The Reduction of Nitroalkenes to Nitroalkanes with Aqueous Sodium Borohydride[1]

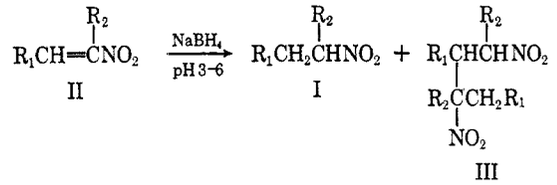
A. I. MEYERS AND J. C. SIRCAR

Department of Chemistry,
Louisiana State University in New Orleans,
New Orleans, Louisiana 70122

Received April 5, 1967

Recently it was shown that heterocyclic systems containing the C=N group[2] (dihydro-1,3-thiazines, 1-pyrrolines) were readily reduced in aqueous acidic sodium borohydride without detrimental side reactions, *e.g.*, ring cleavage. Since these systems gave good yields of reduced products, it was of interest to determine the behavior of nitroalkenes with sodium borohydride. Reductions of nitroalkenes with complex metal hydrides had been reported[3] earlier as an attractive route to primary and secondary nitroalkanes. Although excellent methods are available for preparing nitroalkanes by direct displacement and oxidation,[4] reduction of nitroalkenes derived from aldehydes affords a method to extend the length of a carbon chain. This is especially useful when RCHO is available and RCH_2CH_2X and RCH_2CHO is not.

Conjugated nitroalkenes (II) can be smoothly and efficiently reduced to the corresponding nitroalkanes (I) using sodium borohydride in aqueous ethanol or acetonitrile at 0–5°. The significant innovation in this technique requires that the pH of the reduction medium be maintained between the limits 3–6. This condition



II I III

inhibits the formation of the α-carbanion in the nitroalkane and retards Michael addition to the nitroalkene, which results in dimeric products,[3] III (Table I). The reduction (Table I) proceeded in good yield for nitroalkenes derived from aliphatic aldehydes (IIa–IIc) and in variable yields for nitroalkenes derived from aromatic aldehydes (IId–IIh). It is significant that, in only two cases investigated, dimeric products were obtained by this reductive procedure. Both nitroalkenes (IId, IIf) which produced dimers are vinyl-unsubstituted β-aryl nitrostyrenes, possessing considerable delocalization toward the nitro group, making them particularly susceptible to Michael addition. The β-pyridyl (IIg) and β-indolyl (IIh) derivatives are most likely protonated to a considerable extent in the acidic medium and therefore incapable of interaction with the nitrovinyl moiety. Unreacted IIh was the only other substance obtained after treatment with sodium borohydride.

TABLE I

NITROALKANES (I) AND DIMERS (III) OBTAINED BY REDUCTION OF NITROALKENES (II) WITH SODIUM BOROHYDRIDE

Compd	R_1	R_2	Yield I,[a,e] % This method	Yield I,[a,e] % Other[h]	Yield III,[a] % This method	Yield III,[a] % Other[h]
IIa	*n*-Propyl	H	68[b]	82	0	11
IIb	*n*-Propyl	CH_3	70[b]	63	0	11
IIc	*n*-Hexyl	H	85	...	0	...
IId	Phenyl	H	48	14	43	24
IIe	Phenyl	CH_3	17	43	0	0
IIf	2,3-Dimethoxyphenyl	H	56[c]	...	30[c]	...
IIg	2-Pyridyl[g]	H	55[b,c]	...	0	...
IIh	2-Indolyl[g]	H	30[d,f]	...	0	...

[a] Yields are based upon pure products isolated by preparative layer chromatography. [b] Reduction was quantitative but losses due to volatility of product were experienced. [c] Analytical data for new compounds are given in Experimental Section. [d] The remainder of material was recovered as starting material. [e] The solvent used for reductions were for IIa, IIb, aqueous ethanol; IIc–IIh, aqueous aceonitrile. [f] Mp 53–54° (lit. mp 53.5°, W. E. Noland and P. J. Hartmann, *J. Am. Chem. Soc.*, **76**, 3227 (1964)). [g] These nitroalkenes are rather unstable to air and darken rapidly. [h] See ref 3.

Of particular interest was the reduction of the pyridyl-substituted nitroalkene (IIg). When the latter was subjected to the usual reaction conditions there was obtained quantitatively an oil which exhibited the expected unconjugated nitro stretching band at 6.43 μ and the complete absence of the conjugated nitro band at 6.6 μ. The nmr spectrum showed a two-proton triplet at τ 5.11 (J = 7 cps). This data was in total agreement with the anticipated product (Ig); yet a search of the literature provided only a single reference to this compound which reported[5] that it melts at 145°. This disclosure states that the treatment of 2-vinylpyridine with sodium nitrite in ethanolic hydrogen chloride leads to 2-(2-nitroethyl)pyridine (Ig). Repeated attempts to duplicate this condensation following the sketchy details given as well as many modifications failed to produce any identifiable compound other than recovered 2-vinylpyridine or its hydrochloride salt. The product reported to melt at 145° could not be obtained. The nitroalkenes (IIa–IIh) employed in this study were obtained through usual route of condensing the appropriate carbonyl compound with a nitroalkane[3] and esterifying the resulting nitro alcohol with acetic anhydride or acetyl chloride. The aryl-substituted nitroalkenes (IId–IIh) were prepared in a single step from the aldehydes and nitroalkanes using ammonium acetate. When the acetates were treated with sodium acetate in ethyl acetate, the nitroalkenes were produced in good yield by separation on preparative layer plates (Experimental Section). The purity of the reduced products removed from the preparative plates was further checked by gas chromatography, cleavage to the aldehydes *via* the Nef reaction,[6] and elemental analyses. Few systematic reports on the chemical shifts of nitro alcohols, nitro acetates, nitroalkenes, and nitroalkanes derived from homolo-

(1) This study was supported by funds granted by the National Institutes of Health (RG-DGMS-06248-08).

(2) A. I. Meyers and J. M. Greene, *J. Org. Chem.*, **31**, 556 (1966); A. I. Meyers and W. Y. Libano, *ibid.*, **26**, 4399 (1961). It has now been shown in this laboratory that dihydro-1,3-oxazines are cleanly reduced to tetrahydro-1,3-oxazines with aqueous sodium borohydride: A. I. Meyers and A. Nabeya, unpublished results.

(3) H. Shechter, D. E. Ley, and E. B. Roberson, Jr., *J. Am. Chem. Soc.*, **78**, 4984 (1956); A. Hassner and C. Heathcock, *J. Org. Chem.*, **29**, 1350 (1964).

(4) N. Kornblum, *Org. Reactions*, **12**, 101 (1962).

(5) F. F. Cislak and L. H. Sutherland, U. S. Patent 2,490,672 (1949); *Chem. Abstr.*, **44**, 4043*i* (1950).

(6) J. V. Nef, *Ann.*, **280**, 263 (1894); K. Johnson and E. F. Degering, *J. Org. Chem.*, **8**, 10 (1943).

TABLE II

CHEMICAL SHIFTS (τ) FOR α AND β PROTONS IN NITRO COMPOUNDS[a,b]

			$R_1C(H_B)(OH)-C(H_A)(R_2)NO_2$		$R_1C(H_B)(OAc)-C(H_A)(R_2)NO_2$		$R_1C(H_B)=C(H_A)(R_2)-NO_2$			$R_1CH_2C(H_A)(R_2)NO_2$
Compd[h]	R_1	R_2	H_B	H_A	H_B	H_A	H_B	H_A	J_{AB}	H_A
a	*n*-Propyl	H	5.75(m)	5.61(d)	4.52(m)	5.42(d)	2.58(m)	3.00(d)	13.5	5.60(t)
b	*n*-Propyl	CH_3	6.00(m)	5.51(m)	4.68(m)	5.28(m)	2.90(t)	7.85(s)[c]	...	5.50(m)
c	*n*-Hexyl	H	5.98(m)	5.62(m)	4.53(m)	5.48(d)	2.67(m)	3.02(d)	14.0	5.67(t)
d	Phenyl	H	*g*		*g*		2.02(d)	2.40	14.0	5.60(t)
e	Phenyl	CH_3	*g*		*g*		2.00(s)	7.62(s)[c]	...	*f*
f	2,3-Dimethoxyphenyl	H	*g*		*g*		1.80(d)	2.27(d)	15.5	5.51(t)
g	2-Pyridyl	H	4.50(q)	5.25(q)			*e*	2.50[d]	...	5.11(t)
h	2-Indolyl	H	*g*		*g*		1.80	2.60[e]	...	5.31(t)

[a] All spectra determined in deuteriochloroform using TMS as internal standard. [b] Signal shapes are given as singlet (s), doublet (d), triplet (t), multiplet (m), quartet (q). [c] Methyl singlet, $R_2 = CH_3$. [d] B portion of AB system masked under aromatic signals. [e] Masked under aromatic signals. [f] Product not isolated and yield (Table I) determined by gas chromatography using dodecane as internal standard. [g] The methods of synthesis gives the nitroalkene without formation of intermediate nitro alcohols. [h] Registry numbers: nitro alcohol a, 2224-37-5; nitro alcohol b, 5448-00-0; nitro alcohol c, 2224-39-7; nitro alcohol g, 14255-55-1; nitro ester a, 3428-90-8; nitro ester b, 14255-57-3; nitro ester c, 5469-20-5.

gous series are available[7] and are therefore recorded in Table II.

Experimental Section

All melting points are corrected and were determined on a Fisher-Johns apparatus. Nmr spectra were taken on a Varian A-60 instrument[8] and infrared spectra were taken on a Beckman IR-5A. Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn. Silica used for preparative layer chromatography was Brinkmann (Merck) PF_{254} and plates were made to 2-mm thickness. The applied product were eluted with an appropriate solvent (see below) and visualized with a short-wavelength (2537 A) lamp.

1-Nitro-2-octanol.—This compound has been previously prepared[9] by vapor phase nitration techniques. In this study the nitro alcohol was prepared by stirring, for 90 hr, a mixture of 14.5 g of *n*-heptaldehyde, 8.5 g of nitromethane, 1.5 ml of 10% sodium hydroxide, and 13 ml of ethanol. Dilution with 50 ml of water and extraction of the organic phase with dichloromethane gave, after drying, 45% yield of the nitro alcohol: bp 105–110° (2.4 mm); λ^{film} 2.90, 6.43, 7.22 μ; nmr (Table II). All the other nitro alcohols in this study were prepared according to this procedure.

2-Acetoxy-1-nitrooctane.—A mixture containing 1.18 g (11.0 mmoles) of acetic anhydride, 2.19 g (10 mmoles) of 1-nitro-2-octanol, and 0.01 ml of sulfuric acid was heated at 60–70° for 2.5 hr. Ether (10 ml) was added and the solution washed with 1% sodium bicarbonate solution, dried, and concentrated to give 2.5 g of the nitro ester: λ^{film} 5.80, 6.43, 7.22 μ; no hydroxyl band was evident; nmr (Table II).

1-Nitro-1-octene.—This procedure, utilizing silica plates for separation and isolation, is novel and, therefore, reported in detail. This was employed for all nitroalkenes reported herein.

A solution of 2.40 g (9.0 mmoles) of the nitro acetate in 200 ml of ethyl acetate was treated with 2.40 g of fused sodium acetate and the mixture stirred at room temperature for 50 hr. The solid material was removed by filtration and the filtrate concentrated to give an oily residue which was dissolved in ether and washed with water. After drying (sodium sulfate) and concentration of the ethereal solution, there was obtained 1.85 g of a mixture of nitroalkene and unreacted nitro acetate (determined by infrared spectroscopy). Examination of this mixture on thin layer plates (silica PF_{254}) showed only a single spot, indicating that elimination of acetic acid from unreacted nitro ester was taking place on silica. Preparative layer chromatography was then carried out as follows. The crude mixture (1.08 g) was applied to a silica plate (20 × 40 cm) of 2-mm thickness and the band eluted with hexane–ether (1:1). The uppermost zone (R_f ~0.6) was cut from the plate and extracted with ether and the extracts were concentrated to give 809 mg (95%) of pure 1-nitro-1-octene as a pale yellow oil: λ^{film} 6.08, 6.57, 7.37 μ; nmr (Table II).

1-Nitrooctane. General Technique of Reduction.—All the nitroalkanes (I) reported were prepared utilizing the following procedure. To a solution of 1-nitro-1-octene (733 mg, 3.6 mmoles) in 20 ml of acetonitrile, previously cooled to 0–5°, was added with magnetic stirring a solution containing sodium borohydride (733 mg), 0.1 ml of 40% sodium hydroxide, and 14 ml of water. The rate of addition of the borohydride solution was determined by the ability to control the pH of the acetonitrile solution. Periodic addition of 3 *N* hydrochloric acid was required to maintain the pH between 3 and 6. Additions were usually within 0.5 hr. The homogeneous solution was stirred for 1–2 hr at 0–5° and then diluted with 100 ml of water. The organic layer was extracted thoroughly with dichloromethane and the latter solution dried (sodium sulfate). Concentration of the extracts gave an oil, 690 mg, which exhibited only a single spot on thin layer plates. When the crude material was applied to a silica plate (20 × 40 cm) of 2-mm thickness and eluted with hexane ether (1:1) there was obtained, after removing the single zone with dichloromethane, 620 mg (85%) of 1-nitrooctane as a colorless oil: λ^{film} 6.45, 6.93, 7.22 μ; nmr (Table II). The purity of the product was also determined using vapor phase chromatography (DC-11 silicone oil, 180°) and only a single peak was observed.

2-(2,3-Dimethoxyphenyl)-1-nitroethane (If) and 2,4-Bis(2,3-dimethoxyphenyl)-1,3-dinitrobutane (IIIf).—A solution of 4.0 g (19 mmoles) of 2,3-dimethoxy-β-nitrostyrene (IIf) in 100 ml of acetonitrile was cooled to 0–5° and treated dropwise with a solution containing 3.64 g of sodium borohydride and 0.1 ml of 40% sodium hydroxide as described in the general procedure. The dichloromethane solution, after concentration, gave 3.80 g of an oil which partly solidified after standing in the refrigerator. The oil was removed by washing with cold dichloromethane (2–3 ml) and the remaining solid recrystallized from methanol yielding 1.2 g (30%) of dimer (IIIf): mp 151–153°; λ^{CHCl_3} 6.27, 6.43, 6.73, 7.24 μ; nmr (deuteriochloroform), 2.90–3.35 (6 H), 5.00–5.65 (4 H), 6.05–6.32 (12 H), 6.95 (2 H).

Anal. Calcd for $C_{20}H_{24}O_8N_2$: C, 57.14; H, 5.75; N, 6.66. Found: C, 57.25; H, 5.86; N, 6.64.

The dichloromethane solution from above was applied to a preparative layer plate and eluted with dichloromethane to give 56% of the reduced nitroalkane (If) as a pale yellow oil: λ^{film} 6.28, 6.45, 6.73, 6.98, 7.22 μ; nmr (Table II).

2,3-Dimethoxyphenylacetaldehyde (Nef Reaction).—A solution of 0.523 g (2.5 mmoles) of the dimethoxyphenylnitroethane (If) in 5 ml of methanol was treated with 10 ml of 4% sodium hydroxide solution and then stored at 0° for 18 hr. The solution was then added dropwise into an aqueous sulfuric acid solution (2.5 ml of concentrated sulfuric acid and 12 ml of water) at 0° and stirred for 30 min. The oil which separated was taken up in dichloromethane, washed several times with water, and dried

(7) W. Hofman, L. Stefaniak, T. Urbanski, and M. W. Tanowski, *J. Am. Chem. Soc.*, **86**, 554 (1964).

(8) Obtained by a grant from the National Science Foundation (GP-3674).

(9) R. M. Sherwood and T. A. Washall, *Anal. Chem.*, **38**, 1009 (1966).

over sodium sulfate. Concentration of the extract and examination of the infrared spectrum of the residue (0.456 g) revealed that it was a mixture of aldehyde and nitroalkane. The mixture was applied to a preparative layer plate containing a 2 mm pad of silica and eluted with hexane–ether (1:1). The uppermost band, after being cut from the plate and washed with ether, produced 0.124 g of 2,3-dimethoxyphenylacetaldehyde as an oil. A 2,4-dinitrophenylhydrazone derivative was prepared quantitatively and, upon recrystallization from methanol, melted at 136–137°.

Anal. Calcd for $C_{16}H_{16}N_4O_6$: C, 53.33; H, 4.48; N, 15.55. Found: C, 53.31; H, 4.45; N, 15.84.

2-(2-Pyridyl)nitroethane (Ig) was prepared quantitatively from the corresponding nitroalkene (IIg)[10] by the general procedure for reduction. However, the compound was rather unstable to air and could be kept for prolonged periods under a nitrogen atmosphere at low temperatures. A satisfactory elemental analysis could not be obtained although its spectrum (Table II) was in total agreement with the assigned structure. Attempts to prepare a hydrochloride gave an unstable salt, mp 106–108°. A picrate salt was prepared, mp 129–130° dec.

Anal. Calcd for $C_{13}H_{11}N_5O_9$: C, 40.95; H, 2.91; N, 18.19. Found: C, 40.80; H, 2.91; N, 18.37.

Registry No.—Ia, 628-05-7; Ib, 14255-44-8; Ic, 629-37-8; Id, 6125-24-2; If, 14255-59-5; Ig, 14255-47-1; Ig hydrochloride, 14255-48-2; Ig picrate, 14255-49-3; Ih, 14255-50-6; IIa, 3156-72-7; IIb, 6065-17-4; IIc, 4550-05-4; IId, 102-96-5; IIe, 705-60-2; IIf, 2815-67-0; IIg, 14255-17-5; IIh, 14255-18-6; IIIf, 14319-56-3; 2,3-dimethoxyphenylacetaldehyde 2,4-dinitrophenylhydrazone, 14255-58-4; sodium borohydride, 1303-74-8.

(10) K. W. Merz and H. J. Janssen, *Arch. Pharm.*, **297**, 307 (1964); *Chem. Abstr.*, **61**, 4306*d* (1964).

Addition of Nitrosyl Chloride to Olefins. Synthesis of Some Chloro Ketones[1]

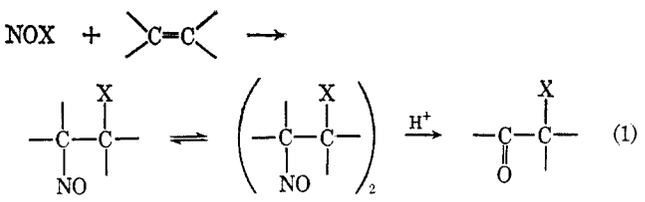
B. W. PONDER AND DAVID R. WALKER

Department of Chemistry, University of Alabama, University, Alabama 35486

Received January 13, 1967

Both acyclic and cyclic α-chloro ketones have been used extensively as intermediates in various synthetic schemes as well as in reaction mechanism studies. These chloro ketones have generally been prepared by passing chlorine gas into a solution of the ketone in ethanol[2] or into an aqueous solution containing the ketone, calcium chloride, and calcium carbonate.[3] These methods usually work satisfactorily in the simple saturated ketone systems, even though significant amounts of di- and polychlorinated products are observed.[3] The above methods become less desirable in systems which are susceptible to the oxidizing action of elemental chlorine.

The addition reaction of nitrosyl halides with olefins[4] (eq 1) yields monomeric and dimeric nitroso chlorides which in most cases can be isolated in good yields as white crystalline solids. These adducts have been converted in some cases[5] to the corresponding chloro ketones by the use of strong acids. The use



(1)

of strong acids for the hydrolysis step subjects this method to the same disadvantage inherent in the previously cited procedures using elemental chlorine, *i.e.*, oxidation and degradation of other vulnerable positions in the molecule. The use of strong acid for this hydrolysis step is not necessary, however, and may be avoided completely by substituting the milder method of levulinic acid hydrolysis.[6] Meinwald and coworkers[7] used the levulinic acid method of hydrolysis successfully in connection with their study of the steric course of addition of nitrosyl halides to olefins. The present study was designed to develop further the sequence of nitrosyl halide addition to olefins followed by levulinic acid hydrolysis into a useful general synthesis of chloro ketones.

Several representative olefins were chosen for study although no attempt was made to elucidate the structural requirements for the reaction. Good yields of the nitroso chloride adducts were obtained consistently; in most instances the adduct precipitated from the reaction solution as the white dimer, although in a few others very little solid was obtained. In these latter cases, an intensely blue solution was observed, indicating the nitroso chloride monomer to be present.

The adducts were hydrolyzed to the corresponding chloro ketones (eq 1), by warming with levulinic acid made 0.1 *N* in hydrochloric acid. The results of these chloro ketone preparations are summarized in Table I. The yields reported for these chloro ketones are based on the starting olefin.

TABLE I

Olefin reacted	Final product	Yield, %	Carbonyl absorption, cm^{-1} Found	Reptd
Cyclopentene	2-Chlorocyclopentanone	59	1755	1755[a]
Cyclohexene	2-Chlorocyclohexanone	63	1725	1722[a]
Cycloheptene	2-Chlorocycloheptanone	93	1715	1716[a]
trans-Stilbene	*trans*-Stilbene	...	...	...
cis-Stilbene	*cis*-Stilbene	...	...	...
Cyclopentadiene	4-Chloro-2-cyclopentenone	11	1725 1740 (sh)	...
Norbornene	*exo*-3-Chlorononcamphor	68	1758	1757[b]
Norbornadiene	*exo*-3-Chlorodehydronorcamphor	65	1750	1748[b]

[a] E. J. Corey, *J. Am. Chem. Soc.*, **75**, 2301 (1953). [b] See ref 7.

Cyclohexene reacts with nitrosyl chloride at 10° to give a mixture of monomeric and dimeric nitroso chlorides. Surprisingly, a significant amount of 2-chlorocyclohexanone was formed directly in this addition reaction, even before hydrolysis. *trans*-Stilbene adds nitrosyl chloride at 20° in carbon tetrachloride to give a white solid, mp 131–132°. The characteristic

(1) Presented in part at the Southeastern Regional Meeting of the American Chemical Society, Louisville, Oct 29, 1966.

(2) M. S. Newman, M. D. Farbman, and H. Hipsher, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p 188.

(3) H. W. Wanzlick, G. Gollmer, and H. Milz, *Chem. Ber.*, **88**, 69 (1955).

(4) W. A. Tilden, *J. Chem. Soc.*, **28**, 514 (1875).

(5) O. Wallach, "Terpene and Campher," 2nd ed, Viet and Co., Leipzig, 1914.

(6) C. H. DePuy and B. W. Ponder, *J. Am. Chem. Soc.*, **81**, 4629 (1959).

(7) J. Meinwald, Y. C. Meinwald, and T. N. Baker, III, *ibid.*, **86**, 4074 (1964).