Novel Double Functional Group Transformation: 'One-flask' Conversion of 1-Nitrocycloalkenes to Terminally Unsaturated Nitriles

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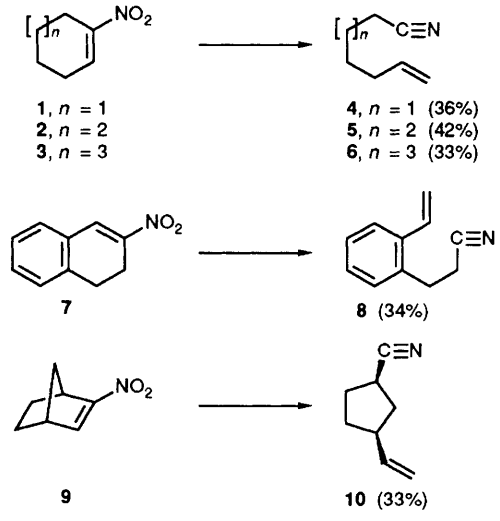
A new method has been developed for the conversion of 1-nitrocycloalkenes to terminally unsaturated nitriles in one flask by use of Me_3SiCH_2MgCl (1.8 equiv.) and PCl_3 (2.5 equiv.) in tetrahydrofuran.

Development of a novel 'double functional group transformation' often involves deliberate design. A representative example is Eschenmoser's transformation of α,β-epoxy hydrazones to carbonyl acetylenes.[1] Herein we report a method for the conversion of 1-nitrocycloalkenes to terminally unsaturated nitriles in one flask. The mechanistic complexity of this newly developed transformation is comparable with that of the Eschenmoser's process; however, the designs for these two transformations are distinct.

We treated 1-nitroalkenes **1–3**, which can be readily prepared by a variety of methods,[2] with Me_3SiCH_2MgCl (1.8 equiv.) in tetrahydrofuran (THF) at −20 °C and then with PCl_3 (2.5 equiv.) at 67 °C *in situ*. The desired nitriles **4–6** were obtained after aqueous workup and purification (Scheme 1). By this 'one-flask' method, we were able to convert monocyclic nitroalkenes **1–3** to nitriles **4–6**, respectively, in 33–42% yields. The same reaction conditions also allowed the generation of nitrile **8** in 34% yield from compound **7**, which contains a nitrostyrene moiety. Further, 1-cyano-3-vinylcyclopentane **10**[3] was generated (33% yield) stereospecifically in the *cis*-form from 1-nitronorbornene **9**. In these 'double functional group transformations,' dimethoxyethane can replace THF as the solvent.

We illustrate our design in Scheme 2, as exemplified in the conversion of 1-nitrocyclohexene **1** to 6-cyanohex-1-ene **4**. The first step involves a Michael addition of Me_3SiCH_2MgCl to **1**; subsequently the resultant nitronate **11** reacts with PCl_3 *in situ* to afford intermediate **12** and Cl^-. The phosphonium species **14** could be generated from intermediate **12** *via* **13**. The electron-deficient phosphonium centre in **14** acts as the initiator to bring about a silicon-directed second-order Beckmann rearrangement to give nitrile **4**. Nishiyama *et al.*[3] reported a similar Beckmann rearrangement of β-trimethylsilyl ketoxime acetates in the presence of $Me_3SiOSO_2CF_3$. Also, Hudrlik *et al.*[4] found that hydroxylamine *O*-sulfonic acid can convert β-trimethylsilyl ketones to alkene nitriles.



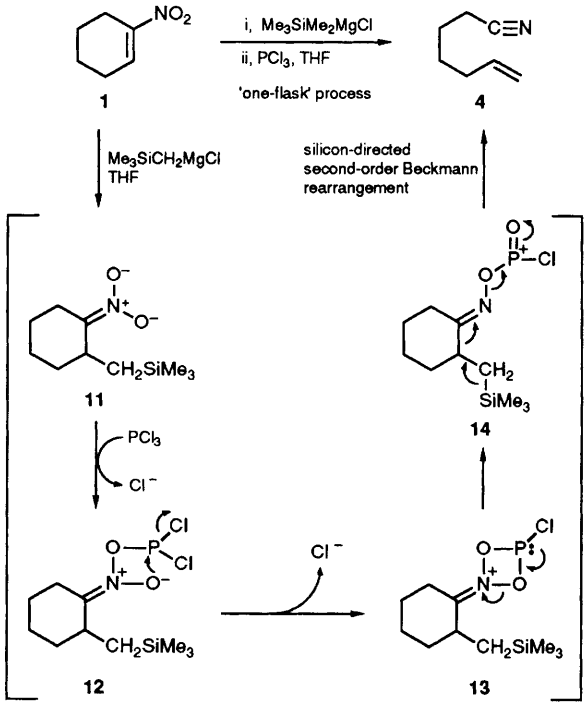
Scheme 1 'One-flask' conversion of various types of 1-nitrocycloalkenes to terminally unsaturated nitriles. *Conditions*: Me_3SiCH_2MgCl, THF, −20 °C; then PCl_3, 67 °C

We considered the possibility that a 1,4-elimination occurred in **12** to lead to a nitrile oxide intermediate. Nevertheless, under various conditions, we did not detect any intra- or inter-molecular nitrile oxide–alkene cycloadducts.

In a control experiment, we added 1-nitrocyclohexene **1** to a THF solution of Me_3SiCH_2MgCl (1.8 equiv.) at −20 °C. The Michael adduct 2-(trimethylsilyl)methyl-1-nitrocyclohexane was obtained in 60% yield. Reversal of the addition order, however, led to the generation of the desired adduct in a low yield.

Phosphorus halides, such as PCl_3[5] and PI_3,[6] can convert primary nitro compounds to nitriles; the halide acting as a nucleophile to attack the nitro group.[5,7,8] We found that terminally unsaturated nitriles can be generated by the reaction of PCl_3 with secondary nitronates (*e.g.* **11**); to the best of our knowledge, this process is unprecedented. In our reactions, PCl_3 acted as an electrophile[9] towards nitronate intermediates. Furthermore, we found that treatment of the isolated 2-(trimethylsilyl)methyl-1-nitrocyclohexane with $P(NMe_2)_3$ in 1,2-dichloroethane[8] also produced hept-6-enenitrile **4**, although the yield was low (17% by GC).

A 'double functional group transformation' allows the combination of several chemical steps into a 'one-flask' reaction and, therefore, isolation of intermediates is not necessary; the present transformation possesses these characteristics. The starting materials are readily available and the cyano group in the products can be converted to a variety of functionalities.[10] Thus this new method could be of value in



Scheme 2 A plausible mechanism for the 'double functional group transformation' of a 1-nitrocycloalkene to a terminally unsaturated nitrile

the synthesis of drugs,[11] especially those for immunologic diseases.

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