–243 dec.	.14	9.02	9.26	3.94	3.79
β-Naphthylamine	245–246 dec.	.04	8.19	7.78	3.58	3.67
Sulfanilamide	245–246 dec.	.1	15.25	15.17	6.66	6.69
2,4-Diaminophenol (di)	250 dec.	.16	10.33	9.99	4.51	3.92[i]
m-Nitroaniline	250 dec.	.09	8.30	8.10	7.25	6.28[i]
Aniline	258–260	.23	9.39	9.40	4.10	3.93
α-Naphthylamine	260 [g]dec.	.1	8.19	7.84	3.58	3.74
Hydrazine (di)	260 dec.	.70	12.13	11.83	5.30	5.58
m-Phenylenediamine (di)	280–290 dec,	.20	10.60	10.70	4.63	4.26
p-Aminoacetanilide	Over 290	1.1	8.04	7.95	7.04	6.97
Benzidine (di)	Over 300	0.11	9.42	9.26	4.12	4.02
p-Phenylenediamine (di)	Stable to 305	.1	10.60	10.51	4.63	4.28
Ethylenediamine (di)	Stable to 305	.11	11.52	11.45	5.03	5.16
Ammonia	Over 310 dec.	1.87	...	...	5.26	5.21
Guanidine	Over 310	0.10	...	...	13.70	13.78
Semicarbazide[k]	205–215	Very sol.	...	...	13.00	4.80 ?

[a] All the salts formed are monosulfonates, unless designated by (di), (tri), etc. Melting points were taken with an enclosed thermometer and uncorrected. [b] The compound persistently forms an oil which requires low temperature and long standing to crystallize. [c] The salt separated as an oil which later crystallized. Recrystallization was from a saturated alcohol solution at 35°. [d] Tends to form an oil which slowly crystallizes. [e] The equivalent of aqueous sulfonic acid was added with vigorous shaking to the pure amine because latter would not readily dissolve in HCl. [f] Decomposition starts at 225° but the compound melts at 252–254°. [g] Decomposition starts at 260° (appar.) but compound melts at 285°. [h] The salt appears to melt and resolidify at 203°. There is no evidence of melting or charring up to 300°. [i] These salts gave consistently low Dumas nitrogen analyses due to excessive carbonization during combustion. [j] The large melting range could not be improved by repeated crystallization from aqueous alcohol. [k] The sulfonate salt was very soluble and on chilling seemed to become contaminated by coprecipitation of dibenzofuran-2-sulfonic acid. Its analysis was consistently low for nitrogen.

could not be separated; semicarbazide appeared to precipitate as the salt (very soluble) but its analysis was consistently bad; guanidine formed an extremely insoluble salt which was very high melting.

Preparation of 3-Nitrodibenzofuran-8-sulfonic Acid and Its Salts.—Dibenzofuran, recrystallized from 95% ethanol and melting at 87°, was nitrated in acetic acid solution by addition of concentrated nitric acid, using the procedure of Gilman.[4] The yellow 3-nitrodibenzofuran melting at 181° was submitted to sulfonation by action of concentrated sulfuric acid at 100° for a 30-minute period. Results of varying the ratio of sulfuric acid to 3-nitrodibenzofuran are shown in Table II.

Experiment 4 represents the conditions originally prescribed by Borsche and Schacke.[5] Smaller amounts of sulfuric acid than specified in expt. 1 were not suitable since then some of the nitro compound failed to dissolve. The conditions in 1 were adopted for all further production of the acid.

TABLE II

SULFONATION OF 3-NITRODIBENZOFURAN AT 100° FOR 30 MINUTES

	3-Nitro cpd., g.	96% Sulfuric acid G.	96% Sulfuric acid Mole	Yield of acid, g.	Per cent. of theory
1	10.0 (0.047 mole)	25.0	0.24	7.5	55.3
2	10.0	50.0	0.48	5.1	38.3
3	10.0	75.0	0.72	5.0	36.2
4	10.0	100.0	0.96	4.0	29.8

As the reaction proceeds the solution becomes bright orange colored: after about 15 minutes the 8-sulfonic acid begins to precipitate. It filters readily from the acid solution, redissolves in hot water and precipitates by chilling. However, this reprecipitated product is virtually unfilter-

TABLE III

3-NITRODIBENZOFURAN-8-SULFONIC ACID AND ITS AMINE SALTS

		Free acid	Salts of the free acid 2 Aniline	3 *p*-Toluidine	4 *p*-Bromoaniline	5 Urea
M.p., °C.		Chars 240	258–260 dec.	250 dec.	258–266 dec.	Over 300 dec.
Neut. equiv.	Calcd.	293.2				
	Found	296.3, 296, 294.2				
N, %	Calcd.	4.78				
	Found	4.80, 5.0				
S, %	Calcd.	10.93	8.30	8.01	6.89	9.07
	Found	10.72	8.25	8.04	6.82	9.18
		10.62	8.40			

TABLE IV

AMINO ACID SALTS OF 3-NITRODIBENZOFURAN-8-SULFONIC ACID

Amino acid	M.p., °C.	Sulfur, % Calcd.	Found
1-Arginine (di)[a]	235–236	8.43	7.98
Creatinine	258	7.89	7.82
1-Cysteine	219	15.47	15.60
1-Cystine (di)	215	15.50	15.70
1-Histidine (di)	248	8.65	8.59
dl-Iso-leucine	246	7.55	7.21
dl-Phenyl-alanine	247	7.00	7.01
l-Leucine	260–262 dec.	7.55	7.58

dl-alanine, α-aminoisobutyric acid, *dl*-lysine, *dl*-methionine, *dl*-norleucine, *dl*-tryptophan[b] and *dl*-valine formed salts which decomposed without melting in the high range of 250–300°

Glycine, aspartic and glutamic acids, tyrosine, proline and hydroxyproline, threonine, asparagine and serine all failed to precipitate from solution upon addition of the nitrosulfonic acid

[a] All salts were monosulfonates except those marked (di). [b] The tryptophan salt of the acid has a brilliant yellow coloration, which may have diagnostic significance; the others were nearly white or pale yellow.

able and very difficult to dry (indications being that it undergoes some hydrolysis of the sulfonic acid group due to the water present). Consequently the crude product was crystallized from glacial acetic acid. Three crystallizations gave a yellow product which could be dried suitably in a vacuum oven at 70°; it had no definite melting point but charred in the region of 240°. Of the analytical values the neutral equivalent seemed to be most reliable (calcd. 293; found 294 to 297).

This acid was tested as an agent for amines and amino acids, the procedure used being the same as given above. The results are given in Table III which lists properties of the free acid and its salts.

Although the analytical values for the acid itself leave something to be desired, the preparation and analysis of the four additional salts 2, 3, 4 and 5 (which crystallize nicely from ethanol) seem to confirm the constitution of the acid.

The acid is soluble in water, methyl and ethyl alcohols, and insoluble in ether, benzene and other non-polar solvents. It precipitates many metal ions from dilute aqueous solutions, *e.g.*, Ag^+, Cu^{+2}, Mg^{+2}, Ca^{+2}, Zn^{+2}, Al^{+3}, Pb^{+2}, Cr^{+3}, Mn^{+2}, Ni^{+2}, Fe^{+2}, Fe^{+3}, Co^{+2}, Sn^{+2} and Ba^{+2}. The sodium and potassium salts of the nitro acid seem to be more soluble than those from dibenzofuran-2-sulfuric acid itself, but quantitative studies were not made.

Although the ammonium salt of dibenzofuran-2-sulfonic acid is crystalline, the addition of ammonium hydroxide to an aqueous solution of 3-nitro acid gave a slimy stringy mass that resembled a thick soap curd. This curious behavior confirmed the considerable difference in solution characteristics of the two acids.

Twenty-four amino acids were tested for precipitability by 3-nitrodibenzofuran-8-sulfonic acid by the same procedure as given above. Table IV lists the results obtained on the salts.

Since the nitrosulfonic acid failed to precipitate nine of the twenty-four amino acids tested, and under the same conditions dibenzofuran-2-sulfonic acid failed in but three cases (7), the advantage of the latter is obvious.

Although the study of the 3-nitro acid was extended to other amines (salt of *n*-butylamine melted 264°, di-*n*-butylamine 167°, diphenylguanidine 225°) the salts formed in many cases showed decomposition without characteristic melting, hence offered little promise for inclusion in this particular study.

Acknowledgment.—A considerable part of this work was done under a research grant from the Research Corporation of New York to whom we express sincere gratitude.

SCHOOL OF CHEMICAL TECHNOLOGY
NORTH DAKOTA STATE COLLEGE
FARGO, NORTH DAKOTA

2-Hydroxymethyl-5-hydroxy-6-acetyl-4-pyrone

BY L. L. WOODS[1]

RECEIVED MARCH 2, 1953

In a previous communication,[2] the attempted synthesis of 2-hydroxymethyl-5-hydroxy-6-acetyl-4-pyrone (6-acetylkojic acid) was reported, but a clean-cut reaction was not obtained and an erroneous conclusion as to the nature of the reaction product was made. This was pointed out by Hurd and Sims.[3] However, their confirmation of the fact that kojic acid does react with acetic anhydride under controlled conditions to form a dark mixture which solidifies only upon aging stimulated our further interest in this acetylation, for such behavior could not be attributed to kojic acid diacetate and can only be accounted for by the formation of other substances along with the

---

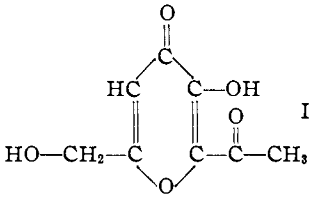
[1] The author wishes to acknowledge the financial assistance given this investigation by the Research Corporation. The kojic acid was furnished through the courtesy of the Corn Products Company.

[2] L. L. Woods, THIS JOURNAL, **70**, 2608 (1948).

[3] C. D. Hurd and R. J. Sims, *ibid.*, **71**, 2440 (1949).

kojic diacetate. Hurd's description of the purification of the reaction product clearly indicates that there is considerable contamination and that kojic acid diacetate is obtained pure only by removing some substance which is considerably more soluble in alcohol. The compound thus removed may have been the desired ketone. Therefore, it was decided that the conditions for creating 6-acetylkojic acid as the major constituent of the reaction product would not be drastically different from those given previously.

Subsequent experiments, which are described in this report, indicate that it is possible to produce 6-acetylkojic acid (I) from kojic acid and acetic anhydride by effecting certain changes in the procedure given originally.[2]



I

Experimental[4]

A mixture consisting of 28.4 g. of kojic acid and 30 g. of 85% phosphoric acid was heated until practically all the kojic acid had dissolved, placed in an oil-bath at 150° and treated with 40.8 g. of acetic anhydride added slowly from a separatory funnel.

The reaction was allowed to proceed at 150° for 10 hours; following which the excess acetic acid and acetic anhydride was removed under reduced pressure until the flask was heavily fogged with the subliming product. After diluting with water and cooling in the ice chest, the product was collected as brown-purple aggregates, 24.7 g. Extraction of the filtrate with ethyl acetate gave an additional 4.2 g.

A sample of the crude material from the ethyl acetate was recrystallized from absolute ethanol and sublimed to a white powder. The compound gave a red coloration with ferric chloride solution, m.p. 119–120°. Treating the brown-purple crystals in a similar manner gave the same substance believed to be principally 2-acetoxymethyl-5-hydroxy-6-acetyl-4-pyrone.

Anal. Calcd. for $C_{10}H_{10}O_6$: C, 53.10; H, 4.32. Found: C, 52.60; H. 4.60.

Hydrolysis of the above mixture was effected by boiling 21 g. with 100 ml. of water for 24 hours. The solution was cooled, treated with charcoal, and filtered. Upon evaporation of the solution to dryness, 16 g. of crude dark brown 6-acetylkojic acid was obtained.

The analytical sample was obtained by sublimation of the impure ketone to a cream colored powder, m.p. 156.5°.

Anal. Calcd. for $C_8H_8O_5$: C, 52.20; H, 4.34. Found: C, 52.21; H, 4.50.

Its infrared spectra (nujol mull) show a sharp absorption band in the C=O region at 1720 cm.$^{-1}$. Another band at 1230 cm.$^{-1}$ may be attributed to the fact that pyrones may be considered to be ester vinylogs.[5] Recently, Zeiss and Tsutsui[6] have shown that the $R_2C{=}C{-}O$ group gives an absorption band at about 1250 cm.$^{-1}$. A $-\overset{\overset{O}{\|}}{C}-C{=}C{-}O$ group, typical of pyrones, should give a similar absorption band, somewhat displaced.

Five grams of crude 6-acetylkojic acid was treated with 10 ml. of acetic anhydride, diluted with 100 ml. of water, and the free acetic acid neutralized with sodium bicarbonate. Extracting the neutral solution with benzene produced 4.8 g. of the completely acetylated compound. The crystals were yellow prisms which when recrystallized twice from benzene gave a m.p. of 98–99°. A sublimed sample gave the same melting point.

Anal. Calcd. for $C_{12}H_{12}O_7$: C, 53.73; H, 4.47. Found: C, 53.90; H, 4.78.

When 6-acetylkojic acid was permitted to react with thionyl chloride, treated with water, and the product recrystallized from benzene, 2-chloromethyl-5-hydroxy-6-acetyl-4-pyrone was formed which gave a strong red purple coloration with ferric chloride and a m.p. of 163–164°.

Anal. Calcd. for $C_8H_7C_4Cl$: C, 47.41; H, 3.45. Found: C, 47.14; H, 3.59.

A small amount of 6-acetylkojic acid (1 g.) was dissolved in 10 ml. of water, treated with 10 drops of acetic acid and 40 drops of phenylhydrazine, heated at reflux for 10 minutes, treated with charcoal and filtered while boiling hot. A clear orange solution was obtained which upon cooling deposited a red substance, m.p. 68–70°.

The analytical results indicate clearly that two molecules of phenylhydrazine have combined with the acetyl compound.

Anal. Calcd. for $C_{20}H_{18}N_4O_2$: N, 16.18. Found: N, 16.07, 16.20.

Consistent results were not obtained using 2,4-dinitrophenylhydrazine. The nitrogen content of the product was always high (22–24%) but always less than that for the pure 2,4-dinitrophenylhydrazine and slightly less than for its hydrochloride.

Fifteen grams of 6-acetylkojic acid was subjected to the conditions of the Clemmensen reduction for six hours following which the solution was diluted with an equal quantity of water and then extracted with ethyl acetate. The solvent layer was washed twice with water. Upon evaporation of the solvent, 3.3 g. of the reduced compound was obtained.

Sublimation of a portion of the sample gave white needles, m.p. 147–149°.

Anal. Calcd. for $C_8H_{10}O_4$: C, 56.47; H, 5.88. Found: C, 56.57; H, 5.69.

The compound gave a dark red coloration with dilute ferric chloride solution.

TEXAS SOUTHERN UNIVERSITY
HOUSTON, TEXAS

---

(4) Analyses were performed by Dr. Carl Tiedcke, Teaneck, New Jersey, and Clark Micro-analytical Laboratory, Urbana, Illinois. All melting points were determined on a Fisher-Johns melting point assembly. Infrared spectrograms were furnished through the courtesy of Samuel P. Sadtler and Son, Philadelphia, Pennsylvania.

(5) L. F. Cavalieri, *Chem. Revs.*, **41**, 525 (1947).

(6) H. H. Zeiss and M. Tsutsui, THIS JOURNAL, **75**, 897 (1953).