The acid amide was boiled under reflux with thirty parts of a 20% alcoholic solution of potassium hydroxide for three hours. The alcohol was replaced by water and evaporated, and the 4-methoxydibenzofuran-1-acetic acid was precipitated from the filtered solution. It was recrystallized from ethanol and appeared as colorless needles, m. p. 223–224°. The yield was 90%.

Anal. Calcd. for $C_{15}H_{12}O_4$: C, 70.28; H, 4.73. Found: C, 70.31; H, 4.43.

UNIVERSITY, VIRGINIA RECEIVED NOVEMBER 21, 1939

The Preparation of Acetyl Bromide*

BY THEODORE M. BURTON WITH ED. F. DEGERING

Acetyl bromide was prepared as early as 1863 by distilling it as formed from a mixture of glacial acetic acid, bromine and phosphorus.[1]

Investigations have shown, however, that acetyl bromide undergoes substitution with bromine to form bromo-acetyl bromides with decrease in the yield of acetyl bromide. Further improvements designed to increase the yield of acetyl bromide have also resulted in increased bromination in the nucleus.[2]

By the elimination of free bromine it was thought possible to increase the yield of acetyl bromide according to the reaction

$$3CH_3CO_2H + PBr_3 \longrightarrow 3CH_3COBr + P(OH)_3$$

Phosphorus tribromide (b. p. 169–170° at 740 mm.) can be prepared readily in 99.5% yield by slowly adding dried bromine from a dropping funnel into a slight excess of freshly washed and dried red phosphorus placed in a round-bottomed flask equipped with a mechanical stirrer and a reflux condenser.

The acetyl bromide was prepared by adding slowly through the dropping funnel, with stirring, a slight excess of 99.5% glacial acetic acid (3.075 moles of CH_3COOH per mole of phosphorus tribromide) to the cold phosphorus tribromide. The mixture separated into two layers which were distilled separately into a common receiver packed in ice. The crude acetyl bromide was rectified in a modified Podbielniak column to produce a water-white fraction boiling from 73–76° at 740 mm. The yield varied from 71.4 to 73.4% of the theoretical.

In other experiments the phosphorus tribromide was purified before use, but yields were increased only by a slight amount to 74.9% of the theoretical. In an effort to test the effect of temperature, the acetyl bromide was distilled from the reaction mixture at room temperature under reduced pressure. The product was collected in a gas bottle immersed in a bath cooled with solid carbon dioxide. No change, however, was observed in the yield. In all cases large amounts of hydrogen bromide were liberated so that the reaction probably does not proceed as indicated in the above equation.

It was found possible to prepare acetyl bromide without the formation of hydrogen bromide by adding phosphorus tribromide slowly, with stirring, to an excess of boiling acetic anhydride. The boiling point dropped as acetyl bromide was formed and when the addition of phosphorus tribromide was completed, the acetyl bromide was distilled from the mixture and rectified as before. The yield was 81.7% of the theoretical.

By using the readily prepared phosphorus tribromide, instead of free bromine with glacial acetic acid, substitution reactions are avoided and the yield of acetyl bromide can be increased to about 80% of the theoretical.

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Hydrogen Bonds Involving the C–H Link. IX.[1] Nitriles and Dinitriles as Solvents for Hydrogen Containing Halogenated Methanes

BY M. J. COPLEY, G. F. ZELLHOEFER AND C. S. MARVEL

Nitriles should be capable of bonding with hydrogen in halogenated methanes of the CH_2X_2 and CHX_3 types and hence should be good solvents for these products. Work reported earlier[1] shows that valeronitrile and benzonitrile do dissolve methylene chloride and monochlorodifluoromethane in excess of the amount calculated from Raoult's law. It is interesting to find that the aliphatic dinitriles, succinonitrile and glutaronitrile, dissolve less than the calculated amounts of these two halogenated methanes. Adiponitrile dissolves almost the exact calculated amount and sebaconitrile takes up more than the calculated amount. These results are interesting when considered with the boiling points of the dinitriles.

*Presented before the Indiana Academy of Science at Terre Haute, Indiana, November, 1939.

(1) H. Gal, *Ann.*, **129**, 53 (1863); M. Hanriot, *Ann. chim. phys.*, [5] **17**, 83 (1879).

(2) H. Gal, *Compt. rend.*, **56**, 1258 (1863); F. Urech, *Ber.*, **13**, 1687 (1880); J. Volhard, *Ann.*, **242**, 144 (1887); C. Hell, *Ber.*, **21**, 1726 (1888); C. F. Ward, *J. Chem. Soc.*, **123**, 2207–2213 (1923); H. B. Watson, *ibid.*, **127**, 2067–2082 (1925); Bernard Gwynn and Ed. F. Degering, *Proc. Indiana Acad. Sci.*, **87** (1939).

(1) For the eighth communication in this series see THIS JOURNAL, **61**, 3550 (1939).

TABLE I

SOLUBILITY OF HALOGENATED METHANES IN NITRILES

Theoretical solubility	Formula	B. p., °C.	CH_2Cl_2 G./g.	CH_2Cl_2 M. F., 0.311	$CHCl_2F$ G./g.	$CHCl_2F$ M. F., 0.381
Caprylonitrile	$CH_3(CH_2)_6CN$	198–200	0.462	0.405	0.875	0.420
Benzonitrile	C_6H_5CN	190.7	.463	.359	See Ref. 1	
Succinonitrile	$CN(CH_2)_2CN$	265–267	.199	.158	.231	.152
Glutaronitrile	$CN(CH_2)_3CN$	285–287	.319	.261	.457	.294
Adiponitrile	$CN(CH_2)_4CN$	295	.364	.316	.560	.428
Sebaconitrile	$CN(CH_2)_8CN$	199–200 (15 mm.)	.425	.435	.730	.522

It is obvious that succinonitrile and glutaronitrile are associated to a considerable extent; this undoubtedly is due to bonding between hydrogens of the methylene groups and the nitrogen atom of the nitrile groups. In succinonitrile the —CH_2— group is alpha to one nitrile residue and beta to another and the cumulative effect is sufficient to give labile hydrogen atoms. In glutaronitrile the further separation of the nitrile groups makes their cumulative effect less on each —CH_2— group. In adiponitrile this effect is fairly well overcome by the distance between the nitrile groups. In sebaconitrile the solubility goes above the calculated value but not as much as might have been expected from the solubility of the mononitriles. This evidence for hydrogen bond association in the dinitriles is of interest in view of the recent estimation that hydrogen cyanide is similarly associated to the extent of 3% at the boiling point.[2]

The solubility determinations were made at 32.2° as described earlier[3] and are reported in the table.

(2) Giauque and Ruehrwein, THIS JOURNAL, **61**, 2626 (1939).
(3) Zellhoefer, *Ind. Eng. Chem.*, **29**, 584 (1937).

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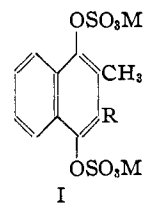
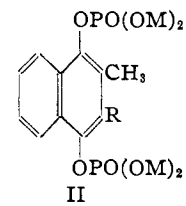
Water-Soluble Antihemorrhagic Esters

BY LOUIS F. FIESER AND EDWARD M. FRY

As a possible means of providing antihemorrhagic compounds which can be administered parenterally in a small volume of aqueous solution, we have prepared a series of water-soluble sulfuric and phosphoric acid ester derivatives of vitamin K_1 and of other quinones of established vitamin K activity. In chick assays conducted by Dr. W. L. Sampson potassium vitamin K_1 hydroquinone disulfate (I, R = phytyl, M = K) was found inactive at a dosage of 500 γ, an observation which perhaps finds a counterpart in the great loss of biological activity attending the conversion of oestrone into oestrone sulfate.[1] Similarly sodium 2,3-dimethyl-1,4-naphthohydroquinone disulfate was inactive at the same high dosage, in contrast to the corresponding quinone which is active at 50 γ. On the other hand, vitamin K_1 hydro-



I



II

quinone diphosphoric acid II (R = phytyl, M = H) shows activity at dosages down to 25 γ, but not at 10 γ, and thus does not fall greatly short of vitamin K_1, which gives a response at 1.5–2 γ by the same procedure. Still more potent is the sodium salt of 2-methyl-1,4-naphthohydroquinone disulfuric acid (I, R = H, M = Na), which shows antihemorrhagic activity at a level of 2 γ (assays at lower dosages are still to be made). The substance crystallizes as a dihydrate, and if the administered material undergoes hydrolysis it could give rise to only 52% of its weight of 2-methyl-1,4-naphthoquinone.

Of the water-soluble substances previously suggested for use in vitamin K therapy, phthiocol[2] suffers from being only weakly active, and free naphthohydroquinone and aminonaphthol derivatives[3] are highly sensitive to oxidation. The above active ester derivatives are colorless solids which are stable in aqueous solution and not sensitive to air or light. Furthermore, 2-methyl-3-phytyl-1,4-naphthohydroquinone diphosphoric acid can be described as a water-soluble form of vitamin K_1.

In a clinical trial conducted by Drs. H. A. Frank, A. Hurwitz and A. M. Seligman at the

(1) Butenandt and Hofstetter, *Z. physiol. Chem.*, **259**, 222 (1939).
(2) Almquist and Klose, THIS JOURNAL, **61**, 1923 (1939).
(3) Doisy, *et al.*, *ibid.*, **61**, 1932, 2563 (1939).