A 0.474-g amount of unreacted starting material was also isolated accompanied by 0.418 g of an amorphous substance which was not identified.

3β,15β-Diacetoxy-14β-hydroxy-5β-bufa-20,22-dienolide (15β-Acetoxybufalin Acetate, 3c). Method A. From 14-Dehydrobufalin Acetate (1a). Olefin **1a** (0.6 g) in acetic acid (36 ml)–water (1.8 ml) was allowed to react with iodine (1.3 g) and silver acetate (1.3 g) as described for the Woodward cis hydroxylation of 14-dehydrobufalin (**1b**). Chromatography of the crude product on silica gel and elution with 5:1 hexane–acetone yielded 0.123 g (20.5%) of diacetate **3c** as an amorphous solid: TLC R_f 0.37 (green to light blue color with sulfuric acid); uv λ_{max} (EtOH) 297 nm (log ϵ 3.22); ir ν_{max} (KBr) 3420 (OH), 1755 (ester CO), 1740–1710 (ester CO and conjugated CO), 1635, 1537 (conjugated C=C), 1260, 1250, 1240, 1230 (ester CO), 1120, 1025, 950, 830, 790, 750 cm^{-1}; NMR (10% solution in $CDCl_3$) δ 0.76 (3 H, s, 18-CH_3), 0.97 (3 H, s, 19-CH_3), 2.03 (3 H, s, 3-OAc), 2.11 (3 H, s, 15-OAc), 5.02 (1 H, broad peak, 3α-H), 5.54 (1 H, broad t, 15α-H), 6.27 (1 H, d, J = 9.5 Hz, 23-H), 7.22 (1 H, d, J = 2.5 Hz, 21-H), 7.84 (1 H, dd, J = 9.5 and 2.5 Hz, 22-H); mass spectrum m/e 486 (M^+), 468 ($M^+ - H_2O$), 426 (M^+ – AcOH), 408 ($M^+ - H_2O$ – AcOH), 348 (M^+ – 2AcOH).

Anal. Calcd for $C_{28}H_{38}O_7$: C, 69.11; H, 7.87. Found: C, 69.37; H, 7.91.

In addition to 15β-acetate **3c**, a 0.231-g amount of unreacted starting material was recovered.

Method B. From 15β-Hydroxybufalin Acetate (3a). A 0.05-g sample of acetate **3a** was acetylated with acetic anhydride (0.7 ml)–pyridine (1.2 ml) at room temperature over 18 hr. The crude product (0.06 g) was purified as described in method A to afford 0.043 g (86%) of diacetate **3c** identical with the specimen obtained by method A.

Method C. From 15β-Acetoxybufalin (3b). Acetylation of acetate **3b** (0.06 g) was conducted as described in method B above and 0.041 g (84%) of diacetate **3c** was isolated and found identical with the product of method A.

15β-Hydroxybufalin (3β,14β,15β-Trihydroxy-5β-bufa-20,22-dienolide, 3d). Method A. From 15β-Hydroxybufalin 3-Acetate (3a). A solution of 3β-acetate **3a** (0.059 g) in 80% ethyl alcohol (33 ml) containing sulfuric acid (0.22 ml) was allowed to remain at room temperature for 5 days. The solution was poured into water, neutralized with dilute sodium bicarbonate, and extracted with chloroform and the combined extract was washed with water. After removal of solvent the residue (0.05 g) was chromatographed on a column of silica gel and the fractions eluted with 3:1 to 2:1 hexane–acetone were recrystallized from acetone–hexane to provide 0.032 g of 15β-hydroxybufalin melting at 267–269° (lit.[6] mp 266–269°) as needles: TLC R_f 0.15 (light blue color with sulfuric acid); uv λ_{max} (MeOH) 297.5 nm (log ϵ 3.23); ir ν_{max} (KBr) 3460, 3428 (OH), 1720, 1700 (conjugated CO), 1635, 1540 (conjugated C=C), 1130, 1040, 1030, 950, 835, 745 cm^{-1}; NMR (10% solution of $CDCl_3$) δ 0.71 (3 H, s, 18-CH_3), 0.91 (3 H, s, 19-CH_3), 4.11 (1 H, broad peak, 3α-H), 4.26 (1 H, broad peak, 15α-H), 6.27 (1 H, d, J = 9.5 Hz, 23-H), 7.22 (1 H, d, J = 2.5 Hz, 21-H), 7.83 (1 H, dd, J = 9.5 and 2.5 Hz, 22-H), mass spectrum m/e 402 (M^+), 384 ($M^+ - H_2O$), 366 ($M^+ - 2H_2O$).

Anal. Calcd for $C_{24}H_{34}O_5$: C, 71.61; H, 8.51. Found: C, 71.55; H, 8.48.

Method B. From 15β-Acetoxybufalin (3b). The preceding experiment was repeated employing 15β-acetate **3b** (0.05 g) in 80% methyl alcohol (60 ml) containing 0.2 ml of 35% hydrochloric acid. The product was purified to yield 15β-hydroxybufalin weighing 0.019 g and melting at 265–268°.

Method C. From 15β-Acetoxybufalin Acetate (3c). The acid hydrolysis reaction of method A was applied to diacetate **3c** (0.025 g) using 30 ml of either 80% ethyl alcohol or methyl alcohol containing sulfuric acid (0.1 ml). In this experiment the 15β-hydroxybufalin (0.008 g, mp 263–267°) was isolated by preparative thin layer chromatography.

The specimens of 15β-hydroxybufalin (**3b**) obtained by means of methods A–C were found to be identical.

3β-Acetoxy-14β-hydroxy-15-oxo-5β-bufa-20,22-dienolide (4). A solution of 15β-hydroxybufalin 3-acetate (**3a**, 0.075 g) in acetic acid (1.5 ml) was treated with a solution of chromium trioxide (0.028 g) in acetic acid (0.5 ml)–water (0.03 ml). After 1.5 hr, stirring was discontinued and 3.5 hr later methyl alcohol (0.3 ml) was added. The mixture was poured into ice–water and extracted with chloroform and the combined extract was washed with water. Solvent was removed and the residue (0.077 g) was chromatographed on a column of silica gel. Elution with 6:1 hexane–acetone and recrystallization of this fraction from acetone led to 0.049 g of 15-ketone **4** as needles melting at 259–261°. The ketone **4** was identical with specimens obtained by analogous oxidation of trans diol **5** and α-epoxide **6**.[8]

Registry No.—**1a**, 22612-50-6; **1b**, 7439-77-2; **2**, 39844-84-3; **3a**, 39844-82-1; **3b**, 55156-32-6; **3c**, 39844-83-2; **3d**, 39844-81-0; **4**, 31444-12-9; osmium trioxide, 20816-12-0; silver acetate, 563-63-3; acetic anhydride, 108-24-7; chromium trioxide, 1333-82-0.

References and Notes

(1) Part 93 of the series, Steroids and Related Natural Products. For Part 92 refer to Y. Kamano, G. R. Pettit, and M. Tozawa, *J. Chem. Soc.*, in press. For Part 29 of the bufadienolide series, see Y. Kamano, G. R. Pettit, and M. Inoue, *J. Org. Chem.*, **39**, 3007 (1974).

(2) We are pleased to acknowledge support of this investigation by the National Cancer Institute, National Institutes of Health (performed pursuant to Contract N01-CM-12308 with the Division of Cancer Treatment, NCI, Department of Health, Education and Welfare), the J. W. Kieckhefer Foundation, and the Fannie E. Rippel Foundation.

(3) (a) Department of Chemistry, School of Medicine, Premedical Course, The Jikei University, Kokuryomachi, Chofushi, Tokyo, 182, Japan; (b) Department of Chemistry, Faculty of Science, Tokyo Metropolitan University, Fukazawa, Setagayaku, Tokyo 158, Japan.

(4) On a recent visit to the People's Republic of China one of us (GRP) saw specimens of *Bufo bufo gargarizans* prominently displayed in medical collections and learned of current applications of Ch'an Su in traditional medical treatment, particularly for its anesthetic, cardiac, and antiinflammatory effects. These interesting observations were made while a member of the National Academy of Sciences Pharmacology Delegation to the People's Republic of China, June 1974.

(5) J. J. Abel and D. I. Macht, *J. Pharmacol. Exp. Ther.*, **3**, 319 (1911).

(6) N. Höriger, D. Živanov, H. H. A. Linde, and K. Meyer, *Helv. Chim. Acta*, **55**, 2549 (1972).

(7) For leading references to the Woodward cis hydroxylation reaction see footnote 11 of Y. Kamano, M. Tozawa, and G. R. Pettit, *J. Org. Chem.*, **40**, 793 (1975).

(8) G. R. Pettit, Y. Kamano, F. Bruschweiler, and P. Brown, *J. Org. Chem.*, **36**, 3736 (1971).

(9) G. R. Pettit, L. E. Houghton, J. C. Knight, and F. Bruschweiler, *J. Org. Chem.*, **35**, 2895 (1970).

(10) G. R. Pettit and Y. Kamano, *J. Chem. Soc., Perkin Trans. 1*, 725 (1973).

(11) M. Okada and Y. Saito, *Chem. Pharm. Bull.*, **17**, 515 (1969).

A New Method for the Dehydration of Nitro Alcohols

Jack Melton and John E. Mc Murry*

Thimann Laboratories, University of California, Santa Cruz, California 95064

Received February 26, 1975

While synthesizing a variety of nitro compounds for use in connection with our recent study of nitro group reduction by titanous ion,[1] we attempted to prepare several nitroolefins by dehydration of the corresponding 2-nitro alcohols. These nitro alcohols are, of course, readily available by aldol-type addition of nitroalkanes to aldehydes and ketones.[2,3] A search of the literature reveals that, although a number of methods have been employed using such reagents as phosphorus pentoxide[4] and phthalic anhydride,[5] such dehydrations are normally carried out by first acetylating the hydroxyl and then effecting elimination with sodium acetate.[6] In our experience, however, yields obtained using this method were low and variable, perhaps because of the severe reaction conditions (5 hr, 120°). We have therefore devised a new, mild method of dehydration which we wish to report here.

We reasoned that the key to effecting dehydration lay simply in transforming the hydroxyl into a better leaving group, and we therefore treated the representative nitro alcohol, 2-nitro-3-pentanol, with 1 equiv of methanesulfonyl chloride in methylene chloride at 0°.[7] After addition of triethylamine and stirring for 15 min at 0°, 2-nitro-2-pentene could be isolated in 80% yield.[8]

Some of our results are given in Table I.

Table I
Dehydration of Nitro Alcohols with Methanesulfonyl Chloride–Triethylamine[a]

Reaction	Yield, %
$CH_3CHOHCH_2NO_2 \longrightarrow CH_3CH{=}CHNO_2$ 3156-73-8 3156-70-5	30
$CH_3CHOHCH(NO_2)CH_3 \longrightarrow CH_3CH{=}C(NO_2)CH_3$ 6270-16-2 4812-23-1	67
$CH_3CH_2CHOHCH(NO_2)CH_3 \longrightarrow$ 20575-40-0 $CH_3CH_2CH{=}C(NO_2)CH_3$ 6065-19-6	80
$CH_3CH_2CHOHCH(NO_2)CH_2CH_3 \longrightarrow$ 5342-71-2 $CH_3CH_2CH{=}C(NO_2)CH_2CH_3$ 4812-22-0	70
$CH_3CH_2CH_2CHOHCH(NO_2)CH_2CH_3 \longrightarrow$ 5462-04-4 $CH_3CH_2CH_2CH{=}C(NO_2)CH_2CH_3$ 6187-24-2	78

[a] Registry no. are given below the compounds.

With the exception of the unhindered and sensitive (toward polymerization) 1-nitro-1-propene, generally good results were obtained. This fact, together with the mildness of the reaction conditions, should make the method of some use in synthesis.

Experimental Section

General Reaction Procedure. *Caution! Nitroolefins are lachrymatory and allergenic. The following procedures should be carried out in a fume hood by a gloved operator.* The nitro alcohol (0.040 mol) was dissolved in 40 ml of methylene chloride at 0° under a nitrogen atmosphere, and 1 equiv of methanesulfonyl chloride (4.6 g, 3.1 ml, 0.040 mol) was added in one portion. Triethylamine (16.0 g, 22 ml, 0.160 mol) was then added dropwise, and the reaction mixture was stirred for 15 min at 0°. The reaction mixture was then transferred to a separatory funnel with the aid of 40 ml of methylene chloride, then washed with water, 5% aqueous HCl, and brine. After concentration at the rotary evaporator, the residual oil was purified by Kugelrohr distillation. In this manner, the following compounds were prepared. Product purity was established by VPC in all cases.

2-Nitro-2-butene from 3-nitro-2-butanol: ir (neat) 1670, 1520 cm^{-1}; NMR (CCl_4) δ 1.88 (d, 3 H, J = 7 Hz), 2.15 (s, 3 H), 7.07 (q, 1 H, J = 7 Hz); bp 80° (20 mm) (Kugelrohr); 2.70 g (67%).

2-Nitro-2-pentene from 2-nitro-3-pentanol: ir (neat) 1670, 1520 cm^{-1}; NMR (CCl_4) δ 1.13 (t, 3 H, J = 7 Hz), 2.13 (s, 3 H), 7.0 (t, 1 H, J = 7 Hz); bp 85° (20 mm) (Kugelrohr); 3.70 g (80%).

3-Nitro-3-hexene from 4-nitro-3-hexanol: ir (neat) 1670, 1550, 1520 cm^{-1}; NMR (CCl_4) δ 6.92 (t, 1 H, J = 7 Hz); bp 90° (18 mm) (Kugelrohr); 3.63 g (70%). The product consisted of a 7:3 mixture of the conjugated and nonconjugated nitroolefins judging from NMR.

3-Nitro-3-heptene from 3-nitro-4-heptanol: ir (neat) 1670, 1550, 1520 cm^{-1}; NMR (CCl_4) δ 7.02 (t, 1 H, J = 7 Hz); bp 90° (20 mm) (Kugelrohr); 4.46 g (78%). The product consisted of 65:35 mixture of conjugated and nonconjugated nitroolefins judging from NMR.

1-Nitropropene from 1-nitro-2-propanol: ir (neat) 1655, 1520 cm^{-1} NMR (CCl_4) δ 1.95 (d, 3 H, J = 6 Hz), 6.83–7.55 (m, 2 H); bp 70° (20 mm) (Kugelrohr); 1.05 g (30%). This reaction worked best when only 0.08 mmol of triethylamine was used per 0.04 mmol of nitro alcohol.

References and Notes

(1) J. E. Mc Murry and J. Melton, *J. Org. Chem.*, **38**, 4367 (1973).
(2) B. Vanderbilt and H. Hass, *Ind. Eng. Chem.*, **32**, 34 (1940).
(3) For a good general procedure, see W. E. Noland, "Organic Syntheses", Collect. Vol. V, Wiley, New York, N.Y., 1973, p 833.
(4) H. Wieland and E. Sakellarios, *Chem. Ber.*, **52**, 898 (1919).
(5) G. D. Buckley and C. W. Scaife, *J. Chem. Soc.*, 1471 (1947).
(6) H. Cerf de Mauny, *Bull. Soc. Chim. Fr.*, **7**, 133 (1940).
(7) R. K. Crossland and K. L. Servis, *J. Org. Chem.*, **35**, 3195 (1970).
(8) Interestingly, Hassner has reported the failure of a steroidal 2-nitro alcohol to dehydrate on treatment with *p*-toluenesulfonyl chloride in pyridine: A. Hassner, J. M. Larkin, and J. E. Dowd, *J. Org. Chem.*, **33**, 1733 (1968).