Cyclopropanation of Electrophilic Alkenes With Nitroalkanes in the Presence of Alumina-Supported Potassium Fluoride

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Alumina-supported potassium fluoride is an effective reagent for Michael addition of nitroalkanes on the electrophilic alkenes, followed by cycloalkylation reaction to give cyclopropanes.

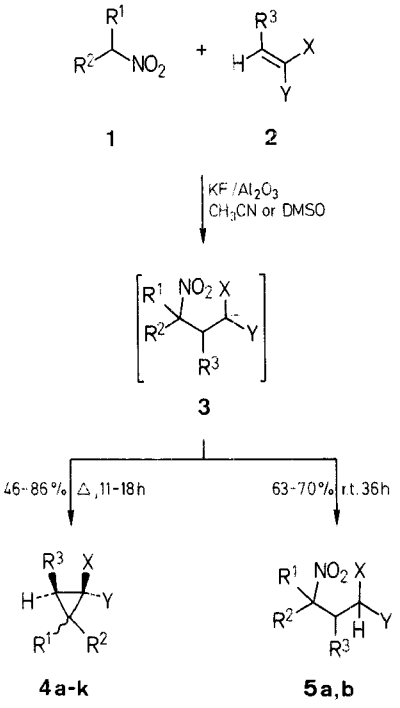
Electrophilic cyclopropanes are of great importance in organic synthesis.[1] In general, the synthesis of such cyclopropanes is performed from phosphorane and α,β-unsaturated esters,[2,3]

from enolates and vinylselenoxides or vinyl selenones,[4] from active methylene compounds and vinylselenones,[5] from 2-lithio-2-phenylsulfonylpropane and electrophilic olefins.[6] Cyclopropanation of olefins with bromomalonic ester,[7] reduction of alkyl-4-bromo-2-cyano-2-pentanoates with sodium borohydride[8] or phase-transfer alkylation[9] leads to cyclopropanes. Tandem Michael addition – cycloalkylation involving malonic ester and methyl bromoacrylate[14] or methyl 2-carbomethoxy-4-bromo-4-methyl-2-pentenoate,[16] methyl-α-bromoacrylate and malonic ester,[14] unsaturated esters and dimethyl bromomalonate[14,15] has been reported to afford cyclopropanes.

Cyclopropane formation by reaction of the α-anion of a nitroalkane with electron deficient olefins has been reported.[10–13] We have shown recently that alumina-supported potassium fluoride is an efficient reagent for the Henry reaction.[17] We now found alumina-supported potassium fluoride to be an effective reagent for the preparation of cyclopropanes by Michael addition – cycloalkylation.

Nitroalkanes **1** and electrophilic alkenes **2**, stirred in acetonitrile, at 80 °C, in the presence of alumina-supported potassium fluoride give cyclopropanes **4** (Table 1). Alumina without potassium fluoride or potassium fluoride without alumina is ineffective. Alumina-supported potassium hydroxide gives low yields of cyclopropanes, with unidentified products.

When X = Y = CO_2CH_3 the anion of the Michael intermediate **3** is not reactive enough and the reaction in the described conditions cannot give the cyclopropane. Then, the Michael adduct **5** is the only product obtained (Table 1). The olefin configuration is reflected in the cyclopropane (R^3 and Y are in *trans* position). The same stereochemistry has been obtained when the cyclopropanes are prepared by the reaction of anion of a nitroalkane with electron deficient olefins, in homogeneous media.[12] When the nitroalkane **1** contains two different alkyl groups, two isomers **4** are formed.



1 2 3 **4a–k** **5a,b**

Alumina-supported Potassium Fluoride:
Anhydrous potassium fluoride (8 g) is dissolved in methanol (150 ml) and chromatographic alumina (16 g, Merck 60 Art 1103) is added with stirring. The solvent is removed under reduced pressure and the result-

Table 1. Cyclopropanes **4a–k** and Michael Adducts **5a, b** Prepared

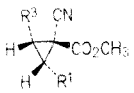
Product	R^1	R^2	R^3	X	Y	Yield (%)[a]	b.p. (°C)/mbar or m.p. (°C)	Molecular Formula[b] or Lit. Data	IR (Neat) ν(cm^{-1})
4a	H	H	*i*-C_3H_7	CN	CO_2CH_3	60	b.p. 40/0.04	$C_9H_{13}NO_2$ (167.2)	2240, 1740
4b	CH_3	CH_3	C_6H_5	CN	CO_2CH_3	86	b.p. 150/0.07; m.p. 58	$C_{14}H_{15}NO_2$[11,12] (229.3)	2235, 1740
4c	C_2H_5	H	*p*-ClC_6H_4	CN	CO_2CH_3	82	m.p. 84[c]	$C_{14}H_{14}ClNO_2$ (263.7)	2235, 1735[d]
4d	CH_3	CH_3	*i*-C_3H_7	CN	CO_2CH_3	86	b.p. 65/0.04	$C_{11}H_{17}NO_2$[11] (195.3)	2240, 1740
4e	CH_3	H	*i*-C_3H_7	CN	CO_2CH_3	86	b.p. 65/0.05[e]	$C_{10}H_{15}NO_2$ (181.2)	2235, 1740
4f	C_2H_5	H	*n*-C_4H_9	CN	CO_2CH_3	86	b.p. 60/0.04[e]	$C_{12}H_{19}NO_2$ (209.3)	2235, 1740
4g	CH_3	CH_3	*n*-C_5H_{11}	CN	CO_2CH_3	69	b.p. 60/0.03	$C_{13}H_{21}NO_2$ (223.3)	2235, 1740
4h	C_6H_5	H	C_2H_5	CN	CO_2CH_3	66	b.p. 90/0.04[e]	$C_{14}H_{15}NO_2$ (229.3)	2240, 1740
4i	CH_3	CH_3	C_6H_5	CN	CN	46	b.p. 135/0.04; m.p. 76	$C_{13}H_{12}N_2$ (196.3)	2240[d]
4j	CH_3	CH_3	*i*-C_3H_7	CN	CN	46	b.p. 40/0.04	$C_{10}H_{14}N_2$[11] (162.2)	2240
4k	CH_3	CH_3	C_6H_5	CN	$P(O)(OC_2H_5)_2$	61	b.p. 110/0.04	$C_{16}H_{22}NO_3P$ (307.3)	2225, 1270, 1170
5a	CH_3	CH_3	C_6H_5	CO_2CH_3	CO_2CH_3	63	m.p. 102	$C_{15}H_{19}NO_6$ (309.3)	1760, 1730, 1535
5b	CH_3	CH_3	*p*-$NO_2C_6H_4$	CO_2CH_3	CO_2CH_3	70	m.p. 107	$C_{15}H_{18}N_2O_8$ (354.3)	1755, 1535, 1520

[a] Yield of isolated product.
[b] Satisfactory microanalyses obtained: C ±0.3, H ±0.2, N ±0.3, Cl ±0.3.
[c] One isomer (A) purified.
[d] Measured in nujol.
[e] Mixture of two isomers.

Table 2. ^{1}H-NMR Spectral Data of Products **4** and **5**

Product	^{1}H-NMR ($CDCl_3$) δ (ppm)
4a	0.70–1.95 (m, 10H); 3.83 (s, 3H, OCH_3)
4b	1.32 (s, 3H, CH_3); 1.46 (s, 3H, CH_3); 3.29 (s, 1H, CH); 3.82 (s, 3H, OCH_3); 7.3 (s, 5H_{arom})
4c	*Isomer A* (90%):[a,b] 1.12 (t, 3H, CH_2-CH_3, J = 7.3 Hz); 1.33, 1.80 (m, 2H, CH_2); 2.28 (m, 1H, $CH-CH_2CH_3$); 7.3 (m, 4H_{arom}) *Isomer B* (10%):[c] 3.15 (d, 1H, *p*-ClC_6H_4-CH, J = 7 Hz)
4d	1.02 (m, 6H, $(CH_3)_2CH$); 1.28 (s, 3H, CH_3); 1.40 (s, 3H, CH_3); 1.25–1.85 (m, 2H, $(CH_3)_2CH-CH$); 3.79 (s, 3H, OCH_3)
4e	*Isomer A* (90%):[a,b,c] 1.05, 1.10 (2d, 6H, $(CH_3)_2CH$, J = 6.3 Hz); 1.33 (d, 3H, CH_3-CH, J = 6.6 Hz); 1.71 (m, 2H, $(CH_3)_2CH-CH$); 2.07 (dq, 1H, CH_3-CH, J = 6.6 Hz, 8.7 Hz); 3.81 (s, 3H, OCH_3)
4f	0.97 (d, 6H, $(CH_3)_2CH$); 1.10 (t, 3H, CH_2-CH_3, J = 7 Hz); 1.25–2.10 (m, 7H); 3.81 (s, 3H, OCH_3)
4g	0.98 (m, 3H, CH_2CH_3); 1.33 (s, 3H, CH_3); 1.43 (s, 3H, CH_3); 1.1–1.8 (m, 8H); 1.96 (t, 1H, J = 7 Hz); 3.83 (s, 3H, OCH_3)[c]
4h[b,c]	*Isomer A* (25%): 1.06 (t, 3H, CH_2-CH_3, J = 7 Hz); 1.8 (m, 2H, CH_2-CH_3); 2.6 (m, 1H, C_2H_5-CH); 3.20 (d, 1H, $CH-C_6H_5$, J = 9 Hz); 3.82 (s, 3H, OCH_3); 7.25 (m, 5H_{arom}) *Isomer B* (75%): 1.20 (t, 3H, CH_2-CH_3, J = 7 Hz); 1.8 (m, 2H, CH_2-CH_3); 2.6 (m, 1H, C_2H_5-CH); 3.00 (d, 1H, $CH-C_6H_5$, J = 7 Hz); 3.50 (s, 3H, OCH_3); 7.25 (m, 5H_{arom})
4i	1.30 (s, 3H, CH_3); 1.62 (s, 3H, CH_3); 3.01 (s, 1H, CH); 7.3 (m, 5H_{arom})
4j	1.05, 1.17 (2d, 6H, $(CH_3)_2CH$, J = 6.5 Hz); 1.42 (s, 3H, CH_3); 1.46 (s, 3H, CH_3); 1.40–1.85 (m, 2H)
4k	1.25–1.80 (m, 2H); 3.20 (d, 1H, CH, J_{PH} = 16 Hz); 4.0–4.5 (m, 4H, $2CH_2-CH_3$); 7.3 (s, 5H_{arom})
5a	1.42 (s, 3H, CH_3); 1.62 (s, 3H, CH_3); 3.30 (s, 3H, OCH_3); 3.63 (s, 3H, OCH_3); 4.26, 4.30 (AB, 2H, J = 11 Hz); 7.3 (s, 5H_{arom})[a]
5b	1.48 (s, 3H, CH_3); 1.68 (s, 3H, CH_3); 3.38 (s, 3H, OCH_3); 3.78 (s, 3H, OCH_3); 4.25, 4.45 (AB, 2H, J = 12 Hz); 7.3–8.3 (m, 4H_{arom})

[a] Measured at 300 MHz using a Bruker AM 300 instrument.

[b] 

Probable structure of isomer A assigned on the basis of coupling constants of CH–CH[18].

[c] Measured as a mixture of isomers A and B.

ing powder is then dried in a vacuum desiccator over calcium chloride (20 mbar, 20°C, 4 h). The catalyst is stored without loss of activity during several weeks. The activity is decreased when alumina-supported potassium fluoride is too strongly dried.

Cyclopropanes 4; General Procedure:

Alumina-supported potassium fluoride (4 g) is added in small portions to a stirred solution of alkene **2**[19] (10 mmol) and nitroalkane **1** (15 mmol) in acetonitrile (9 ml). The mixture is refluxed for 13 h (11 h for **4a**, 18 h for **4k**), then cooled to room temperature and the solid is separated by filtration on celite layer. The solid is washed with acetonitrile (2 × 20 ml) and the combined organic extract is concentrated to give the crude cyclopropane **4** which is purified by short path distillation or by recrystallization (Table 1). ^{1}H-NMR data are given in Table 2.

Michael Adducts 5; General Procedure:

A mixture of alkene **2**[20] (10 mmol), 2-nitropropane (**1**; $R^1 = R^2 = CH_3$; 1.33 g, 15 mmol) and alumina-supported potassium fluoride (4 g) is suspended in dimethylsulfoxid (8 ml) and this suspension is stirred for 36 h at room temperature. Ether (50 ml) is added and the mixture is filtered on celite. The solid is washed with ether and the organic extract is washed with water (3 × 50 ml). It may be necessary to add saturated sodium chloride solution (1–2 ml) to break a possible emulsion. The organic phase is dried with magnesium sulfate and concentrated under reduced pressure. Products **5a, b** are crystallized from hexane/chloroform (20:1) (Table 1).

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