NOTES

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

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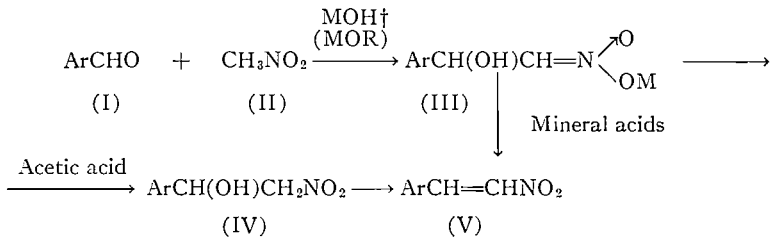
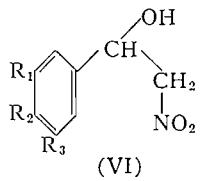
It has been known for many years that aromatic aldehydes (I) and nitromethane (II) will undergo a condensation reaction, under alkaline conditions, to yield the alkali metal derivatives of the *aci*-form of the monohydric nitroalcohols (III). The free nitroalcohols (IV) can be liberated on acidification 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: $R_1+R_2 = OCH_2O$; R_3 = H) (2, 3, 4, 5); 3,4-diacetoxy-α-nitromethylbenzyl alcohol (VI: $R_1 = R_2 = OCOCH_3$; R_3 = H) (6); and 4-benzyloxy-3-methoxy-α-nitromethylbenzyl alcohol (VI: $R_1 = OCH_3$; $R_2 = OCH_2C_6H_5$; R_3 = 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).



(VI)

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.

TAB

Preparation of nitroalcohols

Nitroalcohol prepared				Reagents used and reaction conditions						
Name	R_1	R_2	R_3	Aldehyde*		(g)	CH_3NO_2 (ml)	95% C_2H_5OH (ml)	10% NaOH aq. (ml)	2% AcOH (ml)
3,4-Methylenedioxy-α-nitromethylbenzyl alcohol	OCH_2O		H	Piperonaldehyde	*a*	10	11	135	20	160
4-Acetoxy-3-methoxy-α-nitromethylbenzyl alcohol	CH_3O	CH_3COO	H	4-Acetoxy-3-methoxybenzaldehyde	*b*	5	3.5	35	10	80
3-Acetoxy-4-methoxy-α-nitromethylbenzyl alcohol	CH_3COO	CH_3O	H	3-Acetoxy-4-methoxybenzaldehyde	*b*	5	3.5	50	10	80
3,4-Diacetoxy-α-nitromethylbenzyl alcohol	CH_3COO	CH_3COO	H	3,4-Diacetoxybenzaldehyde	*c*	5	3	25	10	90
4-Benzyloxy-3-methoxy-α-nitromethylbenzyl alcohol	CH_3O	$C_6H_5CH_2O$	H	4-Benzyloxy-3-methoxybenzaldehyde	*d*	1	0.7	7	1.55	13
3,4,5-Trimethoxy-α-nitromethylbenzyl alcohol	CH_3O	CH_3O	CH_3O	3,4,5-Trimethoxybenzaldehyde	*e*	3	2.1	21	5.55	48
4-Acetoxy-3,5-dimethoxy-α-nitromethylbenzyl alcohol	CH_3O	CH_3COO	CH_3O	4-Acetoxy-3,5-dimethoxybenzaldehyde	*f*	1	0.7	18	1.65	13.5

*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

derivatives have been prepared: 4-acetoxy-3-methoxy-α-nitromethylbenzyl alcohol (VI: $R_1 = OCH_3$; $R_2 = OCOCH_3$; $R_3 = H$); 3-acetoxy-4-methoxy-α-nitromethylbenzyl alcohol (VI: $R_1 = OCOCH_3$; $R_2 = OCH_3$; $R_3 = H$); 3,4,5-trimethoxy-α-nitromethylbenzyl alcohol ($R_1 = R_2 = R_3 = OCH_3$) and 4-acetoxy-3,5-dimethoxy-α-nitromethylbenzyl alcohol ($R_1 = R_3 = OCH_3$; $R_2 = OCOCH_3$). 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-

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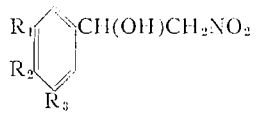


Reaction time (sec)	Yield of purified product (g)	Crystalline form	m.p. (°C)	Literature m.p. (°C) (if known)	Analysis: Found C	Found H	Found N	Calculated C	Calculated H	Calculated N
60	9.3	Fine colorless needles from benzene	95	91(5),‡ 95–96(4), 91(3), 94(2)	51.34	4.44	6.61	51.19	4.30	6.63
45	5.5	Fine colorless needles from benzene	90.5		51.90	5.12	5.59	51.77	5.14	5.49
30	4	Fine colorless needles from benzene	103–104		51.87	5.21	5.43	51.77	5.14	5.49
30	4.9	Colorless plates from ethanol	153–155	155(6)	50.99	4.59	5.02	50.88	4.63	4.95
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
45	2.4	Colorless fine needles from benzene	109		51.60	5.84	5.33	51.36	5.88	5.45
20	1	Fine colorless needles from ethanol	200		50.74	5.39	5.07	50.52	5.30	4.91

(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).

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**

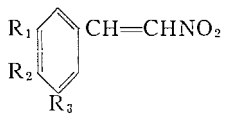
(*i*) *Nitroalcohols.*—Aqueous sodium hydroxide (10%; 1.05 mole) was added with vigorous stirring to a mixture of the aldehyde (1.0 mole) and nitromethane (2–3 mole) dissolved in 95% ethanol at ca. 5°; the reaction mixture was vigorously stirred for a short time (⩾3 minutes), accurately timed on a stop 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 ω-nitrostyrenes



ω-Nitrostyrene prepared				Amount of nitro-alcohol used in g	Properties of product			Analysis					
					Yield of purified product (g)	Crystalline form (from 95% ethanol)	m.p. (°C)	Found			Calculated		
Name	R_1	R_2	R_3					C	H	N	C	H	N
4-Acetoxy-3-methoxy-ω-nitrostyrene*	CH_3O	CH_3COO	H	2	1.5	Fine yellow needles	166–167	55.62	4.62	5.90	55.69	4.68	5.91
3-Acetoxy-4-methoxy-ω-nitrostyrene	CH_3COO	CH_3O	H	0.85	0.7	Yellow needles	142	55.51	4.61	5.75	55.69	4.68	5.91
4-Acetoxy-3,5-dimethoxy-ω-nitrostyrene	CH_3O	CH_3COO	CH_3O	0.3	0.25	Pale yellow plates	177	54.01	4.87	5.21	53.93	4.90	5.24
3-Ethoxycarbonyloxy-4-methoxy-ω-nitrostyrene	C_2H_5OCOO	CH_3O	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-ω-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-nitromethylbenzyl alcohol 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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PREPARATION AND DEHYDRATION OF DI-(1-HYDROXYCYCLOALKYL)-ALKANES[1]

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1-Alkylcycloalkanols have been employed (1, 2) as intermediates in the extension of monofunctional aliphatic chains. An obvious extension of this synthetic method would be the use of di-(1-hydroxycycloalkyl) compounds in chain extension of α,ω-dicarboxylic acids of the aliphatic series. Although there is no record (3) of the use of such intermediates for this purpose, diols of the requisite structural type have been made in isolated previous investigations. We have now prepared diols having five-, six-, seven-, and eight-membered rings and with 2 to 10 methylene groups connecting them, using procedures already described. The results are summarized in Table I.

Method A, reaction of a diester with two moles of a Grignard reagent from a dihalide, has been studied previously only in the synthesis of 1,1′-ethylenedicyclopentanol and 1,1′-ethylenedicyclohexanol from ethyl succinate and respectively tetramethylene dibromide and pentamethylene dibromide (4). We attempted to use hexamethylene dibromide and 1,3-dibromo-2,2-dimethylpropane in similar syntheses but in each case obtained no crystalline product but the major outcome was evidently a polymer. Diethyl 2,2-dimethylglutarate was successfully condensed with 2 moles of the derived Grignard reagent from pentamethylene dibromide although one might have expected the gem dimethyl group to hinder or deactivate one of the ester groups sterically.

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