TABLE II

β-(DIALKYLAMINO)-ETHOXYETHYL p-AMINOBENZOATE MONO-HYDROCHLORIDES

No.	Compound	Color	M. p., °C.	Chlorine, % Calcd.	Chlorine, % Found
A	$p\text{-}H_2NC_6H_4CO_2CH_2CH_2OCH_2CH_2N(CH_3)_2\cdot HCl$	Greenish-yellow	150–152	12.28	12.28
B	$p\text{-}H_2NC_6H_4CO_2CH_2CH_2OCH_2CH_2N(C_2H_5)_2\cdot HCl$	Light yellow	150–152	11.21	11.24
C	$p\text{-}H_2NC_6H_4CO_2CH_2CH_2OCH_2CH_2N(C_3H_7)_2\cdot HCl$	Light yellow	128.5–130	10.30	10.32
D	$p\text{-}H_2NC_6H_4CO_2CH_2CH_2OCH_2CH_2N(C_4H_9)_2\cdot HCl$	Deep yellow	134–136	9.53	9.67

The results of the pharmacological study are summarized in Table III which also includes the data on novocaine and cocaine for comparison.

TABLE III

PHARMACOLOGICAL ACTION OF DIALKYLAMINOETHOXYETHYL p-AMINOBENZOATE MONO-HYDROCHLORIDES

Compound (see Table II)	Toxicity (intravenous mice) mg./kg.	Anesthesia (min.)		Irritation	
		Intracutaneous guinea pig	Rabbit cornea	Rabbit eye	Rabbit skin
A	55	13	None	None	None
B	55	31	20	None	None
C	25	26	16	None	None
D	10	40	43	None	Mild
Novocaine	40	24	None	None	None
Cocaine	17.5	41	20	None	None

Examination of the toxicity column in the above table shows that increasing the size of the alkyl group attached to nitrogen causes an increase in toxicity. This effect parallels that observed for novocaine analogs (formula I).[4] Anesthetic action also increased as the size of the alkyl group increased, although the increase is not a regular one. It is interesting that the dimethyl derivative did not cause topical anesthesia. The present data do not show the optimum size of the alkyl group since none of the compounds with groups larger than butyl could be obtained.

Summary

The monohydrochlorides of dialkylaminoethoxyethyl p-aminobenzoates of the general formula $(p)H_2NC_6H_4COOCH_2CH_2OCH_2CH_2NR_2$ have been prepared in which the R group has been varied from methyl to n-butyl. The toxicity and local anesthetic action of these compounds increased as the size of the alkyl group was increased.

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[4] Schmitz and Loevenhart, *J. Pharm. Exp. Therap.*, **24**, 159 (1924).

URBANA, ILLINOIS RECEIVED MAY 22, 1935

[CONTRIBUTION NO. 127 FROM THE MASSACHUSETTS INSTITUTE OF TECHNOLOGY, RESEARCH LABORATORY OF ORGANIC CHEMISTRY]

Pyrylium Derivatives by the Condensation of Saturated Ketones

BY TENNEY L. DAVIS AND CATHERINE BATES ARMSTRONG

In the preparation of *sym*-trianisylbenzene by the condensation of p-methoxyacetophenone under the influence of a mixture of concentrated sulfuric acid and potassium pyrosulfate by the method of Odell and Hines[1] we have found that about 11% of the material is converted into the desired product and another 11% of it into a bright scarlet crystalline material readily soluble in water to yield a strongly fluorescent solution. Colored material of similar appearance but of undetermined composition has been reported by Schneider and Seebach[2] as formed in condensations leading, under the influence of a sulfoacetic acid reagent, to *sym*-trianisylbenzene. We find that the colored salt is 2,4,6-trianisylpyrylium acid sulfate, a salt of the same base which Dilthey[3] prepared in the form of the chloride–ferric chloride double salt by the reaction of anisal-p-methoxyacetophenone with p-methoxyacetophenone in the presence of ferric chloride and acetic anhydride. Our substance yields a picrate and a chloroplatinate identical with those prepared from the salt produced by Dilthey's method.

When a pyrylium derivative is prepared by Dilthey's method, the product contains all of the carbon atoms which were present in the reagents; the ferric chloride acting as an oxidizing agent removes only hydrogen atoms. But when three molecules of p-methoxyacetophenone react to form one molecule of the pyrylium salt, one methyl group is lost. Since analysis does not distinguish sharply between a simple trianisylpyrylium salt and one which contains an additional methyl

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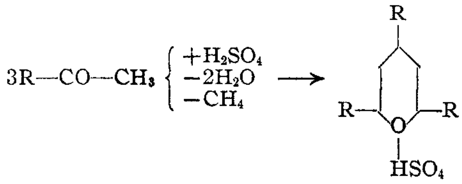
[1] Odell and Hines, THIS JOURNAL, **35**, 82 (1913).

[2] Schneider and Seebach, *Ber.*, **54**, 2298 (1921).

[3] Dilthey, *J. prakt. Chem.*, **94**, 53 (1916); **95**, 116 (1917).

group, we have prepared a 3-methyl-2,4,6-trianisylpyrylium salt by the method of Dilthey, characterized it by analysis of the picrate and chloroplatinate, and have found that the compounds differ from the corresponding derivatives of trianisylpyrylium. The results show that the methyl group has not migrated to a new position in the molecule but has actually been lost during the reaction.



The condensation of acetophenone in the presence of a mixture of concd. sulfuric acid and potassium pyrosulfate yields a yellow salt, 2,4,6-triphenylpyrylium acid sulfate, identified by comparison of the chloroplatinate with the chloroplatinate prepared from a salt procured by Dilthey's method. In this case, also, one methyl group is lost from three molecules of the methyl aryl ketone.

We have studied the reaction further in an effort to determine what happens to the methyl group, but have not been able to find any evidence of methane, methyl alcohol, formaldehyde, carbon monoxide, etc., or indeed any evidence that carbon in a volatile compound escapes from the reaction mixture.

Experiments

2,4,6-Trianisylpyrylium acid sulfate was prepared by warming together 25 g. of *p*-methoxyacetophenone, 52 g. of potassium pyrosulfate, and 4 g. of concd. sulfuric acid in a stoppered flask at 45° for twenty-four hours. The reaction mixture was recrystallized from glacial acetic acid, and the *sym*-trianisylbenzene extracted with hot xylene. The residue, recrystallized from water, yielded bright scarlet crystals of the acid sulfate, 11% of the theoretical. Similar results were obtained when the reaction mixture was not warmed but was allowed to stand in a stoppered flask at room temperature for several days.

2,4,6-Trianisylpyrylium Picrate.—The acid sulfate was dissolved in water, and the pyrane oxide precipitated by the addition of a small amount of sodium hydroxide. This was recrystallized from a mixture of alcohol and ether, taken up in ether, and treated with picric acid in excess. The picrate was recrystallized from alcohol, m. p. 283–284° (corr.).

A sample of the 2,4,6-trianisylpyrylium chloride–ferric chloride double salt, prepared by the method of Dilthey, was recrystallized from water, whereby it lost ferric chloride, and the resulting chloride was converted into the picrate in the same manner; m. p. 283–284° (corr.); mixed m. p. of the two picrates 283–284° (corr.).

2,4,6-Trianisylpyrylium chloroplatinate was prepared by adding an equivalent amount of chloroplatinic acid to a dilute acetone solution of the pyran oxide prepared from the acid sulfate. The precipitate was washed repeatedly with acetone and ether until constancy of melting point was attained; m. p. 258.5–259.5° (corr.) with decomposition.

Anal. Calcd. for $C_{52}H_{46}O_8PtCl_6$: Pt, 16.2. Found: Pt, 16.3, 16.4.

A chloroplatinate was prepared similarly from the chloride double salt procured by the procedure of Dilthey, m. p. 261.5–263.5° (corr.) with decomposition.

Anal. Calcd. for $C_{52}H_{46}O_8PtCl_6$: Pt, 16.2. Found: Pt, 16.3, 16.4.

The mixed m. p. of the two chloroplatinates was 257.5–263.5° (corr.) with decomposition.

3 - Methyl - 2,4,6 - trianisylpyrylium Picrate.—Anisal-*p*-methoxyacetophenone was prepared by mixing 10 g. of anisic aldehyde with 11 g. of *p*-methoxyacetophenone and pouring the mixture into a cold solution of 20 g. of 40% sodium hydroxide in 80 g. of alcohol. The precipitate which collected during a period of twenty minutes was recrystallized from alcohol. To a mixture of 5 g. of anisal-*p*-methoxyacetophenone and 3 g. of *p*-methoxypropiophenone, 6 g. of ferric chloride hydrate was added and then, in small portions at a time and with vigorous cooling, 20 cc. of acetic anhydride. The product, recrystallized from water, yielded 3-methyl-2,4,6-trianisylpyrylium chloride. The chloride was dissolved in water, the pyran oxide precipitated by alkali, dissolved in ether, and treated with picric acid in excess. The picrate was recrystallized from alcohol, m. p. 190.4–195° (corr.).

Anal. Calcd. for $C_{33}H_{27}O_{11}N_3$: N, 6.55. Found: N, 6.58, 6.44.

3-Methyl-2,4,6-trianisylpyrylium chloroplatinate was prepared by adding chloroplatinic acid to a dilute acetone solution of the pyran oxide. The product was washed with acetone and ether until impurities were removed; m. p. 239–240° (corr.) with decomposition.

Anal. Calcd. for $C_{54}H_{50}O_8PtCl_6$: Pt, 15.8. Found: Pt, 16.0, 16.1.

2,4,6-Triphenylpyrylium Chloroplatinate.—Acetophenone was treated with potassium pyrosulfate and concd. sulfuric acid, and the mixture was allowed to stand for several days at room temperature. The yellow salt was extracted with hot water, the liquid made alkaline, and extracted with ether. Chloroplatinic acid was added to the ether extract and the resulting chloroplatinate was purified by washing with acetone and ether, m. p. 244–245° (corr.) with decomposition.

A chloroplatinate, prepared from the 2,4,6-triphenylpyrylium salt procured by Dilthey's method from the reaction of acetophenone with benzalacetophenone, melted at 243–244° (corr.) with decomposition; mixed m. p. of the two chloroplatinates 244–245° (corr.) with decomposition.

Effort to Find Volatile Products.—The condensation of *p*-methoxyacetophenone to trianisylpyrylium acid sulfate was carried out in a vessel to which a dry-ice trap and a pneumatic trough were attached. A small amount of the ketone was condensed but no reaction product was collected either in the trap or at the trough. The reaction product was mixed with water, the water distilled, and the first fraction collected. Qualitative tests for methyl alcohol and for formaldehyde were negative. The same condensation was carried out in an all-glass system to which a mercury manometer was attached, but no rise in pressure was observed in the manometer during the progress of the reaction.

Summary

Acetophenone and *p*-methoxyacetophenone, in the presence of concentrated sulfuric acid and potassium pyrosulfate, yield 2,4,6-triarylpyrylium acid sulfates in yields about equal to those of the *sym*-triarylbenzenes which are produced at the same time.

In the formation of the pyrylium derivatives one methyl group is lost from three molecules of the methyl aryl ketone, but we have not been able to determine what happens to it or to find that any volatile compound of carbon is produced by the reaction.

CAMBRIDGE, MASS. RECEIVED JUNE 14, 1935

[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

The Use of the Concentration Cell in Quantitative Analysis. I. The Estimation of Small Amounts of Chloride in Salts

BY N. HOWELL FURMAN AND GEORGE W. LOW, JR.[1]

The application of the measurement of the e. m. f. of a concentration cell to problems of quantitative analysis appeared to the authors to offer possibilities of the development of an improved technique for the determination of amounts of certain substances ranging from minute traces to small percentages. The primary condition is that the substance to be determined shall be capable of affecting an electrode in a reversible manner.

We deal in this paper with a detailed illustration of the general method in its application to the estimation of small amounts of chloride which appear as impurities in salts. The technique is quite different from any previously used method and it gives results which are reproducible and satisfactory. The usual method for determining small amounts of chloride is the nephelometric procedure, and as has been frequently pointed out[2] this technique is not always satisfactory, especially in the presence of foreign salts. The electrometric procedure described in this paper, on the other hand, is just as applicable in the presence of foreign salts as in their absence.[3]

Theoretical.—The procedure consists in measuring the e. m. f. between two silver–silver chloride electrodes, one of which is dipping into a solution containing the unknown amount of chloride whereas the other dips into a solution containing the unknown amount of chloride *plus* a definite known amount of chloride which is added. Thus a concentration cell is set up, the e. m. f. of which is given by the following expression, at 25°

$$E = 0.0591 \log [f_1(x + a)/f_2(x)] \qquad (1)$$

where x is the molar concentration of the unknown amount of chloride, a the molar concentration of the known amount of chloride added, f_1 and f_2 the chloride ion activity coefficients in the respective sides and E the observed e. m. f. of the cell. The activity coefficients, f_1 and f_2, depend upon the total ionic strength of the solutions and in the present series of measurements the total ionic strength in each side of the concentration cell is practically identical so that $f_1 = f_2$. Equation 1 therefore becomes

$$E = 0.0591 \log [(x + a)/x] \qquad (2)$$

In these e. m. f. measurements there are two other factors besides activities which must be considered, namely, the liquid junction potential and the solubility of the electrodes. In the present series of measurements the conditions were regulated so that the liquid junction was entirely negligible. This was done by making the solutions into which the two silver–silver chloride electrodes dipped *identical* except for the fact that one side of the cell has chloride of concentration x and the other $x + a$. Now x varies from 10^{-5} to 10^{-3} M and a is 10^{-2} M; and the total ionic strength throughout the cell is at no time lower than 0.25 M and is usually much larger than this.

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[1] J. T. Baker Chemical Co. Fellow in Analytical Chemistry, 1933–1934.

[2] P. V. Wells, *Chem. Rev.*, **3**, 331 (1927); C. R. Johnson, *J. Phys. Chem.*, **35**, 2237 (1931).

[3] Iodides and bromides would be expected to interfere with the determination of chloride by this method.