[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, ST. LOUIS UNIVERSITY]

The Preparation and Properties of Some Furfuryl Quaternary Ammonium Compounds[1,2]

BY EARL A. WEILMUENSTER[3] AND CHAS. N. JORDAN

In 1938 Nabenhauer[4] obtained a patent on some dimethyl alkyl furfuryl ammonium salts in which the alkyl groups were the short chain radicals, methyl, ethyl, *n*-propyl, isopropyl, *n*-butyl and *n*-amyl. It was claimed that these compounds have therapeutic value in that they exert cholinergic or muscarinic properties and stimulate the neuro-muscular mechanism through the parasympathetic nervous system. Alkyl(C_8-C_{18})dimethylbenzylammonium chlorides had previously been shown by Domagh[5] to possess marked germicidal properties. In view of the fact that certain types of long chain quaternary compounds are known to have a considerable effect in lowering surface tension while some have bactericidal properties, our work was undertaken with the idea of extending the furfuryl compounds and particularly to compare the influence of replacing the benzyl group on germicidal and physical properties.

TABLE I

DATA ON SOME DIMETHYLALKYLFURFURYLAMMONIUM IODIDES

Alkyl	Reaction time, hr.	Yield, %	Melting point, °C.	Analyses, % Iodine Calcd.	Iodine Found	Nitrogen Calcd.	Nitrogen Found
Methyl	1	96[a]	116–117	47.56	47.55	5.24	5.33
Ethyl	1	97[a]	103–104	45.19	45.10	4.98	5.15
Propyl	4	95[a]	107–108	43.05	43.13	4.75	4.86
i-Propyl	8	89[a]	150–151	43.05	43.10	4.75	4.80
Butyl	8	97[a]	110–111	41.10	41.07	4.53	4.56
i-Butyl	8	91[a]	114–115	41.10	41.08	4.53	4.64
Amyl	12	91[b]	108–109	39.31	39.25	4.33	3.91
i-Amyl	12	90[b]	115	39.31	39.27	4.33	4.33
Hexyl	12	98[b]	74–75	37.68	37.67	4.15	4.08
Heptyl	12	93[b]	66–67	36.18	36.19	3.98	3.86
Octyl	12	..[b]	Oil	34.79	...	3.83	..
Nonyl	12	..[b]	Oil	33.51	...	3.69	..
Decyl	12	93[b]	46–50	32.57	32.35	3.56	3.45
Undecyl	12	94[b]	55–57	31.20	31.04	3.44	3.42
Lauryl	12	98[b]	58–60	30.16	30.23	3.32	3.28
Myricyl	12	98[b]	74–76	28.28	28.26	3.12	3.10
Cetyl	12	98[b]	80–82	26.62	26.42	2.97	2.64
Octadecyl	22	98[b]	97–99	25.10	25.07	2.63	2.48

[a] Crystallized from ethanol–ethyl acetate. [b] Crystallized from ethanol–petroleum ether.

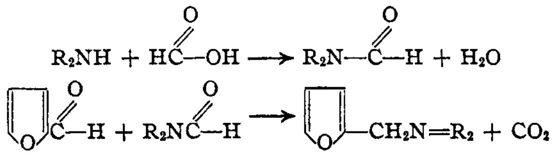
TABLE II

DATA ON SOME DIETHYLALKYLFURFURYLAMMONIUM IODIDES

Alkyl	Reaction time, hr.	Yield, %	Crystallization solvent	Melting point, °C.	Analyses, % Iodine Calcd.	Iodine Found	Nitrogen Calcd.	Nitrogen Found
Methyl	2	98[a]	EtOH–EtOAc	124–125	43.05	43.01	4.74	4.83
Ethyl	3	98[a]	EtOH–EtOAc	137	41.10	41.12	4.53	4.59
Propyl	8	88[a]	EtOH–EtOAc	147–148	39.31	38.34	4.33	4.38
Butyl	16	70[a]	EtOH–EtOAc	128–129	37.68	37.64	4.15	3.90
Amyl	24	70[b]	EtOH–Pet. ether	83 (impure)	36.18	...	3.98	..
Hexyl	24	...	....	Oil	34.79	...	3.83	..
Heptyl	24	...	....	Oil	33.51	...	3.69	..
Octyl	24	...	....	Oil	32.57	...	3.56	..
Nonyl	24	...	....	Oil	31.20	...	3.44	..
Decyl	24	...	....	Oil	30.16	...	3.32	..
Undecyl	24	...	....	Oil	29.42	...	3.21	..
Lauryl	24	77[b]	EtOH–Pet. ether	65–67	28.28	28.10	3.12	3.05
Myricyl	24	70[b]	EtOH–Pet. ether	72–74	26.62	26.55	2.93	2.85
Cetyl	24	74[b]	EtOH–Pet. ether	79–81	25.10	25.25	2.77	2.71
Octadecyl	24	79[b]	EtOH–Pet. ether	91–93	23.82	23.73	2.62	2.63

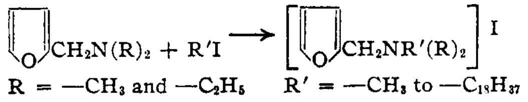
[a] Crystallized from ethanol–ethyl acetate. [b] Crystallized from ethanol–petroleum ether.

The best method of synthesis proved to be through furfuryl dialkyl amines which can be made in fair yields by the Leuckart synthesis.[6] The course of the reaction may be illustrated as



$$R_2NH + HC(=O)—OH \longrightarrow R_2N—C(=O)—H + H_2O$$

In our studies only N,N-dimethylfurfurylamine and N,N-diethylfurfurylamine were used. These amines reacted with alkyl iodides to give quaternary salts.



R = —CH_3 and —C_2H_5 R′ = —CH_3 to —$C_{18}H_{37}$

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(1) Presented at the Detroit meeting of the American Chemical Society in April, 1943.

(2) From the Ph.D. dissertation of Earl A. Weilmuenster.

(3) Present address, Cleveland Industrial Research, Inc., Cleveland, Ohio.

(4) U. S. Patent 2,185,220.

(5) Domagh, *Deut. Med. Woch.*, **61**, 829 (1935).

(6) Leuckart and Janssen, *Ber.*, **18**, 2341 (1885); **22**, 1409 (1889).

Experimental

Preparation of Amines: N,N-Dimethylfurfurylamine and N,N-Diethylfurfurylamine.—One mole of the desired dialkyl amine (dimethylamine and diethylamine), liberated from the corresponding hydrochloride, was bubbled slowly with stirring into one mole of formic acid (87%, sp. gr. 1.20) in the cold. The mixture was then distilled up to a temperature of 135°, the residues being for the most part crude N,N-dimethylformamide and N,N-diethylformamide. The residue in each case was placed in a one-liter round-bottom flask. One-fifth of a mole of furfural was added slowly over a period of thirty minutes. The mixture was heated under reflux on an oil-bath at a temperature of 150–170° for three to four hours, at which time the reaction had subsided. The mixture was cooled and diluted with 200 ml. of water, made strongly alkaline with sodium hydroxide and distilled until all volatile substances were carried over by the steam. The residue was then steam distilled, the volatile dimethylfurfurylamine in the one case and diethylfurfurylamine in the other distilling over. The distillate was then treated with strong alkali and extracted with ether. The ether-base mixture was dried over solid sodium hydroxide. The ether was removed by distillation. The resulting di-alkylfurfurylamine was purified by distillation. For dimethylfurfurylamine: b. p. 142–145°[7]; yield 20.5 g. (85%). For diethylfurfurylamine; b. p. 169–172°; yield 20 g. (68%). The corresponding picrates of the above amines were prepared as suitable derivatives. Dimethylfurfurylamine picrate, m. p. 102–103°. *Anal.* Calcd. for $C_{13}H_{14}N_4O_8$: N, 15.82. Found: N, 15.71. Diethylfurfurylamine picrate, m. p. 84–85°. *Anal.* Calcd. for $C_{15}H_{18}N_4O_8$: N, 14.66. Found: N, 14.55.

Preparation of Trialkylfurfurylammonium Iodides.—Dimethylalkylfurfurylammonium iodides and diethylalkylfurfurylammonium iodides were prepared by the following general method. The alkyl group varied from methyl to stearyl inclusive. To 0.02 mole of the dialkylfurfurylamine, in a 25-ml. round-bottom flask equipped with condenser, was added 0.02 mole of the appropriate alkyl iodide. The mixture was heated at 40–100° for one to twenty-four hours, depending on the volatility and reactivity of the allyl iodide in question. The tri-alkylfurfurylammonium iodides obtained in good yields (av. 95%) were recrystallized from absolute alcohol–ethyl acetate or absolute alcohol–petroleum ether (see table).

Summary

1. Dimethylfurfurylamine and diethylfurfurylamine were prepared. The corresponding picrates were prepared as suitable derivatives of these amines.

2. A series of dimethylalkylfurfurylammonium iodides and of diethylalkylfurfurylammonium iodides were prepared.

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[7] All temperatures listed are corrected.

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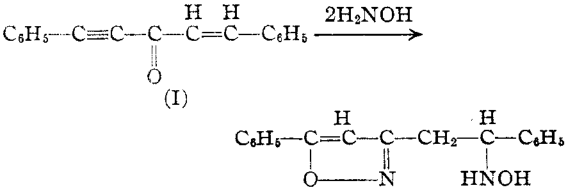
The Synthesis of Acetylenic Ketones from Acid Anhydrides and Sodium Phenylacetylene

BY DOROTHY NIGHTINGALE AND FRANCIS WADSWORTH[1,2]

This investigation was undertaken preliminary to a problem requiring acetylenic ketones in large amounts. The reaction of sodium phenylacetylene with low molecular weight acid chlorides[3] is troublesome and yields are variable. Ethyl phenylpropiolate for use with a Grignard reagent as described by Hurd and Cohen[4] is not readily available. Kroeger and Nieuwland[5] reported a 40–45% yield of phenylethynyl methyl ketone from phenylethynylmagnesium chloride and acetic anhydride, but all attempts in this Laboratory to prepare the ketone by this method, either by adding the anhydride to the Grignard reagent or *vice versa*, have resulted only in bis-phenylethynylmethylcarbinol.

Sodium phenylacetylene reacts smoothly with acid anhydrides and gives consistently better yields of ketone than do the corresponding acid chlorides. Nef[3] reports a satisfactory yield of ketone from acetic anhydride but apparently the use of anhydrides in this reaction has not been extended.

The product (I) of the reaction of sodium phenylacetylene with cinnamic anhydride differs markedly in its properties from the cinnamoylphenylacetylene reported by Worrall.[6] (I) has the composition required for cinnamoylphenylacetylene and reacts with hydroxylamine hydrochloride presumably as follows



(I)

(I) gives a dark red color with cold concentrated sulfuric acid rather than the purple color produced with Worrall's compound, and the sulfuric acid solution has only a slight fluorescence. Our ketone (I) does not give a color with Folin's reagent whereas Worrall's compound gives a positive test at once. The properties listed by Worrall for his compound, notably its behavior with the Grignard reagent and the fact that it does not react with hydroxylamine hydrochloride, are

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[1] Present address: Pan American Oil Company, Texas City, Texas.

[2] (a) Presented at the 105th meeting of the American Chemical Society, Detroit, Michigan, April, 1943. (b) Abstract of a portion of the dissertation to be submitted by Francis Wadsworth in partial fulfillment of the requirement for the degree of Doctor of Philosophy at the University of Missouri.

[3] Nef, *Ann.*, **308**, 275 (1903).

[4] Hurd and Cohen, THIS JOURNAL, **53**, 1068 (1931).

[5] Kroeger and Nieuwland, *ibid.*, **58**, 1861 (1936).

[6] Worrall, *ibid.*, **60**, 1266 (1938).