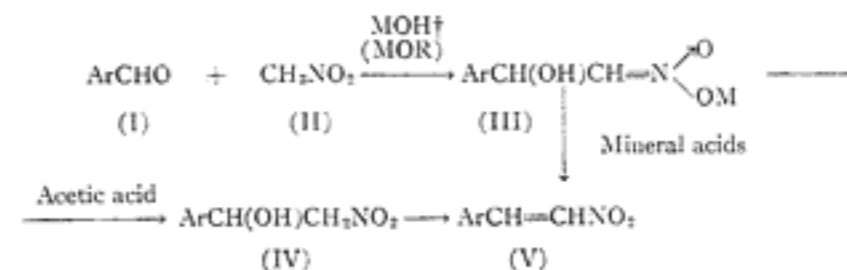


NOTES

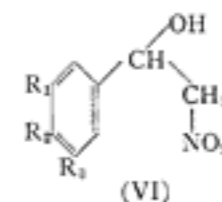
A NOTE ON THE PREPARATION OF SOME 1-PHENYL-2-NITROETHANOL DERIVATIVES

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It has been known for many years that aromatic aldehydes (I) and nitromethane (II) will undergo a condensation reaction, under alkaline conditions, to yield the alkali metal derivatives of the *aci*-form of the monohydric nitroalcohols (III). The free nitroalcohols (IV) can be liberated on acidification of the alkali metal derivative with acetic acid; however, the products will often dehydrate with extreme ease to form the corresponding ω -nitrostyrenes (V), unless certain precautions are taken (cf. ref. 1).



In this laboratory, we have been primarily interested in obtaining certain alkyl, acyl, and aroyl derivatives of 1-(3,4-dihydroxyphenyl)-2-nitroethanol and 1-(3,4,5-trihydroxyphenyl)-2-nitroethanol. A few of these nitroalcohols had previously been described in the literature namely: 3,4-methylenedioxy- α -nitromethylbenzyl alcohol (VI: $R_1 + R_2 = \text{OCH}_2\text{O}$; $R_3 = \text{H}$) (2, 3, 4, 5); 3,4-diacetoxy- α -nitromethylbenzyl alcohol (VI: $R_1 = R_2 =$



OCOCH_3 ; $R_3 = \text{H}$) (6); and 4-benzyloxy-3-methoxy- α -nitromethylbenzyl alcohol (VI: $R_1 = \text{OCH}_3$; $R_2 = \text{OCH}_2\text{C}_6\text{H}_5$; $R_3 = \text{H}$) (7). The 3,4-diacetoxy derivative was obtained using aqueous sodium bicarbonate as the condensing agent (6); however, the other nitroalcohols were prepared either using sodium methoxide under anhydrous conditions or aqueous alcoholic potassium hydroxide to effect the condensation (1, 2, 3, 4, 5, 7).

Some of the aforementioned procedures are rather tedious to carry out and this note reports a rapid and simple method for preparing nitroalcohols of this general type in good yield. The procedure involves the condensation of a suitable aldehyde with excess nitromethane at about 5° in the presence of sodium hydroxide in aqueous alcoholic solution. The optimum reaction time, which was of very short duration (> 3 minutes), varied from case to case and was determined empirically.

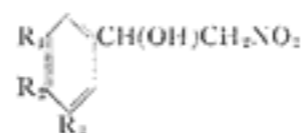
As well as the nitroalcohols mentioned above, the following new 1-phenyl-2-nitroethanol

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† M = Na or K.

TABLE I

Preparation of nitroalcohols



| Nitroalcohol prepared | | | Reagents used and reaction conditions | | | | | | | Properties of products | | | Analysis | | | | | | | | |
|--------------------------------------------------------------|---------------------|-------------------------------------------------|---------------------------------------|-------------------------------------|-----|-----------------------------------------|-------------------------------------------------|-------------------------|--------------------|---------------------------|-------------------------------------|---------------------|-------------------------------------|---------------------------------------|-------------------------------------|-------|------|------------|-------|------|------|
| Name | R ₁ | R ₂ | R ₃ | Aldehyde* | (g) | CH ₃ NO ₂ (ml) | 95% C ₂ H ₅ OH (ml) | 10% NaOH aq. (ml) | 2% AcOH (ml) | Reaction time (sec) | Yield of purified product (g) | Crystalline form | m.p. (°C) | Literature m.p. (°C) (if known) | Found | | | Calculated | | | |
| | | | | | | | | | | | | | | | C | H | N | C | H | N | |
| 3,4-Methylenedioxy- α -nitro-methylbenzyl alcohol | OCH ₃ O | H | H | Piperonaldehyde | a | 10 | 11 | 135 | 20 | 160 | 60 | 9.3 | Fine colorless needles from benzene | 95 | 91(3), 95-96(4), 91(3), 94(2) | 51.34 | 4.41 | 6.61 | 51.19 | 4.30 | 6.63 |
| 4-Acetoxy-3-methoxy- α -nitromethylbenzyl alcohol | CH ₃ O | CH ₃ COO | H | 4-Acetoxy-3-methoxybenzaldehyde | b | 5 | 3.5 | 35 | 10 | 80 | 45 | 5.5 | Fine colorless needles from benzene | 90.5 | | 51.90 | 5.12 | 5.59 | 51.77 | 5.14 | 5.49 |
| 3-Acetoxy-4-methoxy- α -nitromethylbenzyl alcohol | CH ₃ COO | CH ₃ O | H | 3-Acetoxy-4-methoxybenzaldehyde | b | 5 | 3.5 | 50 | 10 | 80 | 30 | 4 | Fine colorless needles from benzene | 103-104 | | 51.87 | 5.21 | 5.43 | 51.77 | 5.14 | 5.49 |
| 3,4-Diacetoxy- α -nitromethylbenzyl alcohol | CH ₃ COO | CH ₃ COO | H | 3,4-Diacetoxybenzaldehyde | c | 5 | 3 | 25 | 10 | 90 | 30 | 4.9 | Colorless plates from ethanol | 153-155 | 155(6) | 50.99 | 4.59 | 5.02 | 50.88 | 4.63 | 4.95 |
| 4-Benzyloxy-3-methoxy- α -nitromethylbenzyl alcohol | CH ₃ O | C ₆ H ₅ CH ₂ O | H | 4-Benzyloxy-3-methoxybenzaldehyde | d | 1 | 0.7 | 7 | 1.55 | 13 | 45 | 0.65† | Colorless small prisms from benzene | 107-108.5 | 107-109(7) | 63.44 | 5.71 | 4.13 | 63.36 | 5.65 | 4.62 |
| 3,4,5-Trimethoxy- α -nitromethylbenzyl alcohol | CH ₃ O | CH ₃ O | CH ₃ O | 3,4,5-Trimethoxybenzaldehyde | e | 3 | 2.1 | 21 | 5.55 | 48 | 45 | 2.4 | Colorless fine needles from benzene | 109 | | 51.60 | 5.81 | 5.33 | 51.36 | 5.88 | 5.45 |
| 4-Acetoxy-3,5-dimethoxy- α -nitromethylbenzyl alcohol | CH ₃ O | CH ₃ COO | CH ₃ O | 4-Acetoxy-3,5-dimethoxybenzaldehyde | f | 1 | 0.7 | 18 | 1.65 | 13.5 | 20 | 1 | Fine colorless needles from ethanol | 200 | | 50.74 | 5.39 | 5.07 | 50.52 | 5.30 | 4.91 |

*Sources of aldehydes: a = Eastman Kodak. b = Prepared by the acetylation of vanillin and isovanillin respectively by an adaptation of the method described by Kanao for the preparation of 3,4-diacetoxybenzaldehyde (6). c = Prepared by the method of Kanao (6). d = 4-Benzyloxy-3-methoxybenzaldehyde (m.p. 64°) was prepared from vanillin by benzylation with benzyl chloride in the presence of aqueous potassium hydroxide. This substance has previously been prepared by alternative routes and the melting point is quoted as 63-64° (9). e = Aldrich Chemical Company. f = Prepared by the acetylation of Syringaldehyde

(Aldrich Chemical Company) by an adaptation of the method described by Kanao for the preparation of 3,4-diacetoxybenzaldehyde (6), m.p. 115°. Freudenberg and Hübner prepared this compound by a different route and quote m.p. 114° (10).

†The crude product, a yellow oil, was stirred with concentrated sodium bisulphite solution for 20 minutes before recrystallization from benzene.

‡The melting point has been incorrectly reported as 98-99° in Chem. Abstr. 48, 13,653 (1954).

derivatives have been prepared: 4-acetoxy-3-methoxy- α -nitromethylbenzyl alcohol (VI: R₁ = OCH₃; R₂ = OCOCH₃; R₃ = H); 3-acetoxy-4-methoxy- α -nitromethylbenzyl alcohol (VI: R₁ = OCOCH₃; R₂ = OCH₃; R₃ = H); 3,4,5-trimethoxy- α -nitromethylbenzyl alcohol (R₁ = R₂ = R₃ = OCH₃) and 4-acetoxy-3,5-dimethoxy- α -nitromethylbenzyl alcohol (R₁ = R₃ = OCH₃; R₂ = OCOCH₃). Attempts to prepare a number of related nitroalcohols by this method were not successful: (i) veratraldehyde gave mainly 3,4-dimethoxy- ω -nitrostyrene, even after cooling the reaction mixture below 0°; (ii) protocatechualdehyde, syringaldehyde, vanillin, and isovanillin did not react with nitromethane under the above conditions. This is not altogether surprising in view of the fact that three of these aldehydes have a para hydroxyl group, which has been reported by several workers to hinder this type of condensation (1, 8); (iii) 3,4-dibenzoyloxybenzaldehyde, 3-benzyloxy-4-methoxybenzaldehyde, 3,4-diethoxycarbonyloxybenzaldehyde, and 3-ethoxycarbonyloxy-4-methoxybenzaldehyde gave oily products, for which satisfactory analyses could not be obtained (for the nitroalcohol) even after distillation in high vacuum. It would appear in these cases that condensation had occurred, but partial decomposition of the products took place in the isolation or distillation stages. The infrared spectra of thin films of these oils showed strong absorption in the 2.79 to 2.81 μ region, probably due to the stretching vibrations of the benzyl alcohol hydroxyl group. (The authenticated nitroalcohols all exhibited marked absorption in this region (2.75 to 2.88 μ)). Recently Axelrod, Senoh, and Witkop have reported the OH stretching fre-

quency of 4-benzyloxy-3-methoxy- α -nitromethylbenzyl alcohol as 2.81 μ in chloroform solution (7).

In a few cases, the corresponding ω -nitrostyrenes had not been previously described in the literature and these derivatives were prepared in good yield, from the nitroalcohol in question, by an adaptation of the method described by Kanao for the preparation of 3,4-diacetoxy- ω -nitrostyrene from 3,4-diacetoxy- α -nitromethylbenzyl alcohol (6).

EXPERIMENTAL

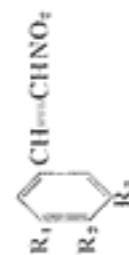
General Procedures*

(i) *Nitroalcohols*. Aqueous sodium hydroxide (10%; 1.05 mole) was added with vigorous stirring to a mixture of the aldehyde (1.0 mole) and nitromethane (2-3 mole) dissolved in 95% ethanol at ca. 5°; the reaction mixture was vigorously stirred for a short time (>3 minutes), accurately timed on a stop watch. Aqueous acetic acid (2%) was added to arrest the reaction and decompose the sodium derivative of the nitroalcohol; the crude product precipitated out as a yellow or colorless solid or oil. After being allowed to stand at 4° for 4-5 hours, the crude product was filtered and purified by repeated recrystallization from a suitable solvent.

(ii) *ω -Nitrostyrenes*.—A suspension of the nitroalcohol and the same weight of fused

*The specific quantities of reagents used and reaction times employed are given in Tables I and II.

TABLE II
Preparation of α -nitrostyrenes



| Name | α -Nitrostyrene prepared | | | Amount of nitro-alcohol used in g | Yield of purified product (g) (95% ethanol) | Crystalline form (from 95% ethanol) | m.p. (°C) | Analysis | | | | | |
|-------------------------------------------------------|-----------------------------------|---------------------|-------------------|-----------------------------------|---------------------------------------------|-------------------------------------|-----------|----------|------|------|------------|------|------|
| | R ₁ | R ₂ | R ₃ | | | | | Found | | | Calculated | | |
| | C | H | N | | | | | C | H | N | C | H | N |
| 4-Acetoxy-3-methoxy- α -nitrostyrene* | CH ₃ O | CH ₃ COO | H | 2 | 1.5 | Fine yellow needles | 166-167 | 55.62 | 4.62 | 5.90 | 55.60 | 4.68 | 5.91 |
| 3-Acetoxy-4-methoxy- α -nitrostyrene | CH ₃ COO | CH ₃ O | H | 0.85 | 0.7 | Yellow needles | 142 | 55.51 | 4.61 | 5.75 | 55.60 | 4.68 | 5.91 |
| 4-Acetoxy-3,5-di-methoxy- α -nitrostyrene | CH ₃ O | CH ₃ COO | CH ₃ O | 0.3 | 0.25 | Pale yellow plates | 177 | 54.01 | 4.87 | 5.21 | 53.93 | 4.90 | 5.24 |
| 3-Ethoxycarbonyloxy-4-methoxy- α -nitrostyrene | C ₂ H ₅ OOC | CH ₃ O | H | † | — | Fine yellow needles | 116 | 54.13 | 4.98 | 5.22 | 53.93 | 4.90 | 5.24 |

*The preparation of this substance has been reported previously by Kobayashi; however, the original Japanese paper is not available to the authors and no preparative details or melting points are given in Chemical Abstracts, but according to Beilstein, the substance was obtained by acetylation of 4-hydroxy-3-methoxy- α -nitrostyrene and had m.p. 161-162° (11).
†A small quantity of the crude reaction mixture from the attempted preparation of 3-ethoxycarbonyloxy-4-methoxy- α -nitrostyrene was used.

sodium acetate in acetic anhydride (five times the weight of one of the other reagents) was boiled under reflux for 10 minutes. After cooling, the reaction mixture was poured into water; a yellow solid separated out, which was filtered off, washed with water, and recrystallized from 95% ethanol.

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