

Counterattack Reagent: Hexamethyldisilathiane in the Conversion of Nitro Compounds into Nitriles

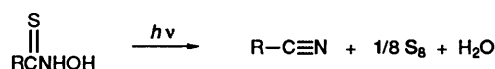
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Various primary nitro compounds have been treated with KH in tetrahydrofuran and then with Me₃SiSSiMe₃ to give potassium thiohydroxamates. These salts were neutralized by an acid and then desulphurized by light to afford nitriles in 78–87% yields. In these reactions, Me₃SiSSiMe₃ acted as a 'counterattack reagent'.

Nitriles can be prepared from the corresponding primary nitro compounds by various methods.¹ Recently, we reported a procedure for the conversion of primary nitro compounds into thiohydroxamic acids in the dark by using Me₃SiSSiMe₃ under alkaline conditions.² Generally, thiohydroxamic acids decompose in the light^{3–6} to give nitriles, sulphur and water (Scheme 1). We have combined these two pieces of information and



Scheme 1

successfully developed a new way to prepare nitriles from nitro compounds. Our method involves application of the 'counterattack reagent' concept; the manipulation procedure is simple and involves mild conditions.^{2,7–11}

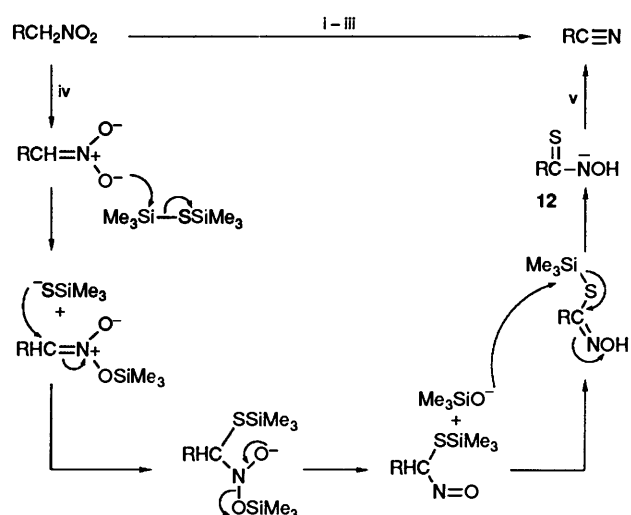
Results

We treated primary nitro compounds **1**, **3**, **5**, **7** and **9** with KH (1.1 equiv.) in THF (tetrahydrofuran) at 0 °C to room temperature. Then Me₃SiSSiMe₃ was added into the reaction flask, which was surrounded with aluminium foil. After being stirred for 3 d, the reaction mixture was neutralized with 10% HCl and exposed to daylight for 3 h. The corresponding nitriles were obtained in 78–87% yields (Table 1). This method was successfully applied to nitro compounds containing various functionalities, including arene, ester and sulphide groups.

By the same strategy, *trans*-β-nitrostyrene **11** was treated with Pr^tSLi (1.5 equiv.) in THF and then with Me₃SiSSiMe₃ (1.5 equiv.) to give the nitrile **10** in 82% yield.

Discussion

In the conversion of primary nitro compounds into nitriles, we first generated thiohydroxamic acids in the dark. These thiohydroxamic acids were then transformed to nitriles by light. In a control experiment, we carried out the reaction with 1-nitrohexane **1** in the light, up to the step leading to the formation of **12** (R = C₅H₁₁), as shown in Scheme 2. The reaction was then quenched with aqueous acid in the dark. A large amount of thiohydroxamic acid C₅H₁₁C(=S)NHOH was obtained. These results indicated that the anionic form of a thiohydroxamic acid, unlike a thiohydroxamic acid itself, did not decompose to a nitrile. On the other hand, we found that arylthiohydroxamic acids (*e.g.*, **5**, **7** and **9**) were desulphurized



Scheme 2 Reagents and conditions: i) KH, THF; ii) Me₃SiSSiMe₃; iii) H₃O⁺, hv; iv) KH; v) H₃O⁺, hv

more readily than alkylthiohydroxamic acids to give the corresponding nitriles in the light.

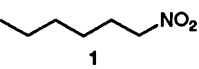
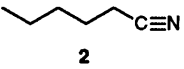
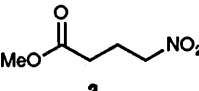
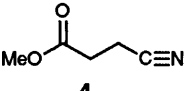
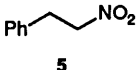
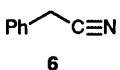
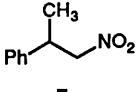
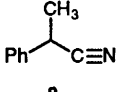
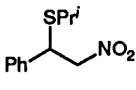
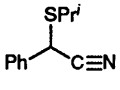
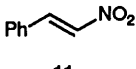
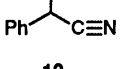
Schemes 2 and 3 show the pathways for generating nitriles from nitro compounds. The Me₃SiSSiMe₃ reagent is first attacked by a nitrate at a silicon centre. The leaving group, Me₃Si⁻, then counterattacks a silylated nitronate intermediate. Thus Me₃SiSSiMe₃ can be regarded as a 'counterattack reagent'^{2,7–11} in these reactions. Although these reactions involved multiple mechanistic steps and several intermediates, none of the latter had to be isolated.

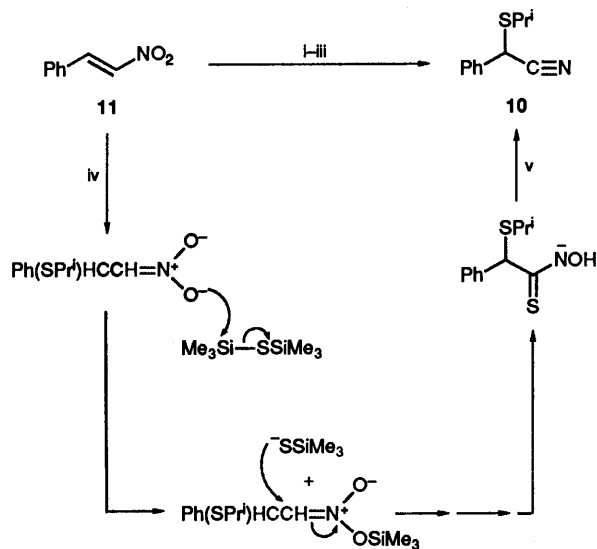
Experimental

General Procedure.—All reactions were carried out in oven-dried glassware (120 °C) under an atmosphere of nitrogen. The starting materials, nitro compounds **5**, **7** and **9**, were prepared from *trans*-β-nitrostyrene.^{12–14} Analytical thin-layer chromatography (TLC) analyses were performed on precoated plates (silica gel GHLF), purchased from Analtech Inc. Gas chromatography analyses were carried out on a Hewlett-Packard 5794 instrument equipped with a 12.5-m cross-linked methyl silicone gum capillary column (0.2-mm i.d.); the injector temperature was set up at 260 °C. Purification by gravity column chromatography was performed with EM Reagents Silica Gel 60 (particle size 0.063–0.200 mm, 70–230 mesh ASTM). Separations by radial thin-layer chromatography were accomplished on a model 7924T Chromatotron from Harrison Research. The plate with 1-mm thickness was coated with EM

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Table 1 Preparation of nitriles from Me₃SiSSiMe₃ and nitroalkanes, or a nitroalkene, under alkaline conditions

Nitro compound	Nitrile	Yield (%)
		85
		78
		85
		80
		87
		82

**Scheme 3** Reagents and conditions: i, LiSPrⁱ, THF; ii, Me₃SiSSiMe₃, heat; iii, H₃O⁺, hv; iv, LiSPrⁱ; v, H₃O⁺, hv

Reagents Silica Gel 60 PF₂₅₄ containing gypsum. ¹H NMR spectra were recorded in CDCl₃ with SiMe₄ as internal standard. *J* Values are given in Hz.

Standard Procedure for the Preparation of Nitriles.—In a one-necked, round-bottomed flask equipped with a stirring bar and a rubber septum, KH (1.1 equiv.) was washed with hexanes (3 × 5 cm³). Hexanes were then removed to give KH as a white powder. A nitro compound (101–155 mg, 1.0 equiv.) and THF (tetrahydrofuran) (0.07–0.10 mol dm⁻³ concentration for

the nitro compound) were added into the flask. After 30 min of stirring at 0 °C followed by 1.0 h at room temperature, hexamethyldisilathiane (1.5 equiv.) was added into the reaction flask, which was surrounded with aluminium foil to avoid light. Stirring was continued at room temperature and the mixture was then heated if necessary. The reaction mixture was diluted with water at 0 °C, neutralized with 10% aqueous HCl, and extracted with CH₂Cl₂ three times. The combined organic layers were washed with saturated brine. The mixture was stirred over MgSO_{4(s)} in daylight for 3 h. After the solution had been filtered and solvents removed, the residue was purified by chromatography to give the desired nitrile.

Hexanenitrile 2. The standard procedure was followed. The reaction mixture was stirred at room temperature for 3 d. After purification by use of a Chromatotron (5% EtOAc in hexanes as eluent), the nitrile 2 was obtained as a pale yellow oil in 85% yield: GC (column program: initial temperature 50 °C, duration 2.00 min; increment rate 15 °C min⁻¹; final temperature 150 °C) *t*_R 2.15 min; δ_H(80 MHz) 0.92 (t, 3 H, *J* 5.8, CH₃), 1.15–1.93 (m, 6 H, 3 × CH₂) and 2.32 (t, 2 H, *J* 6.6, CH₂CN); ν_{max}(neat)/cm⁻¹ 2955s, 2931m, 2861m, 2238w (CN), 1461w, 1425w and 1375w. Physical properties and spectroscopic characteristics are consistent with those of an authentic sample.¹⁵

Methyl 3-cyanopropionate 4. The standard procedure was followed. The reaction mixture was stirred at room temperature for 3 d. After purification by use of a Chromatotron (5% EtOAc in hexanes as eluent), the nitrile 4 was obtained as a yellow oil in 78% yield: GC (column program: initial temperature 50 °C, duration 2.00 min; increment rate 15 °C min⁻¹; final temperature 150 °C) *t*_R 3.42 min; δ_H(80 MHz) 2.68 (br s, 4 H, CH₂CO + CH₂CN) and 3.57 (s, 3 H, CH₃); ν_{max}(neat)/cm⁻¹ 2943s, 2919s, 2849s, 2249w (CN), 1743s (C=O), 1549m, 1437s, 1367m, 1315w, 1268m, 1226s (C–O), 1206s (C–O), 1179s (C–O) and 1060w; *m/z* 113 (M⁺, 31%), 99 (28), 86 (39), 71 (79), 55 (81), 43 (82) and 41 (100). Physical properties and spectroscopic characteristics are consistent with those of the same compound reported in the literature.¹⁶

Benzyl cyanide 6. The standard procedure was followed. The reaction mixture was stirred at room temperature for 24 h and then was heated to reflux for 48 h. After purification by use of a Chromatotron (10% EtOAc in hexanes as eluent), the nitrile 6 was obtained as a yellow oil in 85% yield: GC (column program: initial temperature 70 °C, duration 2.00 min; increment rate 15 °C min⁻¹; final temperature 200 °C) *t*_R 4.60 min; TLC *R*_F 0.41 (20% EtOAc in hexanes); δ_H(80 MHz) 3.58 (s, 2 H, CH₂) and 7.18 (s, 5 H, Ph); ν_{max}(neat)/cm⁻¹ 3049m (=CH), 3037m (=CH), 2943w, 2919w, 2243m (CN), 1600m (C=C), 1494s (C=C), 1453s, 1413s, 1075m, 1026m, 939w, 733s (CH) and 693s (CH). Physical properties and spectroscopic characteristics are consistent with those of an authentic sample.¹⁷

α-Methylbenzyl cyanide 8. The standard procedure was followed. The reaction mixture was stirred at room temperature for 24 h and then was heated to reflux for 48 h. After purification by use of a Chromatotron (10% EtOAc in hexanes as eluent), the nitrile 8 was obtained as a yellow oil in 80% yield: GC (column program: initial temperature 70 °C, duration 2.00 min; increment rate 15 °C min⁻¹; final temperature 200 °C) *t*_R 4.91 min; TLC *R*_F 0.48 (20% EtOAc in hexanes); δ_H(80 MHz) 1.64 (d, 3 H, *J* 7.3, CH₃), 3.90 (q, 1 H, *J* 7.3, CH) and 7.39 (s, 5 H, Ph); ν_{max}(neat)/cm⁻¹ 3084w, 3060m (CH), 3037m (=CH), 2978s, 2931m, 2860w, 2238m (CN), 1684m, 1490m (C=C), 1449s, 1373m, 1261w, 1237w, 1085w, 1073w, 1026w and 691s (=CH). Physical properties and spectroscopic characteristics are consistent with those of the same compound reported in the literature.¹⁸

α-(Isopropylthio)benzyl cyanide 10. Method A. The standard procedure was followed. The reaction mixture was stirred at

room temperature for 24 h and then was heated to reflux for 48 h. After purification by use of a Chromatotron (20% EtOAc in hexanes as eluent), the nitrile **10** was obtained as a yellow oil in 87% yield: GC (column program: initial temperature 70 °C, duration 2.00 min; increment rate 15 °C min⁻¹; final temperature 250 °C) *t*_R 7.94 min; TLC *R*_F 0.20 (20% EtOAc in hexanes); δ_H(80 MHz) 1.22 (d, 6 H, *J* 6.7, 2 × CH₃), 2.85 (hep, 1 H, *J* 6.7, CH), 5.12 (s, 1 H, CHCN) and 7.00–7.65 (m, 5 H, Ph); ν_{max}(CCl₄)/cm⁻¹ 3 042w (=CH), 3010w (=CH), 2966s, 2931s, 2861s, 2225w (CN), 1443m (C=C), 1437m, 1378m, 1343m, 1237m, 1149m, 1114s, 1067m, 903m, 711s (=CH) and 690s (=CH) [Found: *M*⁺, 191.0768. Calc. for C₁₁H₁₃NS: *M*, 191.0769].

Method B. One-Flask Preparation of the Nitrile 10. BuLi (2.5 mol dm⁻³ solution in hexanes; 401 mm³, 0.992 mmol, 1.5 equiv.) was added dropwise to a solution of propane-2-thiol (77 mg, 0.99 mmol, 1.5 equiv.) in THF (10.0 cm³) at -78 °C under an atmosphere of nitrogen. After 30 min at the same temperature, *trans*-β-nitrostyrene **11** (101 mg, 0.662 mmol, 1.0 equiv.) in THF (1.0 cm³) was injected into the reaction flask. The solution was stirred at room temperature for 3 h. The flask was surrounded with aluminium foil to avoid light, to which hexamethyldisilathiane (181 mg, 0.992 mmol, 1.5 equiv.) was added. The reaction mixture was stirred at room temperature for 24 h and was then heated to reflux for 48 h. After purification by use of a Chromatotron (20% EtOAc in hexanes as eluent), the nitrile **10** was obtained as a yellow oil in 82% yield (104 mg, 0.543 mmol).

Acknowledgements

For financial support, we thank the donors of Petroleum Research Fund, administered by the American Chemical Society; the National Institutes of Health for a Biomedical Research Support Grant S07 RR7041, as well as a grant supporting the purchase of a VG 70-S mass spectrometer; the National Science Council of Republic of China; and Academia Sinica.

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Paper 0/04767H

Received 24th October 1990

Accepted 16th November 1990