Lewis Acid-induced Nucleophilic Substitution Reactions of Aliphatic Nitro Compounds with Carbon Nucleophiles

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Tertiary, benzyl, and allylic nitro compounds undergo nucleophilic substitution reactions with carbon nucleophiles such as electron rich aromatic compounds, allylsilanes, or silyl enol ethers in the presence of $SnCl_4$.

Nitro groups activate carbon–carbon bond formation and thus the direct displacement of nitro groups by nucleophiles is a useful process in organic synthesis.[1] In a previous paper we reported that tertiary and benzyl nitro groups are displaced by a phenylthio group on treatment with Me_3SiSPh in the presence of a Lewis acid.[2] We now report the Lewis acid-induced substitution of nitro compounds by carbon nucleophiles. Tertiary, benzyl, and allylic nitro compounds undergo Friedel–Crafts type of reactions with electron rich aromatic compounds. On stirring a mixture of $R–NO_2$, ArH (5

Table 1. Intermolecular Friedel–Crafts reactions of nitro compounds.

Entry	R^1	R^2	R^3	ArH	Time/h	% Yield of (**1**)[a]
1	Me	Me	Me	Anisole	1	74
2	Ph	Me	H	Toluene	1	75
3	Ph	Me	H	*o*-Xylene	1	65
4	Ph	Me	H	Benzene	1	60
5	Ph	$[CH_2]_2CO_2Me$	H	Toluene	2	85
6	Ph	$[CH_2]_2C(=O)Me$	H	Toluene	2	80
7	Me	Me	$CH=CH_2$	Toluene	15 min (−10 °C)	65[b]

[a] *p*-Substituted toluene or anisole was produced predominantly. [b] p-Me-$C_6H_4CH_2CH=CMe_2$ was produced when 1 equiv. of $SnCl_4$ was used.

equiv.), and $SnCl_4$ (2 equiv.) at room temperature, the alkylated products (**1**) were obtained in good yields as summarized in Table 1, equation (1). Best results were obtained when $SnCl_4$ was used; other Lewis acids such as $AlCl_3$, $TiCl_4$, and $ZnCl_2$ were less effective for this reaction.[3]

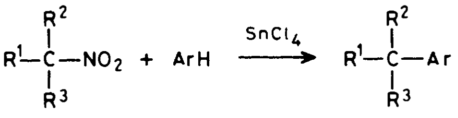
This Friedel–Crafts type of alkylation can also be extended to intramolecular systems as shown in equation (2). The requisite starting compounds were prepared by alkylation of nitro compounds (Michael addition or nitro–aldol condensation),[4] and cyclization took place smoothly at room temperature in the presence of $SnCl_4$ (2 equiv.). The results are summarized in Table 2.

The above results suggest that other carbon nucleophiles may allow similar alkylations catalysed by $SnCl_4$. In fact, allylic nitro compounds reacted with allyltrimethylsilane very rapidly,[5] the reaction being complete in 10 min at −10 °C in the presence of $SnCl_4$ (1 equiv.). Nucleophiles attack the less hindered site predominantly to give the products (**3**) as shown in equation (3). Tertiary nitro groups are also displaced by an allyl group by this procedure, equation (4). When silyl enol ethers were used as nucleophiles, α-alkylation of the analogous carbonyl compound occurred, when allyl nitro compounds act as electrophiles, equation (5).[6] This reaction therefore expands the scope of allylic alkylations. Reactions using enolate ions as nucleophiles with nitro compounds have been limited to the tertiary compounds; however, the present reaction can be extended to the use of secondary nitro compounds, equation (6).

Thus, nitro groups are displaced by carbon nucleophiles, after the nitro compounds were prepared by carbon–carbon bond forming reactions using nitro compounds as nucleophiles

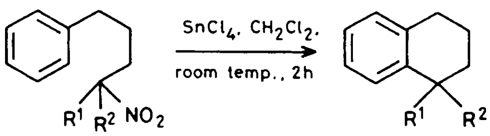
Table 2. Intramolecular Friedel–Crafts reactions of nitro compounds.

Entry	R^1	R^2	Time/h	% Yield of (2)
1	Me	Me	2	55
2	Ph	H	2	74
3	Ph	$[CH_2]_2CO_2Me$	2	48



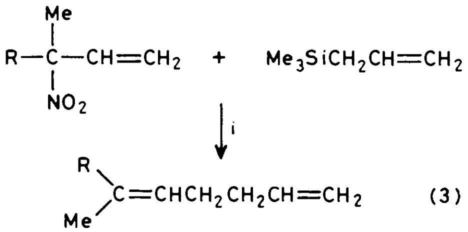
(1)

(1)



(2)

(2)

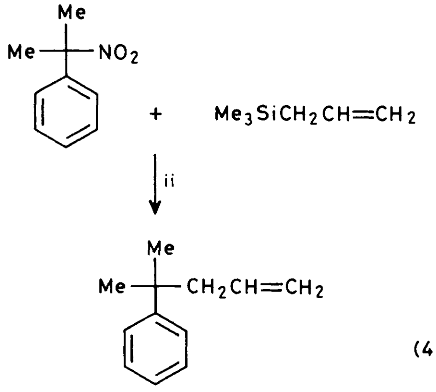


(3)

(3)

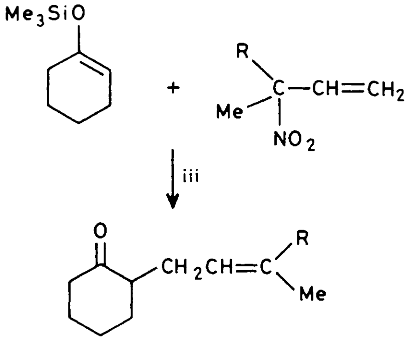
R = C_6H_{13} (65%)
R = $[CH_2]_2CO_2Me$ (70%)

Reagents, for equations (3)—(6): $SnCl_4$ (1 equiv.), CH_2Cl_2. *Conditions:* i, −10 °C, 10 min; ii, −10 °C, 30 min; iii, −20 °C, 30 min.



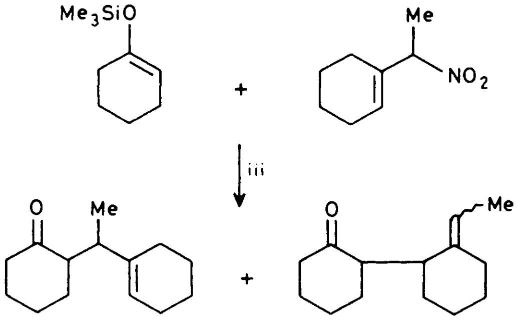
(4)

(4) (40%)



(5)

R = Me (75%)
R = $[CH_2]_2CO_2Me$ (70%)



(6)

(62%)
35 : 65

[see entries 5 and 6, Table 1, entry 3, Table 2, and equations (3), (5), and (6)].†

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4 Sulphones have similar reactivitity to 1,1-dipole synthons, B. M. Trost and M. R. Ghadiri, *J. Am. Chem. Soc.*, 1984, **106**, 7260; 1986, **108**, 1098.

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† The use of nitro compounds as electrophiles will be reported elsewhere. *E.g.*, when Me_3SiY (Y = CN or N_3) was used in the presence of $SnCl_4$, the nitro group was found to be displaced by a cyano or an azide group, respectively.