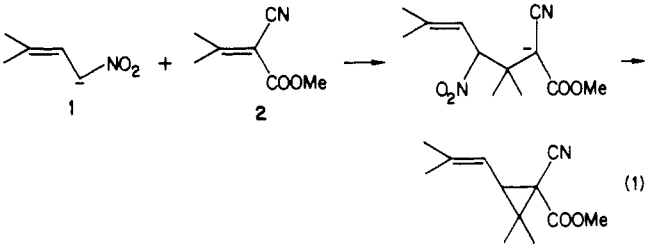
Nitro Compounds as Nucleophilic Alkylidene Transfer Reagents

Summary: Nitro compounds can be used as useful and general nucleophilic alkylidene transfer reagents for the preparation of various cyclopropanes.

Sir: The base-catalyzed reaction of nitroalkanes with electron-deficient olefins is well-known as the Michael reaction and it has been used extensively in organic synthesis.[1] In spite of the numerous examples of Michael additions, there is only one report of cyclopropane formation by the reaction of the α-anion of a nitroalkane with electron-deficient olefins.[2] The yield of cyclopropanes prepared by this method was generally low (10–20%) except for alkenes derived from steroides; the only nitroalkanes investigated were nitromethane and nitroethane.[2] Here we describe the general use of nitroalkanes as alkylidene transfer reagents.

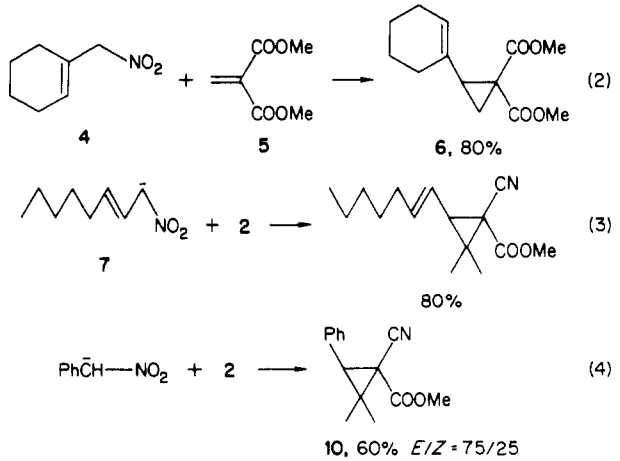
As allylic nitro compounds undergo palladium-catalyzed allylic alkylation with stabilized carbanions,[3] it might be expected that the reaction of the α-anion of 4-nitro-2-methyl-2-butene (1) with 2 in the presence of $Pd(PPh_3)_4$ would give cyclopropane 3 via sequential Michael addition and palladium-catalyzed allylic alkylation. In fact, 3 was



(1)

3, 86% *E*/*Z* = 90/10

obtained in good yield on treatment of the potassium salt of 1 with 2 in the presence of 5 mol % of $Pd(PPh_3)_4$. However, we have found that the palladium catalyst is unnecessary. Simply stirring a mixture of the potassium salt of 1 and 2 in dimethyl sulfoxide (Me_2SO) at room temperature for 3 h gave 3 in 86% yield. The potassium salt was prepared in situ by the reaction of 1 with *t*-BuOK or KOH in Me_2SO. This reaction can be extended to a variety of allylic nitro compounds and conjugated alkenes.



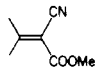
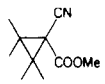
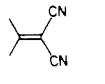
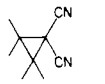
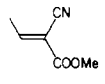
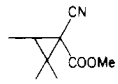
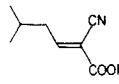
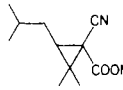
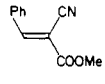
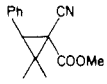
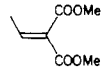
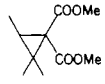
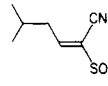
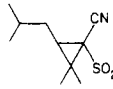
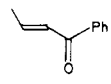
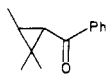
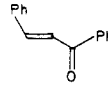
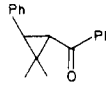
10, 60% *E*/*Z* = 75/25

(1) "Houben-Weyl, Methoden der Organischen Chemie, 4th Ed."; Muller, E., Ed.; George Thieme Verlag: Stuttgart, 1971; Vol X/Part I. Bergmann, E. D.; Ginsberg, D.; Rappo, R. *Org. React. (N.Y.)* **1959**, 10, 179.

(2) Annen, K.; Hofmeister, H.; Laurent, H.; Seeger, A.; Weichert, R. *Chem. Ber.* **1978**, *111*, 3094.

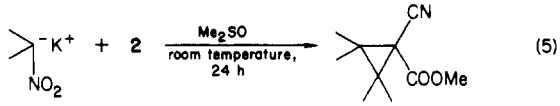
(3) Ono, N.; Hamamoto, I.; Kaji, A. *J. Chem. Soc., Chem. Commun.* **1982**, 821. Tamura, R.; Hegedus, L. S. *J. Am. Chem. Soc.* **1982**, *104*, 3727.

Table I. Preparation of *gem*-Dimethylcyclopropanes Using 2-Nitropropane

olefin	time, h	product	isolated yield, %
			65
			70
			63 (*E* only)
			61 (*E* only)
			58 (*E* only)
			65
			68 (*E* only)
			30 (*E* only)
			5 (*E* only)

Some typical examples are shown here. Phenylnitromethane was also used as an alkylidene transfer reagent to give the corresponding cyclopropane in good yield. Thus, the nitro group at the allylic and benzylic positions is activated to nucleophilic replacement.[4]

Anticipating the formation of *gem*-dimethylcyclopropane (11), we carried out the reaction of the potassium salt of 2-nitropropane with 2. The reaction was carried out in dilute Me_2SO solution with avoidance of proton sources to minimize side reactions, dimerization, and Michael addition.[5] Compound 11 was obtained in 65% yield under these conditions. Various *gem*-dimethylcyclopropanes can



11, 65%

be prepared by this method and the results are summarized in Table I. Isopropylidene transfer using 2-nitropropane is an extremely useful process for organic synthesis. Although the potassium salt of 2-nitropropane lacks the reactivity of typical isopropylidene transfer reagents such as diphenylsulfonium isopropylide[6] or sulfoximine isopropylides,[7] 2-nitropropane is commercially available

(4) The nitro group at an allylic position is readily replaced by good nucleophiles such as thiophenoxide ion without the aid of Pd(0): Ono, N.; Hamamoto, I.; Yanai, T.; Kaji, A. *J. Chem. Soc., Chem. Commun.* **1985**, 523.

(5) A mixture of the potassium salt of 2-nitropropane (10 mmol) and 2 (5 mmol) in 200 mL of Me_2SO was stirred at room temperature for 24 h. When the reaction was carried out in 10 mL of Me_2SO, the yield of 3 was reduced to 30%.

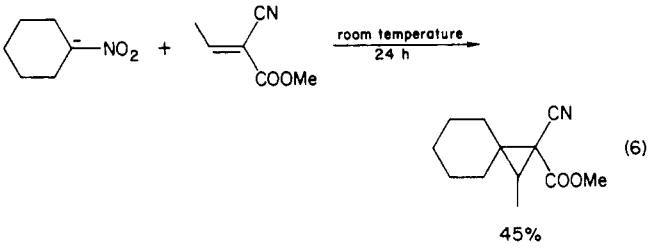
(6) Corey, E. J.; Jautelat, M. *J. Am. Chem. Soc.* **1967**, *89*, 3912.

(7) Johnson, C. R.; Janiga, E. R. *J. Am. Chem. Soc.* **1973**, *95*, 7692.

0022-3263/85/1950-2806$01.50/0

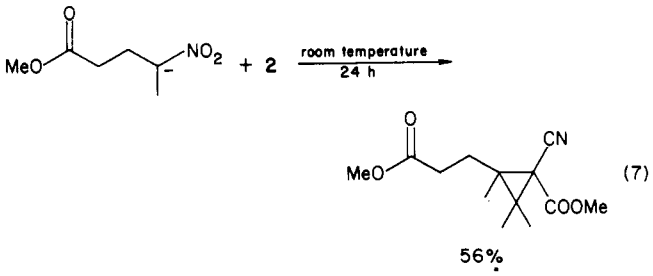
and cheap; the nitronate is stable and easy to handle.

As the α-anion of 2-nitropropane is much more stable than the α-anion of ketones, the reaction of the potassium salt of 2-nitropropane with alkenes substituted with only one keto group is thermodynamically unfavored for the formation of cyclopropanes. Nevertheless, *gem*-dimethylcyclopropanes were obtained in 5–10% yields even in such cases. The present alkylidene transfer reaction is not limited to the examples presented above but can be further extended. When nitro cycloalkanes are used, spiro compounds are prepared as in eq 6. Nitro compounds



(6)

45%



(7)

56%

having other functional groups also follow this reaction, as, for example, methyl 4-nitropentanoate, which results in the regioselective formation of cyclopropanes. When primary nitroalkanes were used, primary alkyl groups could be transfered in 50–60% yields. Only alkenes were successful substrates, activated by two electron-withdrawing groups. The stereochemistry of the present alkylidene transfer reaction is noteworthy. The stereochemistry of alkenes was retained in the course of the reaction when they were prepared by the Knoevenagel reaction. This means that the reaction proceeds via the similar intermediates as those of the Knoevenagel reaction.[8] The studied reaction of nitro groups so closely parallels the sulfone cyclopropanation.[9] The former method has merits over the latter one in that various alkyl groups are transfered regioselectively.

Thus, the nitro group at allylic, benzylic, and tertiary positions is especially readily replaced by intramolecular nucleophiles to form cyclopropanes. This fact strongly suggests that the present ring closure proceeds via single-electron transfer as in other reactions of nitro compounds with nucleophiles.[10] Further studies are currently in progress on the mechanism of the ring closure along with the synthetic application of the present reaction.

Registry No. 1-K, 96914-56-6; **2**, 6666-75-7; (*E*)-**3**, 96914-59-9; (*Z*)-**3**, 96914-73-7; **4**, 5330-61-0; **5**, 3377-21-7; **6**, 96914-60-2; **7**-K, 96914-57-7; (*Z*)-**10**, 96914-62-4; (*E*)-**10**, 96914-63-5; **11**, 96914-64-6; $PhCH(K)NO_2$, 66045-11-2; $(CH_3)_2CH(K)NO_2$, 28273-55-4; (*E*)-$CH_3CH{=}C(CN)CO_2Me$, 51977-58-3; $(CH_3)_2C{=}C(CN)_2$, 13166-10-4; (*E*)-$(CH_3)_2CHCH_2CH{=}C(CN)CO_2Me$, 96914-67-9; (*E*)-$PhCH{=}C(CN)CO_2Me$, 14533-86-9; $CH_3CH{=}C(CO_2Me)_2$, 17041-60-0; (*E*)-$(CH_3)_2CHCH_2CH{=}C(CN)SO_2Ph$, 96914-69-1; (*E*)-CH3CH=CHC(O)Ph, 35845-66-0; (*E*)-PhCH=CHC(O)Ph, 614-47-1; $MeO_2C(CH_2)_2C(K)CH_3NO_2$, 96914-58-8; 3-cyano-2,2-dimethyl-1-(1-heptenyl)-3-(methoxycarbonyl)cyclopropane, 96914-61-3; nitrocyclohexane potassium salt, 12385-03-4; methyl 1-cyano-2-methylspiro[2.5]octan-1-oate, 96914-65-7; 3-cyano-1,1,2,2-tetramethyl-3-(methoxycarbonyl)cyclopropane, 96914-64-6; 3,3-dicyano-1,1,2,2-tetramethylcyclopropane, 1195-70-6; *trans*-1-cyano-1-(methoxycarbonyl)-2,2,3-trimethylcarbonyl)cyclopropane, 96914-68-0; *trans*-1-cyano-2,2-dimethyl-1-(methoxycarbonyl)-3-phenylcyclopropane, 96914-63-5; 1,1-dimethyl-2,2-bis(methoxycarbonyl)-3-methylcyclopropane, 24512-15-0; *trans*-1-cyano-2,2-dimethyl-3-isobutyl-1-(phenylsulfonyl)cyclopropane, 96914-70-4; *trans*-1-benzoyl-2,2-dimethyl-3-methylcyclopropane, 96914-71-5; *trans*-1-benzoyl-2,2-dimethyl-3-phenylcyclopropane, 50299-81-5; methyl *trans*-1-cyano-2,2,3-trimethyl-1-[(methoxycarbonyl)-cyclopropyl]propionate, 96914-72-6.

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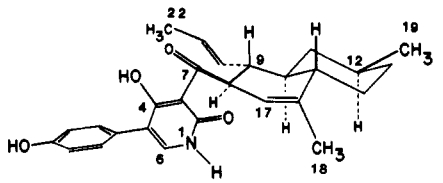
Total Synthesis of (±)-Ilicicolin H

Summary: The first total synthesis of ilicicolin H (**1**) is described. An intramolecular Diels–Alder strategy provides high regio- and stereoselectivity.

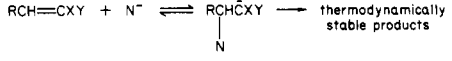
Sir: Extracts from the mycelium of the imperfect fungus, *Cylindrocladium ilicicola*, have led to the isolation and characterization of the novel antifungal antibiotic known as ilicicolin H (**1**).[2] Bassianin, tenellin, and funiculosin



Ilicicolin H **1**

have been identified as related members of this family of natural products,[3] and extensive biosynthetic studies of tenellin and ilicicolin H have established a unique ring expansion rearrangement leading to these α-pyridone metabolites.[4] These studies present a convergent route

(8) See: Apeloig, Y.; Miriam, K.; Rappoport, Z. *J. Am. Chem. Soc.* **1983**, *105*, 2784. Tanikaga, R.; Tamura, T.; Nozaki, Y.; Kaji, A. *J. Chem. Soc., Chem. Commun.* **1984**, *87*.



(9) Trost, B. M.; Melvin, L. S., Jr. "Sulfur Ylides"; Academic Press: New York, 1975. Campbell, R. V. M.; Crobie, L.; Pattenden, G. *J. Chem. Soc., Chem. Commun.* **1971**, 218.

(10) The nitro group at allylic, benzylic, and tertiary positions is readily denitrated by radical reactions, see: Ono, N.; Miyake, H.; Tamura, R.; Kaji, A. *Tetrahedron Lett.* **1981**, *22*, 1705. Nucleophilic substitution of tertiary nitroalkanes with stabilized carbanions proceeds via single-electron-transfer processes, see: Kornblum, N.; Erickson, A. S. *J. Org. Chem.* **1981**, *46*, 1047 and references therein. The synchronous process also cannot be excluded for the present cyclization.

(1) Alfred P. Sloan Fellow (1983–1986).

(2) Matsumoto, M.; Minato, H. *Tetrahedron Lett.* **1976**, 3827.

(3) Wat, C.-K.; McInnes, A. G.; Smith, D. G.; Wright, J. L. C.; Vining, L. C. *Can. J. Chem.* **1977**, *55*, 4090. Ando, K.; Matsuura, I.; Nawata, Y.; Endo, H.; Sasaki, H.; Okytomi, T.; Sachi, T.; Tamura, G. *J. Antibiot.* **1978**, *31*, 533.

(4) Tanabe, M.; Urano, S. *Tetrahedron* **1983**, *24*, 3569. Leete, E.; Kowanko, N.; Newmark, R. A.; Vining, L. C.; McInnes, G.; Wright, J. L. C. *Tetrahedron Lett.* **1975**, 4103. McInnes, A. G.; Smith, D. G.; Walter, J. A.; Vining, L. C.; Wright, J. L. C. *J. Chem. Soc., Chem. Commun.* **1974**, 282.

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