p.s.i. The catalyst was removed by filtration and the sirup obtained on solvent removal was dried by repeated distillation of added ethanol under reduced pressure and finally in a desiccator under reduced pressure. The product was dissolved in 180 ml. of freshly distilled and dried pyridine and 80 ml. of this was removed under reduced pressure in order to further dry the reaction mixture. The solution was cooled to 0°, 100 ml. of acetic anhydride was added in small amounts under vigorous shaking, and the whole was maintained at 5° for 82 hr. The viscous acetylation mixture was then poured into 800 ml. of ice and water and the separated sirup was removed by decantation and washed by decantation with several portions of cold water. The resultant solid was dissolved in chloroform and washed successively with water, dilute aqueous cadmium chloride (to remove pyridine as the insoluble cadmium chloride complex) and again with water, dried over Na_2SO_4 and concentrated under reduced pressure. The resultant sirup was frothed and dried in a vacuum desiccator to an amorphous, white solid; yield 22.1 g.

An amount of 3.0 g. of the above acetate mixture was dissolved in 50 ml. of benzene and chromatographed on a 240 × 54 mm. (diam.) column of Magnesol-Celite (5:1 by wt.) by development with 1500 ml. of benzene-*t*-butyl alcohol (75:1 by vol.). By means of the alkaline permanganate[11] streak three zones were located on the extruded column: (A), on the bottom half; (B), one-third of a column length from the top; and (C), at the column top.

The acetone eluate material from each zone was isolated. That from zone A was recrystallized from absolute ethanol and was identified as sorbitol hexaacetate; yield 1.52 g., m.p. 98–99° unchanged on admixture with an authentic specimen, $[\alpha]^{26}D$ +9.3° (*c* 3.0, chloroform).

The sirup from zone B was dissolved in 85 ml. of benzene and rechromatographed as before, employing 2300 ml. of developer. Three zones were obtained. The lower one yielded a further small amount (50 mg.) of sorbitol hexaacetate (m.p. 98–99°) isolated in the same manner. Crystallization from absolute ethanol of the material from the top zone produced maltitol nonaacetate[10,16]; yield 420 mg., m.p. 83–85° unchanged on admixture with an authentic specimen, $[\alpha]^{24}D$ +84.2° (*c* 1.0, chloroform).

The sirup (0.66 g.) from zone C was dissolved in 50 ml. of benzene and added at the top of a 210 mm. × 44 mm. (diam.) column of Silene-EF[12]-Celite (5:1 by wt.). The chromatogram was developed with 900 ml. of benzene-*t*-butyl alcohol (100:1 by vol.). The alkaline permanganate streak located three zones on the extruded column. The acetone eluate from the lowest zone yielded a further amount of maltitol nonaacetate; yield 32 mg., m.p. 82–83°. The acetone eluate from the next higher zone was rechromatographed in the same manner and again yielded two zones. The acetone eluate of the lower zone was dissolved in abs. ethanol and from this isomaltitol nonaacetate crystallized; yield 17 mg., m.p. and mixed m.p. with an authentic specimen (m.p. 114–115°) 113–114°.

COLUMBUS 10, OHIO RECEIVED AUGUST 23, 1951

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF GENERAL MILLS, INC.]

The Reaction of α,β-Unsaturated Aldehydes with Nitro Compounds[1,2]

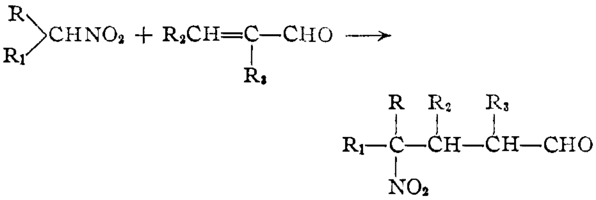
BY DONALD T. WARNER AND OWEN A. MOE

The reactions of primary and secondary nitroparaffins with α,β-unsaturated aldehydes in alcohol solutions containing basic catalysts have been found to yield γ-nitrobutyraldehydes. These aldehyde products have been characterized as their 2,4-dinitrophenylhydrazones. One of the compounds, γ-nitrocaproaldehyde, was converted to the corresponding 4-amino-1-hexanol and this reduction product showed no evidence of vicinal hydroxyl and amino groups in the test with periodic acid. γ-Nitrocaproaldehyde was also hydrogenated at elevated temperatures, and one of the reduction products was α-ethylpyrrolidine. The γ-nitroaldehyde structure has therefore been clearly substantiated.

Several references to the reactions of α,β-unsaturated aldehydes with nitroparaffins have appeared recently.[3,4,5] In all of the experiments recorded, the conditions which were employed apparently resulted in the formation of unsaturated nitro alcohols by the addition of the nitroparaffin to the carbonyl group of the α,β-unsaturated aldehyde.

On the basis of previous studies involving malonate systems and α,β-unsaturated aldehydes,[6] it seemed probable that under the proper conditions, the nitroparaffins might also react with α,β-unsaturated aldehydes to yield nitroaldehyde compounds resulting from the 1,4-addition of one mole of nitroparaffin to one mole of α,β-unsaturated aldehyde. Accordingly, this possibility was first studied with secondary nitro compounds, in which the presence of the single hydrogen atom on the α-carbon atom might be expected to promote the 1,4-addition with fewer side reactions. 2-Nitropropane was selected for these tests. By carrying out the addition in alcoholic solution and in the presence of a small molar ratio of a strong alkaline catalyst, the desired γ-nitroaldehydes were obtained in modest yields.

From these encouraging results, the reaction was extended to primary nitroparaffins such as 1-nitropropane. In each of the instances studied, 1-nitropropane also reacted with the α,β-unsaturated aldehydes in the 1,4-manner to yield γ-nitrobutyraldehydes. The compounds studied and their structures may be summarized in accordance with the general equation



$$\begin{matrix}R\\R_1\end{matrix}\!>\!\mathrm{CHNO_2} + \mathrm{R_2CH{=}}\underset{R_3}{\underset{|}{\mathrm{C}}}\mathrm{{-}CHO} \longrightarrow \mathrm{R_1{-}}\underset{NO_2}{\underset{|}{\overset{R}{\overset{|}{\mathrm{C}}}}}\mathrm{{-}}\overset{R_2}{\overset{|}{\mathrm{CH}}}\mathrm{{-}}\overset{R_3}{\overset{|}{\mathrm{CH}}}\mathrm{{-}CHO}$$

I, $R = R_1 = CH_3$; $R_2 = R_3 = H$
II, $R = R_1 = R_3 = CH_3$; $R_2 = H$
III, $R = R_1 = R_2 = CH_3$; $R_3 = H$
IV, $R = C_2H_5$; $R_1 = R_2 = R_3 = H$
V, $R = C_2H_5$; $R_1 = R_2 = H$; $R_3 = CH_3$
VI, $R = C_2H_5$; $R_1 = R_3 = H$; $R_2 = CH_3$

The isolation of the aldehyde compounds I–VI was accomplished by distillation of the crude reaction mixtures after neutralization and washing.

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[1] Paper No. 117, Journal Series, General Mills, Inc., Research Dept.

[2] Presented at XIIth International Congress of Pure and Applied Science, New York City, September, 1951.

[3] E. F. Degering and A. Sprang, U. S. Patent 2,332,482, Oct. 19, (1943).

[4] F. J. Villani and F. F. Nord, THIS JOURNAL, **69**, 2608 (1947).

[5] G. Fort and A. McLean, *J. Chem. Soc.*, 1907 (1948).

[6] D. T. Warner and O. A. Moe, THIS JOURNAL, **71**, 2586 (1949).

TABLE I

PHYSICAL PROPERTIES OF γ-NITROALDEHYDES AND THEIR 2,4-DINITROPHENYLHYDRAZONES

	Aldehydes										2,4-Dinitrophenylhydrazones						
					Analyses												
	B.p.				Carbon		Hydrogen		Nitrogen			Carbon		Hydrogen		Nitrogen	
Compound	°C.	Mm.	$n^{25}D$	Yield, %	Calcd.	Found	Calcd.	Found	Calcd.	Found	M.p., °C.	Calcd.	Found	Calcd.	Found	Calcd.	Found
I	58–60	0.1	1.4443	33[a]	49.63	49.99	7.64	7.28	9.65	9.55	133–134[b]	44.31	44.33	4.65	4.70	21.54	21.41
II	60–66	.5	1.4444	20[c]	52.81	51.95	8.23	7.83	8.80	9.13	137[d]	46.01	46.12	5.05	4.87	20.64	20.53
III	58–60	.1	1.4513[i]	34[e]	...	...	..	..	..	..	110–111	46.01	46.59	5.05	5.04	20.64	20.49
IV	52–53	.25	1.4413	30[f]	49.63	49.08	7.64	7.65	9.65	9.73	101–102	44.31	44.39	4.65	4.49	21.54	21.63
V	50–51	.2	1.4390	31[g]	52.81	51.80	8.23	8.03	8.80	8.96	107–108[h]	46.01	46.15	5.05	5.09	20.64	20.93
											125–126[h]	46.01	45.88	5.05	4.99	20.64	20.61
VI	60–75	.23	1.4501[i]	15	...	...	..	..	..	..	120–121	46.01	46.01	5.05	4.78	20.64	20.79

[a] Based on 2-nitropropane used and a product which distilled at 52–61° (0.1 mm.). [b] Crude derivative (m.p. 130–131°) obtained in 91% yield from distilled aldehyde. [c] Based on product distilling at 58–75° (0.5–0.66 mm.). [d] Crude derivative (m.p. 135–136°) obtained in 82% yield from distilled aldehyde. [e] Based on product distilling at 57–64° (0.06–0.18 mm.). [f] Based on product distilling at 52–56° (0.25–0.30 mm.). [g] Based on product distilling at 48–51° (0.2 mm.). [h] Two products corresponding to the two racemic modifications were obtained and purified. [i] These products contained traces of crotonic acid. Therefore the refractive indices may be slightly in error and the aldehydes were not analyzed.

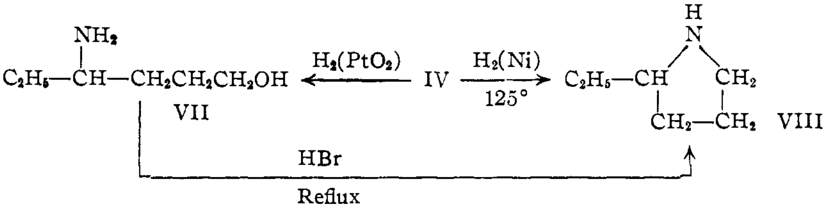
The freshly distilled products were nearly water-white liquids. In the case of compound IV, an attempt was made to isolate a probable second component of the reaction mixture by further distillation. When the distillate temperature reached 150° (1.8 mm.), the residue decomposed rather violently with a rapid increase in temperature so that further attempts to examine the residue by distillation were avoided as hazardous.

Each of the aldehyde compounds obtained in the present study was characterized as its crystalline 2,4-dinitrophenylhydrazone. These derivatives formed very readily from all of the distilled products. The aldehyde compounds I, II, III and IV apparently yielded only a single derivative. On the other hand, aldehyde compounds V and VI yielded well crystallized materials which were probably mixtures of the products from the two racemic modifications. From the derivative of V, both of the 2,4-dinitrophenylhydrazones were obtained pure and analyzed. The physical properties of the aldehydes and their derivatives are presented in Table I.

Compound IV was studied in greater detail to substantiate the γ-nitroaldehyde structure. The purified 2,4-dinitrophenylhydrazone was prepared from the distilled product in 93% yield, indicating virtual absence of unsaturated nitro alcohol product.[7] The nitroaldehyde was hydrogenated using platinum oxide at 45 p.s.i. at room temperature to yield an amino alcohol which analyzed correctly for $C_6H_{15}ON$. This reduction product formed a bis-3,5-dinitrobenzoyl derivative which melted at 193–194°. The amino alcohol was then treated with periodic acid; and no periodate was consumed. This result indicated the absence of vicinal amino and hydroxyl groups in the molecule, and the exclusive presence of the 4-amino-1-hexanol in the reduction product.[8]

Compound IV was also hydrogenated over Raney nickel catalyst at 125–130° with an initial hydrogen pressure of about 700 p.s.i. Under these conditions a poor yield of α-ethylpyrrolidine (VIII) was obtained from the steam-volatile fraction together with some higher boiling material which was not identified. The α-ethylpyrrolidine was characterized as the p-toluenesulfonyl derivative melting at 76.5–77.5° (literature value, 76.9°).[9] The formation of α-ethylpyrrolidine is additional evidence for the proposed structure of Compound IV.

The preparation of VIII was more conveniently accomplished by refluxing the amino alcohol VII with hydrobromic acid (48%) and steam distilling the alkalized hydrolysate. The yield based on VII was 44%. The phenylthiourea derivative was also prepared, m.p. 87–87.6° (literature value, 89°).[9]



Experimental[10,11]

Preparation of γ-Nitroaldehydes.—The general reaction conditions employed in the synthesis of γ-nitroaldehydes are illustrated by the preparation of γ-nitrocaproaldehyde (IV).

An alcoholic solution of sodium ethoxide (prepared from 120 ml. of absolute ethanol and 0.07 g. of metallic sodium) was mixed with 62.3 g. (0.07 mole) of 1-nitropropane. The mixture was cooled to 0° and 39.2 g. (0.07 mole) of freshly distilled acrolein was added dropwise over a period of 1.5 hours at a temperature of approximately 5°.[12] After an additional one-half hour at 10°, the reaction mixture was acidified by the addition of 1.5 ml. of glacial acetic acid. The solution was concentrated *in vacuo* to a thin sirup. This sirup was dissolved in 200 ml. of benzene and washed with four 50-ml. portions of water. The benzene solution was dried over anhydrous sodium sulfate. Removal of the solvent *in vacuo* yielded a residual oil weighing 95.7 g. This crude product (93.2 g.) was distilled. The first fraction (35.5 g.) was collected at 65–90° (0.3–0.4 mm.) and mostly at 65–75°. A second intermediate fraction (12.6 g.) was collected at 90–138° (0.4–1.4 mm.) with gradual rise in temperature and some evidence of decomposition. A third fraction was being collected at about 138–145° (1.4–1.8 mm.) when the distillation temperature rose rather rapidly to about 175°. A rather sudden decomposition took place in the distilling flask and a brown decomposition product was carried over into the distillate. The flask residue was a

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(7) Similarly Compounds I and II were converted to their respective 2,4-dinitrophenylhydrazones in 91 and 82% yields.

(8) B. H. Nicolet and L. A. Shinn, THIS JOURNAL, 61, 1615 (1939).

(9) A. Muller and H. Wachs, *Monatsh.*, 53, 420 (1929).

(10) All melting points uncorrected, except as indicated.

(11) Analyses by J. R. Kerns.

(12) In reactions employing methacrolein and crotonaldehyde, the addition was usually conducted at 25–30°.

viscous tar. The sudden occurrence of this decomposition indicates the potential hazard involved in carrying the distillation too far.[13]

The first fraction (35.5 g.) was redistilled through a short Vigreux column, and 30.1 g. of IV was collected at 52–56° (0.25–0.3 mm.), yield 29.6%. A center cut (15.8 g.) boiled at 52–53° (0.25 mm.), n^{25}D 1.4413. This product was analyzed.

Another portion of redistilled γ-nitrocaproaldehyde (1.51 g.) was treated with 2.03 g. of 2,4-dinitrophenylhydrazine in 160 ml. of boiling 95% ethanol containing 1 ml. of concentrated hydrochloric acid. The resulting derivative weighed 3.14 g. (93% yield) and melted at 101.5–102.5°. An analytical sample melted at 101.5–102° (crystallized from ethanol).

4-Amino-1-hexanol (VII).—Compound IV (14.5 g., 0.1 mole) was dissolved in 100 ml. of absolute ethanol and 0.7 g. of Adams platinum oxide catalyst was added. After approximately two moles of hydrogen had been consumed an additional 0.6 g. of catalyst was added and the hydrogenation was resumed. Approximately 3.8 moles of hydrogen was consumed after a total of 48 hours. The catalyst was removed by filtration, and the filtrate was concentrated *in vacuo*. The crude product yielded 6.3 g. of distillate at 61–63° (0.27 mm.) and 2.2 g. at 63–65° (0.27 mm.). The combined fractions represent a yield of 73%. The first fraction was analyzed.

Anal. Calcd. for $C_6H_{15}ON$: C, 61.5; H, 12.9; N, 11.93. Found: C, 61.96; H, 12.69; N, 12.04.

The reaction of the reduced product with 3,5-dinitrobenzoyl chloride yielded the bis-3,5-dinitrobenzoyl derivative of VII melting at 193–194° after recrystallization from an ethanol–ethyl acetate solvent mixture.

Anal. Calcd. for $C_{20}H_{19}O_{11}N_5$: C, 47.5; H, 3.8; N, 13.9. Found: C, 47.88; H, 3.76; N, 13.99.

Periodate Treatment of 4-Amino-1-hexanol (VII).—4-Amino-1-hexanol (0.1646 g.) was treated with 40 ml. of 0.44 *M* periodic acid solution at room temperature. Aliquot samples taken after one-half hour and three-fourths hour showed no periodate uptake in the reaction mixture.

α-Ethylpyrrolidine (VIII). A.—Product IV (13.8 g.) was dissolved in 60 ml. of absolute ethanol and 4.0 g. of a moist paste of Raney nickel was added. The hydrogenation was carried out at an initial pressure of 700 p.s.i. at 125–130° over a period of four hours. The catalyst was removed by filtration and the filtrate was acidified with hydrochloric acid and concentrated *in vacuo*. The residual sirupy material was dissolved in 200 ml. of water and made alkaline with 4.8 g. of NaOH. The mixture was steam distilled and one liter of distillate was collected containing a small quantity of insoluble oil. The distillate was acidified and concentrated *in vacuo* to a thin sirup. This sirup was treated with 50 ml. of 40% KOH solution and the oil which separated was taken up in ether (100 ml.). The ether layer was dried over anhydrous sodium sulfate. After removal of the ether through a Vigreux column the α-ethylpyrrolidine distilled at 121–128° (740 mm.), n^{15}D 1.4425; given[9] for pure α-ethylpyrrolidine, n^{15}D 1.4442, weight 0.75 g., 8% yield. Some higher boiling material was obtained at 200–225° (740 mm.). This product was not characterized.

Crude α-ethylpyrrolidine was reacted with *p*-toluenesulfonyl chloride in aqueous sodium hydroxide. The product separated in the alkaline media, as would be expected of a secondary amine derivative. After two recrystallizations from 80% ethanol it melted at 76.5–77.5° (corrected); given[9] for the *p*-toluenesulfonyl derivative of α-ethylpyrrolidine, m.p. 76.9°.

Anal. Calcd. for $C_{13}H_{19}O_2SN$: C, 61.63; H, 7.56. Found: C, 62.03; H, 7.45.

B.—Compound VII (4.79 g.) was refluxed for 16 hours with 30 ml. of 48% hydrobromic acid. The light brown hydrolyzate was concentrated *in vacuo* to a thin paste. This paste was dissolved in 500 ml. of water and made alkaline with 10 g. of sodium hydroxide. The mixture was steam distilled and then processed further as described under Method A.

α-Ethylpyrrolidine, VIII (1.78 g., 44%), was collected at 121–126° (736 mm.), n^{15}D 1.4427. VIII was again converted to the *p*-toluenesulfonate (m.p. 75.5–76.5°) and also to the phenylthiourea derivative, m.p. 87–87.6°.

Anal. Calcd. for $C_{13}H_{18}N_2S$: C, 66.62; H, 7.74; N, 11.96. Found: C, 66.93; H, 7.68; N, 12.69.

MINNEAPOLIS, MINNESOTA RECEIVED JULY 6, 1951

[13] A similar decomposition was observed by Fort and McLean, see reference 5.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF FORDHAM UNIVERSITY]

The Willgerodt Reaction in the Heterocyclic Series. III. Temperature Studies with Thienyl Ketones

BY JOSEPH A. BLANCHETTE AND ELLIS V. BROWN

2-Thienyl methyl ketone has been found to undergo the Willgerodt reaction with the yield dependent on the operation temperature. Temperature studies with 2-thienyl methyl ketone, 2,5-dimethyl-3-thienyl methyl ketone and 3,4-dimethyl-2-thienyl methyl ketone have shown that the yields of the corresponding amides decrease sharply above 160°. When these amides were subjected to the conditions of the Willgerodt reaction at a temperature of 190° only small amounts could be recovered. Lengthening of the aliphatic chain of 2-thienyl ketones was accompanied by a decrease in the yield of amide. A comparison of the yields obtained from the thiophene compounds investigated is included.

In previous reports[1] we have shown that α-vinyl, α-acetonyl- and α-(1-hydroxyethyl)-thiophenes yielded the respective amides by the Willgerodt reaction in yields of 20–35%. 5-Alkyl-2-thienyl methyl ketone and 2,3-dimethyl-5-thienyl methyl ketone gave 40–55% yields of the corresponding amides by the Willgerodt reaction. However, the compounds which contained an alkyl group in the β-position ortho to the α-carbonyl group were converted to the respective amides in yields of only 25–35%. When both α-positions contained alkyl substituents yields of 70–90% were obtained with these 3-thienyl methyl ketones while 3-thienyl methyl ketone itself gave the lowest yield, 5–13%. Earlier in this study, a series of experiments with 2-acetothienone was carried out but no amides could be isolated from the reaction mixtures. This observation has also been reported by several investigators[2,3,4] who used the morpholine and sulfur modification of the Willgerodt reaction. This failure of 2-thienyl methyl ketone to react while other α-monosubstituted thiophenes were converted to the corresponding amides required a reasonable explanation. Any assumption that

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[1] J. A. Blanchette and E. V. Brown, THIS JOURNAL, **73**, 2779 (1951); **72**, 3414 (1950).

[2] E. Schwenk and D. Papa, *J. Org. Chem.*, **11**, 798 (1946).

[3] Buu-Hoi and Nguyen-Hoan, *Rec. trav. chim.*, **68**, 5 (1949).

[4] B. H. Ford, G. C. Prescott and D. R. Colingwsorth, THIS JOURNAL, **72**, 2109 (1950).