troleum ether (b.p. 30–60°), m.p. 190.5–191°. This product is not appreciably soluble in 5% aqueous sodium bicarbonate.

Anal. Calcd. for $C_{16}H_{22}Cl_2N_2O_3$: C, 53.20; H, 6.14. Found: C, 53.46; H, 6.27.

2,5-Dipivalamido-3,6-dichlorophenol.—In a manner similar to that used for the 2,5-dipivalamido-3,4-dichlorophenol, formic acid was added to 0.5 g. of 2,5-dichloro-*p*-quinonedipivalimide to give an adduct which upon hydrolysis yielded 0.23 g. (44%) of 2,5-dipivalamido-3,6-dichlorophenol. The product was purified from chloroform with addition of petroleum ether (b.p. 30–60°), m.p. 199.5–200.5°. This product is not appreciably soluble in 5% aqueous sodium bicarbonate.

Anal. Calcd. for $C_{16}H_{22}Cl_2N_2O_3$: C, 53.20; H, 6.14. Found: C, 53.39; H, 5.98.

2,3,5,6-Tetrachloro-*p*-phenylenedipivalamide.—A solution of 2.5 g. of tetrachloro-*p*-phenylenediamine,[2b] and 2.5 g. of pivalyl chloride in 25 ml. of pyridine was refluxed for 4.5 hours, then cooled and poured into ice and hydrochloric acid. The crude diamide weighed 4.0 g. (95%). It was recrystallized from 95% ethanol and finally from chloroform; platelets, m.p. 335–335.5°. This product proved to be identical to that formed by addition of hydrogen chloride to the 2,3,5-trichloro diimide.

Addition of Hydrogen Chloride to 2,3,5-Trichloro-*p*-quinonedipivalimide.—Hydrogen chloride was passed into a solution of 0.25 g. of 2,3,5-trichloro-*p*-quinonedipivalimide in petroleum ether (b.p. 80–110°). The precipitate that formed was removed by filtration, and identified as tetrachloro-*p*-phenylenedipivalamide, 0.12 g. (44%). Concentration of the filtrate gave 0.11 g. (45%) of colorless needles which were crystallized from petroleum ether (b.p. 80–110°) and aqueous ethanol; m.p. 225°. The product analyzed for the corresponding oxazole, 2-*t*-butyl-4,5,7-trichloro-6-pivalamidobenzoxazole.

Anal. Calcd. for $C_{16}H_{19}Cl_3N_2O_2$: C, 50.87; H, 5.07; N, 7.42. Found: C, 50.58; H, 4.96; N, 7.84.

Upon refluxing this product for 4 hours with 10% aqueous sodium hydroxide and acidifying, a low yield of a phenol resulted.

URBANA, ILLINOIS

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE OHIO STATE UNIVERSITY]

Addition Reactions of Nitroalkanes with Acrolein and Methyl Vinyl Ketone. Selective Reduction of Nitrocarbonyl Compounds to Nitrocarbinols

BY HAROLD SHECHTER, DEAN E. LEY[1] AND LAWRENCE ZELDIN[1,2]

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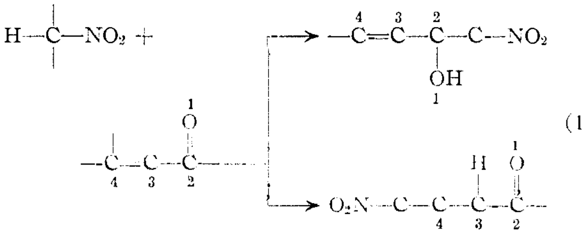
Reactions of nitromethane, nitroethane and 2-nitropropane with methyl vinyl ketone and acrolein in the presence of benzyltrimethylammonium hydroxide or sodium methoxide result principally in 1,4-addition to give the corresponding nitrocarbonyl compounds. General techniques have been developed for the selective reduction of aliphatic primary, secondary and tertiary mononitro and primary and secondary *gem*-dinitro aldehydes and ketones to their corresponding mononitro and dinitrocarbinols by reaction with (1) aluminum isopropoxide in 2-propanol or toluene or (2) sodium borohydride in water–methanol.

Discussion

The present investigation consists of (1) a continuation of a study of addition reactions of acidic nitroalkanes with acrolein and methyl vinyl ketone[3] and (2) the development of general methods for the selective reduction of the nitrocarbonyl compounds produced therefrom into the corresponding nitrocarbinols.

Nitrocarbonyl Compounds.—Reaction of a nitroalkane with an α,β-unsaturated carbonyl compound (Equation 1) may occur with (1) the carbonyl group to yield the unsaturated nitrocarbinol and (2) the carbon–carbon double bond to give the corresponding saturated nitrocarbonyl derivative. In the base-catalyzed condensation of nitroparaffins with conjugated unsaturated ketones, it has been demonstrated that the principal reaction is addition of the nitro compound to the olefinic linkage.[3,4] The reaction of nitroalkanes with certain substituted α,β-unsaturated aldehydes is reported to involve either or both 1,2- and 1,4-addition[5]; this system, however, has not been extensively studied.



(1)

In the present study it has been found that reactions of 2-nitropropane, nitroethane and nitromethane with acrolein and methyl vinyl ketone, catalyzed by benzyltrimethylammonium hydroxide or sodium methoxide, result principally in addition to the olefinic groups of the conjugated carbonyl compounds (Table I). The yields of 1:1 addition products obtained from the nitroalkanes decrease in the order: 2-nitropropane > nitroethane > nitromethane, and are much greater with methyl vinyl ketone than with acrolein. The variation in yields obtained with the nitroalkanes is attributed to the difference in the number of replaceable hydrogens of the acidic nitro compounds. Thus, 2-nitropropane gives rise to only 1:1 addition products, whereas nitroethane and nitromethane also yield 1:2, and 1:2 and 1:3 adducts, respectively. Maximum yields of the 1:1 adducts were realized when higher

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[1] Taken in part from the (a) M.S. thesis of D. E. Ley, August, 1951, and (b) Ph.D. Dissertation of L. Zeldin, June, 1951.

[2] Financial support of the research of L. Zeldin was supplied by the Office of Naval Research.

[3] H. Shechter and L. Zeldin, THIS JOURNAL, **73**, 1276 (1951).

[4] E. P. Kohler, *ibid.*, **38**, 889 (1916); **46**, 503 (1924); E. P. Kohler and H. F. Engelbrecht, *ibid.*, **41**, 1379 (1919); E. P. Kohler and H. E. Williams, *ibid.*, **41**, 1644 (1919); E. P. Kohler and M. S. Rao, *ibid.*, **41**, 1697 (1919); E. P. Kohler and L. I. Smith, *ibid.*, **44**, 624 (1922); M. C. Kloetzel, *ibid.*, **69**, 2271 (1947).

[5] E. F. Degering and A. Sprang, U. S. Patent 2,332,482 (October 19, 1943); G. Fort and A. McLean, *J. Chem. Soc.*, 1907 (1948); F. J. Villani and F. F. Nord, THIS JOURNAL, **69**, 2608 (1947); D. T. Warner and O. A. Moe, *ibid.*, **74**, 1064 (1952).

mole ratios of nitroalkane to unsaturated carbonyl compound were used (see Table I). In general, a higher mole ratio of nitroalkanes was also needed in condensations with acrolein (readily polymerized) than with methyl vinyl ketone.

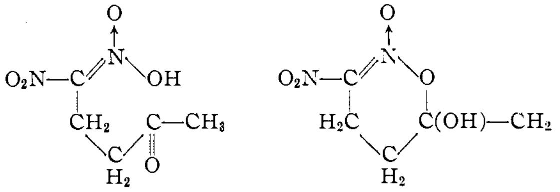
The products isolated from reactions of the nitroalkanes with acrolein and methyl vinyl ketone were all shown to be nitrocarbonyl compounds derived from 1,4-addition (and not the isomeric olefinic nitro alcohols from 1,2-addition) by: (1) infrared analysis (strong absorption for carbonyl (5.8 microns) and mononitro (6.4 microns) groups; no absorption for olefinic (6.0 microns) or hydroxyl (2.9 microns) groups), (2) conversion into either the corresponding semicarbazones or 2,4-dinitrophenylhydrazones in high yields, and (3) selective reduction into the corresponding nitrocarbinols (see following section). Additional chemical proof of structure of 5-nitro-2-hexanone, derived from nitroethane and methyl vinyl ketone, was provided by conversion of its sodium salt into 2,5-hexanedione by the action of sulfuric acid (the Nef reaction)[6]; 2,5-hexanedione was identified as 2,5-hexanedione dioxime[7] after reaction with hydroxylamine.

Nitrocarbinols.—Previous studies have shown that nitroaromatic aldehydes and ketones[8] and nitrocyclopropyl ketones[9,10] are selectively reduced by metal alkoxides to the corresponding nitro alcohols. It has also been demonstrated that conversion of *m*-nitrobenzaldehyde to *m*-nitrobenzyl alcohol is effected by sodium borohydride.[11] In the present investigation it has been found that aliphatic primary, secondary and tertiary mononitro and primary and secondary *gem*-dinitro aldehydes and ketones (Table II) may be selectively reduced to the corresponding aliphatic mononitro and dinitrocarbinols by the action of either (1) aluminum isopropoxide in 2-propanol or toluene or (2) sodium borohydride in water–methanol.

The reduction of non-acidic nitrocarbonyl compounds, such as tertiary mononitro and secondary *gem*-dinitro aldehydes and ketones with aluminum isopropoxide, may be accomplished efficiently by the usual techniques[8] in refluxing 2-propanol. In general, the nitro aldehydes undergo reduction much more rapidly than nitro ketones; however, the yields are usually lower. With sensitive acidic compounds such as 5-nitro-2-pentanone and 5-nitro-2-hexanone, reduction occurs slowly in 2-propanol and extensive decomposition of reagents and products results. It was found, however, that these compounds were reduced efficiently upon rapid addition to a refluxing mixture of toluene and aluminum isopropoxide and subsequent minimum exposure after reduction was complete. The yields of reduction product obtained with aluminum isopropoxide may be related to the type of nitro group in the carbonyl compound, and for mononitro carbonyl compounds are in the order: tertiary > secondary > primary.

The selective reduction of aliphatic nitrocarbonyl compounds (Table II) with aqueous methanolic sodium borohydride is effected rapidly and efficiently at 0–25° over the *p*H range 3–10.5. No particular difficulty has been experienced in hydrolyzing the borate esters of the primary and secondary alcohols produced nor have any serious hazards been encountered in any reductions. In general, use of sodium borohydride is to be preferred over aluminum isopropoxide for reduction of sensitive compounds.

It is of interest that 5,5-dinitro-2-pentanone is reduced slowly to 5,5-dinitro-2-pentanol (Table II) by acidic sodium borohydride. Even with large excesses of reducing agent (300%) and long reaction times, reduction is incomplete, and the product contains unreacted *gem*-dinitro ketone. The difficulty in reduction of 5,5-dinitro-2-pentanone, a relatively strong acid,[12] is in marked contrast to the ease of reduction of acidic mononitro and other *gem*-dinitro compounds (Table II) under comparable conditions. It is suggested[13] that the slow reduction of 5,5-dinitro-2-pentanone is related to ring-chain tautomerism of the type



in which the usual reactivity (or the effective concentration) of the carbonyl group is diminished by participation of the primary nitro-nitronate anion with the formation of the pseudo nitronic ester. On the basis of the well-established reversible condensation of acidic nitroalkanes and carbonyl compounds resulting in both carbon and oxygen alkylation,[14] keto–lactonol tautomerism of 5,5-dinitro-2-pentanone is to be expected and, thus, be analogous to that observed with β-formylpropionic acid, 2-benzoylbenzoic acid, phthalonic acid, and other similar derivatives which exhibit both normal and pseudo acid properties.[15]

The structures assigned to the nitrocarbinols prepared by reduction with either aluminum isopropoxide or sodium borohydride have been verified by: (1) quantitative and infrared analysis (strong absorption of the products (0.2 M in carbon tetrachlo-

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[6] J. U. Nef, *Ann.*, **280**, 263 (1894).

[7] A. Lipp and E. Scheller, *Ber.*, **42**, 1967 (1909).

[8] A. L. Wilds, "Reduction with Aluminum Alkoxides," in R. Adams, "Organic Reactions," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1946, pp. 178-223.

[9] L. I. Smith and V. A. Engelhardt, THIS JOURNAL, **71**, 2676 (1949); L. I. Smith and E. R. Rogier, *ibid.*, **73**, 3837 (1951).

[10] Nitrocyclopropanes are much weaker pseudo acids than are primary or secondary nitroalkanes. *Cf.* H. Shechter, Ph.D. Dissertation, Purdue University, 1946, and H. Stone, Ph.D. Dissertation, The Ohio State University, 1950.

[11] S. W. Chaikin and W. G. Brown, THIS JOURNAL, **71**, 122 (1949).

[12] The ionization constants for 1,1-dinitroalkanes usually range from 10^{-4}-10^{-6}; H. Ley and A. Hantzsch, *Ber.*, **39**, 3149 (1906); G. E. K. Branch and M. Calvin "The Theory of Organic Chemistry," Prentice-Hall, Inc., New York, N. Y., 1941, p. 269. The ionization constants for mononitroalkanes are of the order: 10^{-9}-10^{-11}; D. Turnbull and S. H. Maron, THIS JOURNAL, **65**, 212 (1943).

[13] The authors should like to acknowledge Dr. R. B. Kaplan for this explanation.

[14] P. Duden and G. Ponndorf, *Ber.*, **38**, 203 (1905); H. Jacobson, Ph.D. thesis, Purdue University, 1942; J. M. Grosheintz and H. O. L. Fischer, THIS JOURNAL, **70**, 1479 (1948); M. L. Wolfrom, S. M. Olin and W. J. Polglase, *ibid.*, **72**, 1724 (1950); R. B. Kaplan, Ph.D. thesis, The Ohio State University, 1950.

[15] J. W. Baker, "Tautomerism," George Routledge and Sons, Ltd., London, 1934, pp. 173-186.

TABLE I

CONDENSATION PRODUCTS OF NITROALKANES WITH METHYL VINYL KETONE AND ACROLEIN

Products[a]	Mole ratio[b]	Yield, %	B.p., °C.	B.p., Mm.	M.p., °C.	n_D (°C.)	d^{20}_{20}	Molar refraction Calcd.	Molar refraction Found	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
5-Methyl-5-nitro-2-hexanone[c]	1:1	69.3	123–125	10		1.4444 (20.6)	1.056	40.17	40.03	52.81	52.53	8.23	8.18	8.80	8.92
2,4-Dinitrophenylhydrazone		65			130.5–131.5					46.02	46.35	5.05	5.12	20.64	20.09
Semicarbazone		72			192–193					44.43	44.75	7.46	7.46	25.91	25.26
5-Nitro-2-hexanone[c]	1:1	49.3	115–117.5	10		1.4396 (19.6)	1.0775	35.55	35.50	49.64	49.64	7.64	7.73	9.65	9.66
2,4-Dinitrophenylhydrazone		75			95.5–96.0					44.31	44.39	4.65	4.76	21.53	21.62
Semicarbazone		86			172–185					41.57	41.62	6.98	6.94	27.71	27.77
5-Nitro-2-pentanone[d]	10:1	50.9	117–120	10		1.4445 (19.0)	1.1174	30.93	31.19	45.79	45.92	6.92	6.98	10.68	10.71
2,4-Dinitrophenylhydrazone		52			135.8–136.5					42.45	42.37	4.21	4.23	22.50	22.36
Semicarbazone		98			140.0–140.7					38.29	38.19	6.43	6.40	29.77	29.79
4-Methyl-4-nitro-1-pentanal[e]	10:1	48.8	88.3–89.5	3		1.4469 (19.5)	1.0968	35.55	35.51	49.64	49.82	7.64	7.62	9.65	9.53
2,4-Dinitrophenylhydrazone		62			130.5–131.0					44.31	44.41	4.65	4.55	21.53	21.53
Semicarbazone		50			140–141					41.57	41.50	6.98	6.89	27.71	27.91
4-Nitro-1-pentanal[f]	30:1	50.9	79–81	3		1.4455 (19.6)	1.1232	30.93	31.09	45.79	45.77	6.92	6.90	10.68	10.69
2,4-Dinitrophenylhydrazone		52			96.0–96.5					42.45	42.48	4.21	4.16	22.50	22.53
4-Nitro-1-butanal[g]	100:1	40.0	87–88.2	2		1.4474 (19.8)	1.1902	26.31	26.36	41.03	41.17	6.03	6.22	11.96	12.06
2,4-Dinitrophenylhydrazone		56			135.3–136.0					40.41	40.36	3.73	3.80	23.56	23.53

[a] Upon final distillation, all products are colorless and may be stored for long periods without appreciable decomposition. [b] Mole ratio of nitroalkane to α,β-unsaturated carbonyl compound. [c] Positive iodoform reaction. [d] At a mole ratio of 1.1:1, the yield was 5.0%; at a mole ratio of 8:1, the yield was 12.4%. [e] At a mole ratio of 1.1:1, the yield was 11.3%. [f] At a mole ratio of 2:1, no product was obtained; at a mole ratio of 15:1, the yield was 14.7%; at a mole ratio of 40:1, the yield was 32.1%. [g] At a mole ratio of 100:1, and using sodium methoxide as the catalyst, the yield was 32.3%.

TABLE II

REDUCTION PRODUCTS OF NITROCARBONYL COMPOUNDS: NITROCARBINOLS

Products[a]	Yield, % $Al(OC_3H_7)_3$	Yield, % $NaBH_4$, H^-	B.p., °C.	B.p., Mm.	M.p., °C.	n_D (°C.)	d^{20}_{20}	Molar refraction Calcd.	Molar refraction Found	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
5-Methyl-5-nitro-2-hexanol[b]	93.3[c]	98.7	98–101	2		1.4490 (19.8)	1.015	41.68	41.38	52.15	52.37	9.38	9.40	8.69	8.73
α-Naphthylurethan (44% yield)					122.0–122.5					65.44	65.47	6.71	6.61	8.48	8.63
p-Nitrobenzoate (70% yield)					118.5–119					54.18	54.16	5.85	5.77	9.03	9.08
5-Nitro-2-hexanol	48.0[d]	50.7	122–125	10		1.4464 (19.5)	1.0607	37.06	37.02	48.97	49.05	8.91	9.03	9.52	9.41
p-Nitrobenzoate (36% yield)					102.5–103.0					52.70	52.62	5.44	5.41	9.46	9.38
3,5-Dinitrobenzoate					59.5–61.0									12.31	12.55
5-Nitro-2-pentanol[e]	24.0[d]	66.6, 61.2[f]	87–88	1		1.4493 (20.0)	1.0988	32.44	32.42					10.52	10.44
4-Methyl-4-nitro-1-pentanol	69.3[c]	54.8	111–115	3		1.4507 (19.4)	1.0951	37.06	36.68	48.97	49.11	8.91	9.03	9.52	9.53
p-Nitrobenzoate (44% yield)					92.5–93.0					52.70	52.65	5.44	5.44	9.46	9.48
3,5-Dinitrobenzoate (15% yield)					62–63									12.31	12.26
4-Nitro-1-pentanol[g]	26.7[c], 17.3[d]	56.3	91–92.5	1		1.4475 (20.0)	1.0951	32.44	32.50	45.10	44.94	8.33	8.03	10.52	10.29
4-Nitro-1-butanol		33.4	103–103.5	2		1.4510 (19.6)	1.1619	27.82	27.71					11.76	11.69
5,5-Dinitro-2-hexanol	87.9[c]	78.2, 54.5[f]	104–104.5	0.6		1.4636 (20.0)	1.240	42.67	42.73	37.50	37.18	6.29	6.02	14.58	14.52
p-Nitrobenzoate (100% yield)					106.0–106.5					45.75	45.67	4.43	4.14	12.31	12.38
4,4-Dinitro-1-pentanol	62.8[c]	67.6[f]	109–110	0.8		1.4669 (20.0)	1.293	38.06	38.22	33.71	33.99	5.66	4.81	15.73	15.82
p-Nitrobenzoate (99% yield)					78.0–78.5					44.04	43.84	4.00	4.27	12.84	12.59
5,5-Dinitro-2-pentanol[h]		48.5	115.5–116.5	1		1.4628 (19.7)	1.2806	38.18	38.33						

[a] Upon final distillation, all products are colorless and may be stored for long periods without appreciable decomposition. [b] Positive iodoform reaction. [c] The solvent reduction medium was 2-propanol. [d] The solvent reduction medium was toluene. [e] Characterized as 4-hydroxy-1-pentanal 2,4-dinitrophenylhydrazone (see Experimental). [f] The reducing agent was neutral-basic sodium borohydride. [g] Characterized as 5-hydroxy-2-pentanone 2,4-dinitrophenylhydrazone, m.p. 146–147°. [h] Reduction was carried out with 300% excess sodium borohydride at *p*H 3–4; the product contained small quantities of 5,5-dinitro-2-pentanone.

ride) for hydroxyl (2.9 microns) and nitro (6.2–6.4 microns) groups; no absorption characteristics of carbonyl (5.7–5.8 microns) groups) and (2) conversion of the alcohols into appropriate derivatives (Table II) in excellent yields. Further proof of structure of 4-nitro-1-pentanol, prepared from nitroethane and acrolein and subsequent reduction, was obtained by conversion of its sodium salt to 5-hydroxy-2-pentanone by the Nef reaction[6]; 5-hydroxy-2-pentanone was characterized by its 2,4-dinitrophenylhydrazone.[16]

Experimental

Reagents.—Nitromethane, nitroethane and 2-nitropropane (Commercial Solvents Corporation) were purified, after extraction with 10% sodium bicarbonate, by rectification over boric acid in a helix-packed column. Immediately prior to their use in the condensation reactions, the nitroalkanes were washed with 10% sodium bicarbonate solution and dried by filtration through anhydrous sodium sulfate. 4,4-Dinitro-1-pentanal and 5,5-dinitro-2-hexanone were prepared by reaction of 1,1-dinitroethane with acrolein and methyl vinyl ketone, respectively, in the presence of benzyltrimethylammonium hydroxide.[3] 5,5-Dinitro-2-pentanone was obtained from R. B. Kaplan.

Acrolein (Shell Chemical Company) was purified by distillation and then stabilized with hydroquinone (1 g. per 100 ml.). Methyl vinyl ketone (85% azeotrope, stabilized with hydroquinone, E. I. du Pont de Nemours and Co.) was used without further purification.

Commercial samples of Triton B (a 40% aqueous solution of benzyltrimethylammonium hydroxide, Rohm and Haas Co.), aluminum isopropoxide (practical grade, Eastman Kodak Company), and sodium borohydride (Metal Hydrides, Inc.) were used without further purification. 2-Propanol was dried by rectification from calcium oxide.

Condensation of Nitroalkanes with α,β-Unsaturated Carbonyl Compounds. Technique.—The condensations of methyl vinyl ketone and the nitroalkanes were usually run in ethyl ether for 15–24 hours at the reflux temperatures of the reaction mixtures. The volume of Triton B used as catalyst ranged from 6–9 ml. per mole of methyl vinyl ketone. Reactions of the nitroalkanes with acrolein were conducted at −20 to −5° and, as soon as the acrolein had been added, the mixtures were neutralized and the products were purified immediately. The volumes of 40% benzyltrimethylammonium hydroxide used as catalyst in the reactions of acrolein ranged from 40–50 ml. per mole of acrolein.

In the distillation of the products from reactions of acrolein with nitromethane and nitroethane, respectively, relatively large amounts of thermally unstable residues were left after removal of the 1:1 adduct. To prevent excessive decomposition and contamination of the product, it is advisable to keep the distillation temperature as low as possible. When large amounts of residue are present, it is often advantageous to force the product rapidly from the residue by use of a direct flame and then redistil the crude product in the usual manner.

4-Nitro-1-butanal. Procedure 1.—A solution of acrolein (9.0 g., 0.16 mole) and nitromethane (183.1 g., 3 moles) was added dropwise in 4 hours to a stirred mixture of nitromethane (793.5 g., 13 moles) and Triton B (7 ml.) at −3 to −8°. After addition was complete, 37% hydrochloric acid (5 ml.) in water (20 ml.) was added. The reaction mixture was washed with saturated sodium chloride solution and filtered through anhydrous sodium sulfate. Distillation of the product at reduced pressures, after removal of the unreacted materials by distillation at a pressure of 20 mm., gave: (1) **4-nitro-1-butanol** (8.0 g., 0.0683 mole) as a light yellow liquid in 42.7% yield, b.p. 86–87.5° (2 mm.) and (2) a black viscous residue (approximately 20 g.) which decomposes suddenly upon attempted distillation.

Procedure 2.—Nitromethane (732.5 g., 12 moles) was added in 5 minutes at temperatures below 10° to a mixture prepared from absolute methanol (50 ml.) and potassium (8.3 g., 0.16 mole). The stirred mixture was cooled to −20° and a solution of acrolein (9.0 g., 0.16 mole) and nitromethane (183.1 g., 3 moles) was added dropwise in 3 hours at −19 to −21°. After the addition was completed, the mixture was acidified with gaseous hydrogen chloride. The mixture was filtered from the potassium chloride that precipitated and then dried by filtration through anhydrous sodium sulfate. Distillation of the product, after distillation of the unreacted materials at a pressure of 20 mm., gave: (1) **4-nitro-1-butanal** (7.9 g., 0.0623 mole) as a yellow liquid in 39.5% yield, b.p. 76–84° (2 mm.) and (2) a black, thermally-unstable residue (13.9 g.).

5-Nitro-2-hexanone.—Methyl vinyl ketone (85% azeotrope, 82.4 g., 1.0 mole) was added dropwise in 3 hours to a refluxing mixture of nitroethane (78.8 g., 1.05 moles), ethyl ether (100 ml.) and benzyltrimethylammonium hydroxide (Triton B, 7 ml.). The reaction mixture was then stirred and heated for 15 hours. The mixture was cooled and washed with water and saturated sodium chloride. The mixture was dried over anhydrous sodium sulfate for 24 hours, then filtered and acidified with concd. hydrochloric acid. Distillation of the product at reduced pressures, after removal of unreacted materials at 43° (17 mm.), gave **5-nitro-2-hexanone** (71.6 g., 0.493 mole) as a light yellow liquid in 49.3% yield, b.p. 115–119° (10 mm.).

Proof of Structure of 5-Nitro-2-hexanone. 2,5-Hexanedione Dioxime.—A solution of 5-nitro-2-hexanone (1 g.), sodium hydroxide (0.4 g.), water (10 ml.) and methanol (5 ml.) at 0–5° was added dropwise to concd. sulfuric acid (2.5 ml.) in water (12 ml.) at 0–5°. The mixture was extracted with ethyl ether and the combined ether extracts were filtered through anhydrous sodium sulfate. The solvents were removed by vacuum evaporation; a colorless oil, crude 2,5-hexanedione, remained. The product was converted into its dioxime upon addition to a solution of hydroxylamine hydrochloride (10 g.), water (30 ml.) and 10% sodium hydroxide (20 ml.) and then heating the mixture at 70–80° for one hour. The mixture was then extracted with ethyl ether. The ether extracts were combined, filtered through anhydrous sodium sulfate, and then evaporated. A white powder remained which, after two recrystallizations from benzene, gave **2,5-hexanedione dioxime**, in 42% yield, m.p. 136–137°, lit.[7] 137°. The melting point of this derivative, when mixed with an authentic sample of 2,5-hexanedione dioxime, was not depressed.

Reductions with Aluminum Isopropoxide. 5-Nitro-2-hexanol.—5-Nitro-2-hexanone (21.8 g., 0.15 mole) was added in 5 minutes to a refluxing mixture of aluminum isopropoxide (30.6 g., 0.15 mole) and anhydrous toluene (100 ml., dried over sodium) in a Hempel column (40 cm. × 2 cm., packed with glass beads) attached to a downward condenser. During the next 30 minutes, the distillate (11 g., theoretical acetone is 8.4 g.) was collected over a temperature range of 58–76°; the mixture was then cooled immediately to 10°. Sulfuric acid (3 *N*, 200 ml.) was then added to the mixture at temperatures below 15°. The aqueous layer was separated and extracted with ethyl ether. The ether extracts and the toluene layer were combined, washed with water, saturated sodium bisulfite solution (2 × 100 ml., 5 minutes with each portion) and saturated sodium chloride solution, and filtered through anhydrous sodium sulfate. Distillation of the product at reduced pressures, after removal of solvents up to 29° (10 mm.), gave **5-nitro-2-hexanol** (10.5 g., 0.072 mole) as a yellow liquid in 48% yield; b.p. 122–127° (10 mm.). Redistillation of this material produced a pure, colorless product (Table II) in only slightly lower yield.

Reductions with Sodium Borohydride. Technique.—Selective reduction of aliphatic nitrocarbonyl compounds may be effected with aqueous methanolic sodium borohydride in either neutral, basic or acidic media (Table II, see Experimental examples). In the usual preferred technique, the reduction is carried out rapidly and simply in the *p*H range 7–10.5. With nitrocarbonyl compounds which are particularly sensitive to alkaline reagents, it is of value to conduct the reductions in acid medium. In the acidic reductions, the *p*H of the reaction mixture is maintained at 3–4 by the addition of 3 *N* sulfuric acid as needed; when the *p*H drops below 3, liberation of hydrogen is excessive and reduction is incomplete.

In the initial reduction experiments, methanolic solutions of sodium borohydride were added to the nitrocarbonyl compounds; however, this proved inconvenient because of the rapid reaction of sodium borohydride with methanol

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(16) D. A. Aten, Ph.D. Dissertation, The Ohio State University, Columbus, Ohio, August, 1951.

during storage at room temperatures. Aqueous solutions of sodium borohydride, stabilized with a few drops of concentrated sodium hydroxide solution, show much greater stability at room temperature, and therefore were employed in the subsequent reductions. The sodium borohydride solutions were prepared in beakers and added to the reaction mixture with a dropper; when a dropping funnel, buret, etc., was used, in which the wetted surface was large, the evolution of hydrogen was excessive. All reductions were conducted in aqueous methanol, the quantity of methanol being just sufficient to keep the nitro compounds in solution. The reduced products were contaminated with traces of the initial carbonyl compounds (determined by infrared analysis). The initial nitrocarbonyl compounds were removed by washing ethereal solutions of the product with several portions of saturated sodium bisulfite solution. It is especially necessary to shake the mixture thoroughly for at least five minutes with each portion of bisulfite solution; a long contact time is necessary to remove the contaminating compound.

4,4-Dinitro-1-pentanol.—Sodium borohydride solution (0.795 g., 0.021 mole, in 10 ml. of water containing one drop of 6 *N* sodium hydroxide) was added dropwise (15 minutes) to a stirred solution of 4,4-dinitro-1-pentanal (7.27 g., 0.0413 mole), methanol (25 ml.) and water (10 ml.) cooled in an ice–water mixture. The *p*H of the mixture, after the reaction was completed, was 9.2. The solution was partially neutralized with urea–acetic acid solution (10 ml., 0.028 mole, each of acetic acid and urea; the *p*H after the addition was 6); the *p*H was then adjusted to 3 by addition of 18 *N* sulfuric acid (2 ml.). The blue-green acidic solution was extracted with ether; the ether extract was dried with sodium sulfate and distilled to give **4,4-dinitro-2-pentanol** (4.97 g., 67.6% yield) (Table II), b.p. 114–118° (1.2 mm.).

5-Nitro-2-pentanol.—A solution of sodium borohydride (2.8 g., 0.075 mole), water (50 ml.), and concd. sodium hydroxide (one drop) was added dropwise in one hour to a slowly stirred mixture of 5-nitro-2-pentanone (19.7 g., 0.15 mole) and methanol (50 ml.). The temperature of the mixture was maintained at 20–25° by external cooling and its *p*H was kept at 3–4 (determined by *p*H meter) by the continuous addition of 3 *N* sulfuric acid. Hydrogen was evolved during addition of the sodium borohydride, and a white precipitate formed. After addition was completed, the mixture was allowed to stand for 5 minutes; excess sodium borohydride was then destroyed by adding concd. sulfuric acid (1 ml.). After the reaction mixture had been diluted to 350 ml. with water and neutralized with concd. sodium hydroxide, the homogeneous solution was extracted with ethyl ether. The ether extracts were combined, washed with saturated sodium bisulfite solution (3 × 150 ml., 5 minutes with each portion) and saturated sodium chloride solution, and filtered through anhydrous sodium sulfate. Benzene was added, and the solvents were removed by distillation. Distillation of the product, after a few crystals of boric acid had been added, gave **5-nitro-2-pentanol** (11.3 g., 0.1 mole) as a colorless liquid in 86.6% yield, b.p. 101–102.5° (2 mm.).

Because of the difficulty of preparing a solid derivative of the nitro alcohol, 5-nitro-2-pentanol was characterized by conversion into 4-hydroxy-1-pentanal 2,4-dinitrophenylhydrazone in the following manner. A solution of 5-nitro-2-pentanol (1 g.), sodium hydroxide (0.4 g.), methanol (5 ml.) and water (10 ml.) at 0–5° was added dropwise to a mixture of concd. sulfuric acid (2.5 ml.) in water (12 ml.) at 0–5°. The mixture was extracted with ethyl ether and the combined extracts were filtered through anhydrous sodium sulfate. The ether was removed by evaporation in a stream of air; crude 4-hydroxy-1-pentanal remained as a colorless oil. The hydroxyaldehyde was converted into its 2,4-dinitrophenylhydrazone by reaction with an ethanolic mixture of 2,4-dinitrophenylhydrazine and concd. sulfuric acid. The resulting precipitate was recrystallized 4 times from hot ethanol to give **4-hydroxy-1-pentanal 2,4-dinitrophenylhydrazone** in 37.3% yield, as fine yellow needles, m.p. 124.0–125.5°.

Anal. Calcd. for $C_{11}H_{14}N_4O_5$: N, 19.85. Found: N, 19.92.

COLUMBUS, OHIO

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, NEW YORK UNIVERSITY]

The Problem of the Configurations of Hydratropic Acid and Atrolactic Acid. Application of the Method of Melting Point–Composition Diagrams

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The solid–liquid phase relationships of (+)-hydratropamide and the enantiomorphous (+)-2-chloro-2-phenylacetamides have been found to differ, in that (+)-hydratropamide forms solid solutions with (+)-2-chloro-2-phenylacetamide but an immiscible mixture with (−)-2-chloro-2-phenylacetamide. This result, considered in context with the fact that (+)-2-chloro-2-phenylacetamide was obtained from L(+)-mandelic acid *via* the use of thionyl chloride, independently confirms prior conclusions regarding the configuration of (+)-hydrotropic acid relative to that of glyceraldehyde. The solid–liquid phase relationships of (−)-atrolactic acid and the enantiomorphous mandelic acids have been investigated and found to be of the same type. An attempt to confirm the configuration of atrolactic acid by the method of melting point–composition diagrams was thus rendered ineffective.

Optically active substances may exhibit a variety of phase relationships with their enantiomers; thus racemic mixtures ("conglomerates"), compounds ("racemates") and solid solutions ("pseudoracemates") are encountered. Differences in phase behavior have often been utilized in the problem of relating the configurations of similarly constituted substances.[1] The basis for such correlations rests on the premise that a significance, capable of being rationalized in terms of molecular configuration, may be attached to any *difference* in the phase behavior of mixtures of configurationally related substances, Cabcx and Cabcy (or xcbaC and ycbaC, the corresponding enantiomers), and in the phase behavior of mixtures of configurationally quasi-enantiomorphous substances, Cabcx and ycbaC (or xcbaC and Cabcy). In practice, only three types of such *differences* in behavior have been noted. As of type 1 one may consider instances where mixtures of Cabcx and Cabcy form solid solutions while mixtures of Cabcx and ycbaC form a compound. The very reasonable conclusion that Cabcx and Cabcy are configurationally related while Cabcx and ycbaC are quasi-enantiomorphous follows from the premise that solid solution formation may be regarded as a consequence of a similarity in over-all geometry (and therefore mutual replaceability in the crystal lattice), while compound formation may be viewed as a phenomenon, *i.e.*, quasi-racemate

[1] For excellent reviews of such work, *cf.* H. Lettré, *Erg. Enzymforsch.*, **9**, 1 (1943), and A. Fredge, in "The Svedberg," Almqvist and Wiksells, Uppsala (Sweden), 1944, pp. 261 ff.