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NUCLEOPHILIC SUBSTITUTION REACTION VIA ONE ELECTRON TRANSFER PROCESSES. II A NEW SYNTHETIC METHOD FOR THE PREPARATION OF α,β-UNSATUPATED ESTERS AND KETONES

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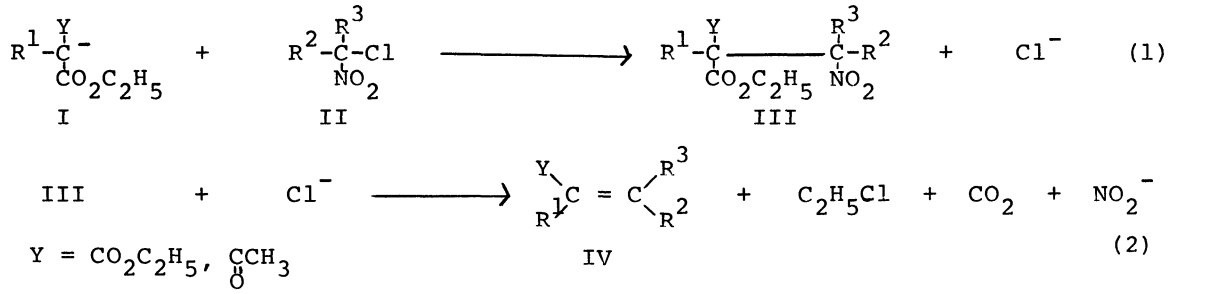
An efficient one-pot synthesis of α,β-unsaturated esters and ketones consisting of the coupling reaction of α-chloronitroalkanes with the anions of diethyl α-alkylmalonates or ethyl α-alkylacetoacetates followed by deethoxycarbonylation and concomitant elimination of the nitro group is described.

The radical chain substitution reaction (S_{RN}) is becoming one of the quite promising process in the synthetic organic chemistry. In a previous paper 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 was described.[1] The synthetic scheme suggested that α,β-unsaturated esters and ketones would also be available by this method. The present report describes a new synthetic method for these compounds. The general synthetic approach is shown in scheme I.

Scheme I



A typical procedure is given below. A mixture of the sodium salt of diethyl 2-ethylmalonate (0.01 mol) and 2-chloro-2-nitropropane (0.01 mol) in 10 ml of HMPA was irradiated with 150 W tungstenlamp under nitrogen at 20° for 3 hr and then the mixture was heated at 120° for 4 hr to affect deethoxycarbonylation. Chloride ion that affects deethoxycarbonylation is produced in the reaction of eq 1. Working up in the usual manner followed by distillation gave ethyl 2-isopropylidenebutyrate in 63% yield, bp 75°/48mmHg, ir(neat): 1700, 1620, 1190, 1195 cm^{-1}; nmr(δ_{TMS}ppm, CCl_4): 0.97(t,3H), 1.29(t,3H), 1.80(s,3H), 1.94(s,3H), 2.29(q,2H), 4.14(q,2H); mass: m/e: 156(M^+).

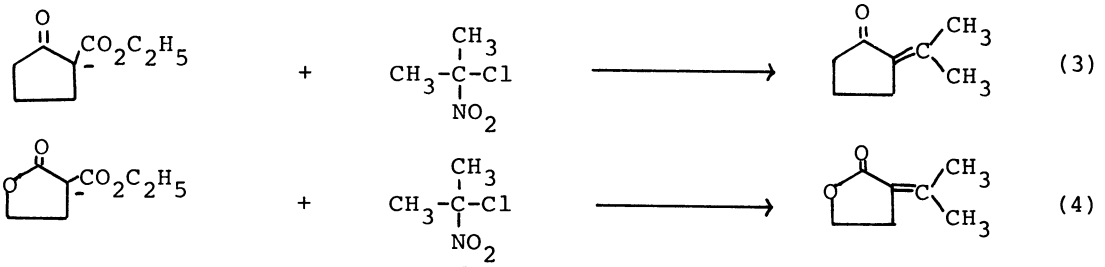
The present reaction furnishes a valuable and simple method for the preparation of highly substituted α,β-unsaturated carbonyl compounds from readily available starting materials.[2] Some typical examples are presented in the Table.

Table

R^1	Y	R^2	R^3	Isolated yield of IV* (%)	Bp (°C/mmHg)
C_2H_5	$CO_2C_2H_5$	CH_3	CH_3	63	75/48
C_2H_5	$CO_2C_2H_5$	$-(CH_2)_5-$		56	102/8
$n\text{-}C_4H_9$	$CO_2C_2H_5$	CH_3	CH_3	69	110/48
$n\text{-}C_4H_9$	$CO_2C_2H_5$	$-(CH_2)_5-$		42	120/9
C_2H_5	CCH_3 (O)	CH_3	CH_3	51	61/20
$n\text{-}C_4H_9$	CCH_3 (O)	CH_3	CH_3	60	90/20

* All compounds exhibited ir, nmr and mass spectrum data in accordance with assigned structure.

The coupling reaction of eq 1 proceeds by S_{RN} mechanism.[3] The reaction is catalyzed by light and inhibited by p-dinitrobenzene as expected for the S_{RN} process. α-Bromonitroalkanes and α-iodonitroalkanes can not be used for this reaction, for halogen transfer reaction from nitrohalides to I and the subsequent complex reactions take place in the reaction mixture, thus reducing the yield of III.[4] The reaction can be carried out in other dipolar aprotic solvents such as DMSO or DMF. However, high temperature(150°) and long reaction time(7hr) are necessary to affect deethoxycarbonylation. Practical uses are found in the preparation of a number of important natural products. The present reaction is the method of choice for the introduction of sec-alkylidene groups alpha to a carbonyl function. 2-Isopropylidenecyclopentanone(bp 85°/11mmHg) and 2-isopropylidene-γ-butyrolactone (bp 109/13mmHg) were prepared in 54 and 50% overall yield as are shown in eq 3 and 4.



References

1) N. Ono, H. Eto, R. Tamura, J. Hayami, and A. Kaji, Chem. Lett., 757(1976).
2) α-Chloronitroalkanes were prepared by chlorination of nitroalkanes. See, for example, N. Kornblum, M. K. Kestner, S. D. Boyd, and L. C. Cattran, J. Am. Chem. Soc., 95, 3356 (1973).
3) For an excellent review of S_{RN}, see, N. Kornblum, Angew. Chem. Int. Edit., 14, 734 (1975).
4) Compounds III can be obtained in good yields by the reaction of α-nitrosulfones or α,α-dinitrocompounds with I. The effects of the leaving groups and nucleophiles will be discussed elsewhere.

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