

Novel Regioselective Generation of Nitroalkane Dianions

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An alteration of the regioselectivity in dianion formation, from the usual α,α -dianions to the uncommon α,β -dianions, of nitroethane and 1-nitropropane was established by changing the order of addition of reagents.

Regioselective C–C bond formation by the reaction of polyanions with electrophiles is interesting with respect to new synthetic methods.¹ Recently, Seebach *et al.*² have made improvements in the Henry reaction and emphasized the usefulness of nitro compounds for regio- and stereo-selective C–C bond formation. However by their double deprotonation method, the formation of α,β -dianions was limited to secondary and β -aryl nitroalkanes.³ From primary nitroalkanes, α,α -dianions (**1**) were prepared regiospecifically in all cases except one.⁴ We were interested in this relatively unexplored regioselective generation of α,β -dianions of primary nitroalkanes (**2**) in connection with our investigation on the photochemistry of nitronate anions⁵ and nitroalkane dianions. The solvent addend hexamethylphosphoric triamide (HMPA) is known to play an important role in changing the regioselectivity of anion formation⁶ and also in affecting the ratio of *E/Z* enolate anion formation by changing the addition sequence of the base. We, hence, re-examined Seebach's double deprotonation technique considering the above points. The change of the addition sequence of reagents showed an interesting alteration of regioselectivity in dianion formation.

Following Seebach's procedure⁸ (procedure A) nitroethane dianion was added to benzaldehyde, *i.e.*, BuⁿLi (22 mmol) was added to a tetrahydrofuran (THF) solution of nitroethane (11 mmol) and HMPA (56.9 mmol) at -90°C and then benzaldehyde (10 mmol) was added. The α -type product (**3**)⁹ derived from the α,α -dianion predominated over the β -type product (**4**)[†] derived from the α,β -dianion [(**3**):(**4**) 85:15]. With the same molar ratio and temperature, but changing the sequence of addition, *i.e.*, addition of nitroethane to a THF

solution of BuⁿLi and HMPA (procedure B), followed by addition of benzaldehyde led to (**4**) almost exclusively [(**3**):(**4**) 5:95] with a total yield of 76%. Also remarkable was the effect of the solvent addend HMPA; a control reaction using procedure B without HMPA gave (**3**) as a single product. The ratio of HMPA to BuⁿLi was also found to direct the regioselectivity. A ratio of HMPA to BuⁿLi of $<1:1$ showed a preference for (**3**) while (**4**) dominated at a ratio $>2:1$. Procedure A did not demonstrate such an effect. However the ratio of epimers (*threo/erythro*) was affected as reported.⁸

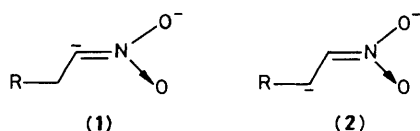
This effect of HMPA was further investigated in the reaction of nitroethane dianion with benzyl bromide by procedure B, which showed a similar tendency to that observed in the reaction with benzaldehyde. Virtually exclusive formation of the β -type product (**6**)¹⁰ was observed for HMPA: BuⁿLi = 2, though the yield was low ($\sim 30\%$).

To extend the scope of this methodology, the reaction of nitroethane dianion generated by procedure B was also carried out with electrophiles: hexanal, cyclohexanone, and benzophenone. In all cases, β -type products predominated with 99% regioselectivity, and isolated yields of 35, 63, and 18% respectively. § 1-Nitropropane showed a similar 99%

Table 1. Effect of HMPA on the ratio of (**3**) to (**4**) by procedure B.^a

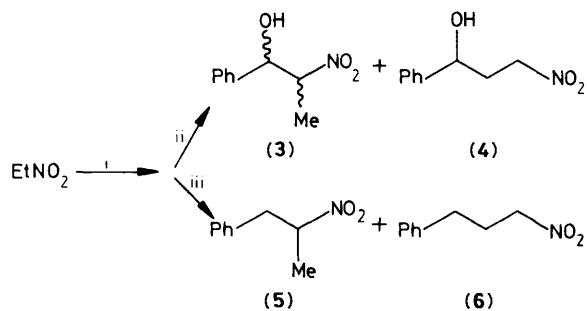
HMPA /Bu ⁿ Li ^b	(3):(4)	Yield, ^c %
0	100:0	57
0.78	84:16	62
1.55	70:30	60
2.10	11:89	57
2.60	5:95	76

^a Nitroethane was added at -90°C and the temperature was raised to -78°C when benzaldehyde was added. The temperature was then quickly raised to -35°C . ^b Molar ratio. ^c Total isolated yield.



† Compound (**4**) was hydrogenated to a known amine.

§ All new compounds gave satisfactory ¹H n.m.r. and mass spectra, and elemental analyses.



Reagents: i, $\text{Bu}^n\text{Li}/\text{HMPA}$; then ii, PhCHO ; or iii, PhCH_2Br .

β -selectivity (isolated yield, 77%) in the reaction with benzaldehyde. \S

Attempts to differentiate between kinetic or thermodynamic control of this regioselectivity were not conclusive. \ddagger To the best of our knowledge, the present finding is the first example of the alteration of regioselectivity in dianion formation as a function of the amount of HMPA. The sequence of additions is the practical key factor to facilitate this interesting regioselectivity, which has a wide synthetic potential.

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\ddagger Dianions were prepared at -80 to -30°C .

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