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NUCLEOPHILIC SUBSTITUTION REACTION VIA ONE ELECTRON TRANSFER PROCESSES. I A NEW SYNTHETIC METHOD FOR THE PREPARATION OF α,β-UNSATURATED NITRILES

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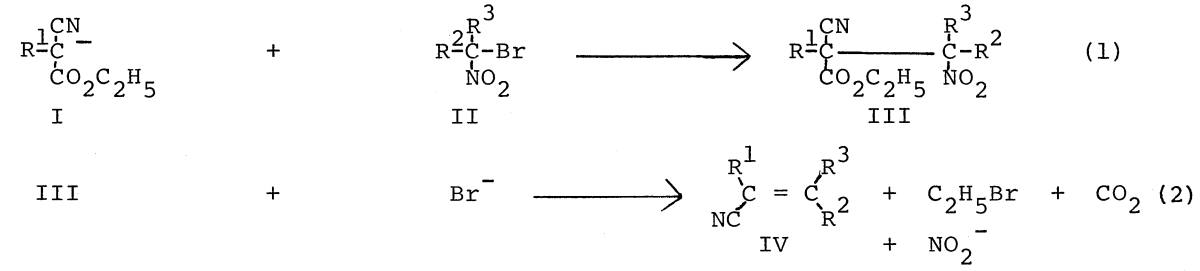
An efficient one-pot synthesis of α,β-unsaturated nitriles consisting of the coupling reaction of α-bromonitroalkanes with the anions of ethyl α-alkylcyanoacetates followed by deethoxycarbonylation and elimination of the nitro group is described.

A newly emerging area of chemistry is found in radical chain substitution reactions at aliphatic carbon atoms(S_{RN}). Generally they give rise to high yields and are of mechanistic and synthetic interests.[1)]

This paper describes the application of S_{RN} to a construction of carbon-carbon linkage on the preparation of α,β-unsaturated nitriles. The procedure consists simply of mixing the sodium salt of ethyl α-alkylcyanoacetates(I, 0.01 mol) with α-bromonitroalkanes(II, 0.01 mol) in hexamethylphosphoric triamide(10 ml) at room temperature under nitrogen and heating the resulting solution at 120° for 1 hr to affect deethoxycarbonylation. After the usual work up, simple distillation affords the pure products(IV) in good yields. Some typical examples are presented in Table.



The coupling reaction(eq 1) is believed to proceed by S_{RN} mechanism.[2)] The reaction is quite rapid. For example, the reaction of 2-bromo-2-nitropropane with the anion of ethyl 2-cyano-3-methylbutyrate was complete within 2 min at room temperature and the coupling product was obtained in almost quantitative yield.[2)] Isolation of III is not necessary. Deethoxycarbonylation promoted by bromide ion in dipolar aprotic solvents proceeds through carbanion intermediate.[3)] Therefore elimination of the nitro group may plausibly proceed by E1CB mechanism.

The reaction can be carried out in other dipolar aprotic solvents such as dimethylformamide or dimethyl sulfoxide. However, high temperature(150°) and long reaction time(6hr) were necessary to affect deethoxycarbonylation. α-Chloronitroalkanes or α-iodonitroalkanes also react with I to give IV in somewhat poor yields. The present method furnishes a valuable and simple method for the preparation of highly substituted α,β-unsaturated nitriles from readily available starting materials.[4] The reactions of other stable carbanions with the α-halonitroalkanes are possible. Studies are now in progress and the results will be published soon.

Table Yields of α,β-unsaturated nitriles (IV)

R^1	R^2	R^3	isolated yields of IV (%)
$i\text{-}C_3H_7$	CH_3	CH_3	70
$i\text{-}C_3H_7$	CH_3	CH_3CH_2	62 (E/Z=1.3)
$i\text{-}C_3H_7$	$-(CH_2)_5-$		63
$n\text{-}C_4H_9$	CH_3	CH_3	72
$n\text{-}C_8H_{17}$	CH_3	CH_3	72
$C_6H_5CH_2$	CH_3	CH_3	75
$C_6H_5CH_2$	CH_3	CH_3CH_2	75 (E/Z=1.2)
$C_6H_5CH_2$	$-(CH_2)_5-$		70

E/Z ratio was determined by nmr.

References

1) N. Kornblum, S. D. Boyd, and N. Ono, J. Am. Chem. Soc., 96, 2580 (1974) and earlier references given therein.

2) The fact that this coupling reaction gives no o-alkylation products and that it is insensitive to steric hindrance supports this mechanism. The reaction is strongly inhibited by the presence of radical inhibitors. Ten mole per cent of di-tert-butyl nitroxide inhibited the reaction of 2-bromo-2-nitropropane with the anion of ethyl 2-cyano-3-methylbutyrate, and only 3% of coupling product was detected in 2 min.

3) M. Asaoka, K. Miyake, and H. Takei, Chem. Lett., 1149 (1975).

4) Ethyl α-alkylcyanoacetates were prepared by alkylation of ethyl cyanoacetates. See, for example, R. B. Millar and B. F. Smith, Synth. Commun., 3, 413 (1973). α-Bromonitroalkanes were prepared by bromination of nitroalkanes. See, for example, N. Kornblum, M.K. Kestner, S. D. Boyd, and L. C. Cattran, J. Am. Chem. Soc., 95, 3356 (1973).

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