

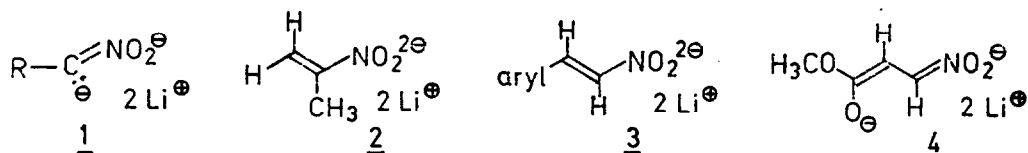
CARBON ALKYLATIONS OF α,α - AND α,β -DOUBLY DEPROTONATED NITROALKANES

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We have recently shown that primary nitroalkanes ($R-CH_2-NO_2$) can be deprotonated twice in the α -position to give 1 which - in contrast to simple nitronates ($R-CH=NO_2^\ominus$) - is C-acylated in good yields¹⁾. If there is only one α -nitro-CH as in 2-nitro propane, the α,β -doubly deprotonated reagent 2 is formed²⁾; the same is true when additionally acidifying groups are present in the β -nitro position as in 2-aryl-1-nitroethane (\rightarrow 3)²⁾. A hitherto unpublished example of this latter type of dianion derived from a nitroalkane is



4 which is readily formed from methyl β -nitro-propionate³⁾ and two moles of lithium diisopropylamide under conditions (THF/HMPT 5:1, $-78^\circ C$, 1h) similar to those used for the generation of 1-3^{1, 2)}. In view of the synthetic potential^{1, 2, 4)} of these novel nucleophilic reagents we report here their successful C-alkylation with alkyl halides and α,β -unsaturated carbonyl compounds.

Secondary nitroalkanes from 1: In our previous experiments¹⁾ we were only able to alkylate 1, $R=C_6H_5S$, while simple nitroalkanes did not give products 6. Obviously, the use of concn. HCl for protonation of the primarily formed nitronate 5 had caused a

a) Part of the projected dissertations of R.H. and F.L., Universität Gießen

Nef-reaction. We now found, that reaction of 1 with alkyl halides (45 min -90° to -78°C , 14 h -78° to $+15^{\circ}\text{C}$) and subsequent addition of a fourfold molar excess of glacial acetic

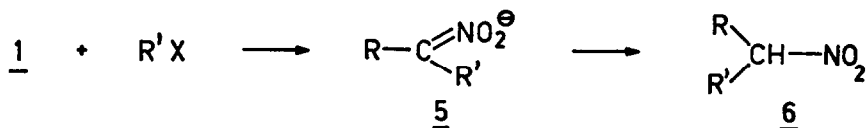


Table 1

alkyl halide (R'X) reacted with <u>1</u>	alkylation product <u>6</u>			
	R	R'	yield [%]	$n_D^{20} / \text{mp. } [^{\circ}\text{C}]$
1-iodo-hexane	H	$\text{C}_6\text{H}_{13}-$	35	1.4274^{22}
benzyl bromide	C_2H_5	$\text{C}_6\text{H}_5-\text{CH}_2-$	53	1.5098^{22}
1-iodo-hexane	C_2H_5	$\text{C}_6\text{H}_{13}-$	51	1.4292^{23}
benzyl bromide	C_5H_{11}	$\text{C}_6\text{H}_5-\text{CH}_2-$	60	1.4990^{22}
1-iodo-ethane	C_5H_{11}	C_2H_5-	50	1.4270^{22}
1-bromo-pentane	C_6H_5	$\text{C}_5\text{H}_{11}-$	80	1.5015^{22}
benzyl bromide	C_6H_5	$\text{C}_6\text{H}_5-\text{CH}_2-$	75	35
1-iodo-ethane	C_6H_5	C_2H_5-	80	1.5132^{22}
1.5-dibromo-pentane	C_6H_5	$\text{Br}(\text{CH}_2)_5-$	40^{a}	1.5360^{22}

a) Besides this "mono-product" a 30% yield of 1.7-dinitro-1.7-diphenyl-heptane was isolated.

acid⁵⁾ (-90°C) before aqueous workup leads to secondary nitroalkanes in yields ranging from 35 to 80% (see table 1). Thus, as in acylations¹⁾, the reagents 1 are powerful carbon-nucleophiles - quite different from simple nitronates which are normally O-alkylated.

Alkylations of 2, 3, and 4: Addition of benzyl bromide to a solution containing 2²⁾ gave 3-nitro-1-phenyl-butane (7a, table 2), the β -benzylation product of 2-nitro propane, while 1-iodo hexane did not produce the corresponding alkylated compound. 3, the hexylation and benzylation of which was already described²⁾, combines with α, β -unsaturated carbonyl compounds in a Michael-addition (\rightarrow 7b, 7c, 7d, table 2). The β -nitro propionic acid derivative 4 could be benzylated as well as alkylated with primary and secondary alkyl

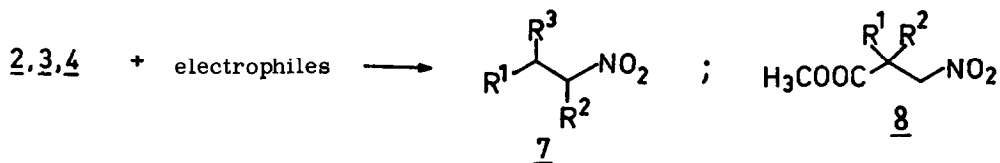
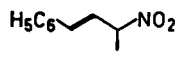
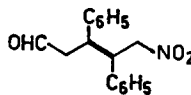
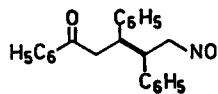
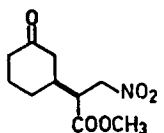
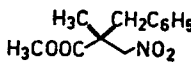
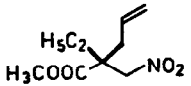


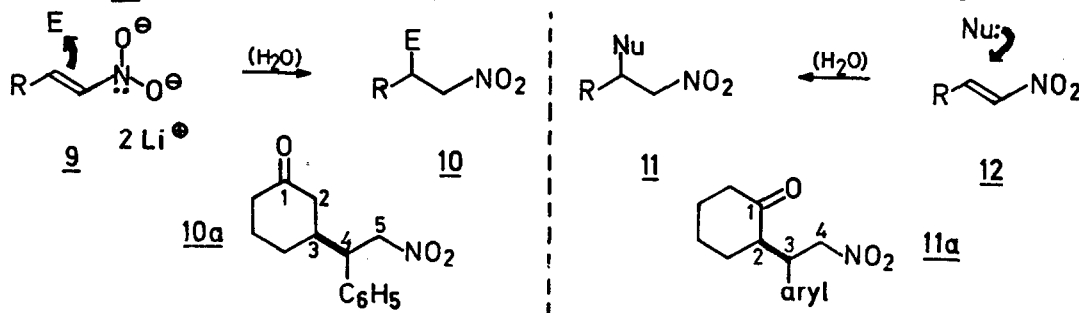
Table 2

dilithio derivative	electrophile	product of type <u>7</u> or <u>8</u>	yield %	physical ^{e)} or spectroscopic data
<u>2</u>	benzyl bromide	<u>7a</u> 	40	$n_D^{22} = 1.5103$
<u>3</u> (aryl=C ₆ H ₅)	cyclohexenone	<u>7b</u> (see formula <u>10a</u>)	49	m. p. 126°C ^{a)}
	cinnamaldehyde	<u>7c</u> 		m. p. 205-206°C ^{a)}
	benzal acetophenone	<u>7d</u> 	45	m. p. 210°C ^{a)}
<u>4</u> ^{b)}	iodo methane	<u>7e</u> , R=CH ₃	74	b. p. 85°C/2mm
	1-iodo octane	<u>7f</u> , R=n-C ₈ H ₁₇	81	b. p. 105°C/0.1mm $n_D^{22} = 1.4460$
	2-iodo propane	<u>7g</u> , R=CH(CH ₃) ₂	78	b. p. 100°C/1.8mm $n_D^{21.5} = 1.4391$
	benzyl bromide	<u>7h</u> , R=C ₆ H ₅ CH ₂	80	b. p. 130°C/0.2mm $n_D^{22} = 1.5145$
		<u>7i</u> 		b. p. 170°C/0.5mm
<u>4</u>	1. iodo methane 2. LDA ^{c)} 3. benzyl bromide ^{d)}	<u>8a</u> 	78	b. p. 120°C/0.13mm $n_D^{22} = 1.5140$
	1. iodo ethane 2. LDA ^{c)} 3. allyl bromide ^{d)}	<u>8b</u> 	62	b. p. 95°C/0.5mm $n_D^{20} = 1.4577$

a) Mixture of two diastereomers. b) After addition of the alkylating reagent at -78°C the temperature was raised within 3h to -30°C before workup. c) For this deprotonation of a monoalkylated derivative a reaction time of 3h between -78°C and -30°C is required. d) Reaction time 15h at -15°C (freezer). e) b. p. = bath temperatures upon micro distillation.

iodide to give in high yields products 7e-h (see table 2); it also furnished the Michael-adduct 7i to cyclohexenone. The monoalkylated methyl β -nitro propionates can be converted once more to dianions of type 4 and alkylated. This leads to the α,α -disubstituted nitro esters 8a and 8b (table 2). The structures of the products 6, 7, and 8 thus obtained are fully compatible with all spectral data; their elemental analyses were correct within 0.3%.

The nucleophiles 2-4 can be described by the resonance formula 9 and may thus be regarded as enamines²⁾ or Li_2O -adducts to ene-nitroso derivatives ($\text{C}=\text{C}-\text{N}=\text{O}$). Their products 10 with electrophiles ($\text{E}^{\oplus}/\text{H}^{\oplus}$) are synthetic counterparts of nucleophile



($\text{Nu}^{\ominus}/\text{H}^{\oplus}$) adducts 11 to nitroolefins 12 [umpolung of nitroalkene reactivity⁶⁾, cf. 10a (\equiv 7b of table 2), the adduct of 3 to cyclohexenone with 11a⁴⁾, obtained from cyclohexanone enolate and an ω -nitro styrene].

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References and footnotes

- 1) D. Seebach and F. Lehr, *Angew. Chem.* **88**, 540 (1976); *Angew. Int. Ed. Engl.* **15**, 505 (1976), and references cited therein.
- 2) R. Henning, F. Lehr, and D. Seebach, *Helv. Chim. Act.* **59**, 2213 (1976).
- 3) Prepared from commercially available β -nitro-propionic acid and $\text{CH}_3\text{OH}/\text{H}_2\text{SO}_4$; b. p. $61^\circ\text{C}/0.7\text{mm}$ [Lit.: b. p. $68^\circ\text{C}/1\text{mm}$; V. M. Belikov, *Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk* 1956, 855; *C. A.* **51**, 1837i (1957)].
- 4) D. Seebach, H. F. Leitz, and V. Ehrig, *Chem. Ber.* **108**, 1924 (1975).
- 5) As recommended by N. Kornblum and G. E. Graham, *J. Amer. Chem. Soc.* **73**, 4041 (1951).
- 6) For recent examples of Michael-additions (cf. 2 and 3) to nitroolefins see ref. 4) and: D. Seebach and V. Ehrig, *Angew. Chem.* **86**, 446 (1974); *Angew. Chem. Int. Ed. Engl.* **13**, 401 (1974); *Chem. Ber.* **108**, 1961 (1975).
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