Regio- and Stereo-selective γ-Substitution of Allylic Nitro Compounds with Lithium Dialkylcuprates

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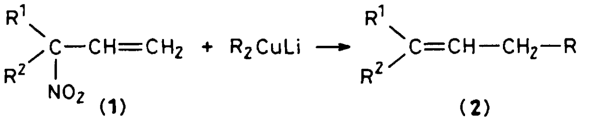
Regio- and stereo-selective γ-substitution of allylic nitro compounds with lithium dialkylcuprates provides a new synthesis for trisubstituted olefins.

Substitution reactions of allylic substrates with organometallic reagents are important in organic synthesis and have been studied extensively. Allylic substrates containing oxygen or sulphur in the leaving group (OAc, $O_3SC_6H_4$-*p*-Me, OR, OH, SO_2R) and allylic halides have commonly been used.[1] In general, high regio- and stereo-selectivity for the alkylation reaction have been reported, although they depend on the structure of the allylic substrate and the organometallic reagent.

Here we report the regio- and stereo-selective γ-substitution of allylic nitro compounds (**1**) with lithium dialkylcuprates to give the trisubstituted olefins (**2**).

The requisite allylic nitro compounds (**1**) were readily prepared either by introduction of a vinyl group into nitroalkanes,[2] or by isomerization of nitro-olefins.[3] The reaction of (**1**) with R_2CuLi gave the substitution products (**2**) which were produced *via* an S_N2' pathway. The regioselectivity was very high for every example tried (Table 1). When R^1 and R^2 were different and one of them was a methyl group, *E*-olefins were formed predominantly.



The following procedure for the preparation of (**2g**) is typical. A hexane solution of Bu^nLi (1.55 M, 2.9 mmol) was added to a stirred suspension of CuI (0.28 g, 1.45 mmol) in diethyl ether (5 ml) at −30 °C under argon. The mixture was stirred for 30 min and ethyl 2-nitro-2-methylbut-3-enoate

Table 1. The reaction of (**1**) with R_2CuLi.

	R^1	R^2	R	Yield of (**2**), %[a]	*E*/*Z* ratio[b]
a	Me	Me	Bu^n	88	
b	Me	Me	Ph	55[c]	
c	$-[CH_2]_4-$		Bu^n	65	
d	$-[CH_2]_4-$		Bu^n	70	
e	Me	$CH_2CH_2CO_2Et$	Bu^n	76	88/12
f	Me	$CH_2CH_2C(=O)Me$	Bu^n	60	83/17
g	Me	CO_2Et	Bu^n	70	96/4
h	Me	CO_2Et	Ph	40[c]	97/3

[a] Isolated yield based on (**1**). [b] Determined by g.l.c. [c] Biphenyl was formed in 20—30% yield as a side product.

(0.23 g, 1.3 mmol) in diethyl ether (3 ml) was added at −30 °C. The mixture was allowed to warm to room temperature and stirred for 15 h. The crude product was chromatographed using hexane–benzene as eluant through a short column of silica gel to yield 0.17 g (70%) of ethyl 2-methyloct-2-enoate (**2g**), whose *E*/*Z* ratio was 96/4. An authentic sample was prepared by the Wittig–Horner reaction using ethyl 2-(*O*,*O*-diethylphosphono)propionate and hexanal,[4] in this case the *E*/*Z* ratio of (**2g**) was 75/25.

Although a number of γ-substitutions of allylic substrates with organometallic reagents have been reported,[1] the present transformations may afford a very useful addition, as nitroalkanes are available from various sources and the nitro group stabilizes an adjacent carbanion to construct a carbon framework much more effectively than any other functional group. The reaction mechanism of the present reaction is also interesting, for there are few examples of the nitro group acting as a leaving group in nucleophilic substitution.[2,3] It is also noteworthy that lithium dialkylcuprates can be used for the substitution reaction with nitro compounds. In general, lithium dialkylcuprates are oxidized to dimers on reaction with nitro compounds.[5]

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