

CARBON-CARBON BOND FORMATION BY MEANS OF SUBSTITUTION AND ADDITION REACTIONS INVOLVING THE  
 POLYMER-SUPPORTED CARBANION FROM METHYL NITROACETATE

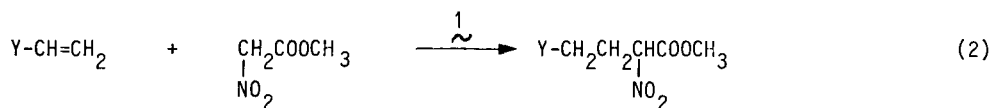
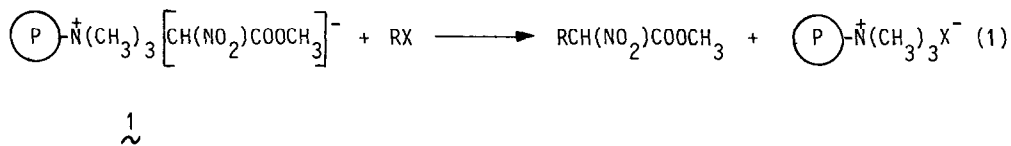
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Summary: A polymer-supported carbanion has been prepared from methyl nitroacetate and reacted with alkyl halides or activated olefins to give  $\alpha$ -nitroesters.

Nitroacetic acid and its derivatives have been the subject of investigations by many synthetic chemists because the presence of the active methylene group makes these compounds useful intermediates for the formation of the carbon-carbon bond<sup>1</sup>. However the yields of the addition and substitution reactions involving the carbanion generated by common procedures are frequently rather poor<sup>2-5</sup>. Our interest in the field of carbon-carbon forming reactions<sup>6</sup> has led us to evaluate the possibility of improving the process by resorting to a polymer-supported carbanion, a type of reagent which has been used only in a very few cases<sup>7</sup>.

We now report that the polymer-supported carbanion **1** can be easily obtained utilizing the commercially available Amberlite IRA 400 (OH<sup>-</sup>) for the anion generation from methyl nitroacetate. The carbanionic resin is stable enough to be isolated in the dry state and stored for months. Furthermore, we have found that the polymeric species **1** reacts with alkyl halides and can be used conveniently in the Michael addition, to give  $\alpha$ -nitroesters according to eqs. 1 and 2:



Y = CN, COOCH<sub>3</sub>

The obtained results are reported in the Table. Yields are higher than or comparable with

T A B L E  
 Synthesis of  $\alpha$ -nitroesters by use of the polymer-supported carbanion 1.

Entry	Electrophile <sup>a</sup>	Solvent <sup>b</sup>	Time (h)	Product	Yield <sup>c</sup> (%)
1	$\text{CH}_3\text{OOC-CH}_2\text{-Br}$	$\text{CH}_2\text{Cl}_2$	27	$\text{CH}_3\text{OOC-CH}_2\text{-}\underset{\text{NO}_2}{\text{CH}}\text{-COOCH}_3$	54
2	$\text{CH}_3\text{OOC-CH}_2\text{-CH}_2\text{-Br}$	$\text{CH}_2\text{Cl}_2$	45	$\text{CH}_3\text{OOC-CH}_2\text{-CH}_2\text{-}\underset{\text{NO}_2}{\text{CH}}\text{-COOCH}_3$	70
3	$\text{C}_6\text{H}_5\text{-CH}_2\text{-Br}$	$\text{CH}_2\text{Cl}_2$	24	$\text{C}_6\text{H}_5\text{-CH}_2\text{-}\underset{\text{NO}_2}{\text{CH}}\text{-COOCH}_3$	45
4	$\text{CH}_3\text{-I}$	$\text{CH}_2\text{Cl}_2$	32	$\text{CH}_3\text{-}\underset{\text{NO}_2}{\text{CH}}\text{-COOCH}_3$	56 <sup>d</sup>
5	$\text{CH}_3\text{-CH}_2\text{-I}$	THF	50	$\text{CH}_3\text{-CH}_2\text{-}\underset{\text{NO}_2}{\text{CH}}\text{-COOCH}_3$	35
6	$\text{CH}_2\text{=CH-CH}_2\text{-Br}$	$\text{CH}_2\text{Cl}_2$	25	$\text{CH}_2\text{=CH-CH}_2\text{-}\underset{\text{NO}_2}{\text{CH}}\text{-COOCH}_3$	40 <sup>d,e</sup>
7	$\text{CH}_2\text{=CH-COOCH}_3$	THF	26	$\text{CH}_3\text{OOC-CH}_2\text{-CH}_2\text{-}\underset{\text{NO}_2}{\text{CH}}\text{-COOCH}_3$	75 <sup>f</sup>
8	$\text{CH}_2\text{=CH-CN}$	THF	20	$\text{NC-CH}_2\text{-CH}_2\text{-}\underset{\text{NO}_2}{\text{CH}}\text{-COOCH}_3$	62 <sup>d,e,f</sup>

a) The reactions with alkyl halides were carried with a 2:1 molar ratio resin/substrate. In the Michael additions equimolecular amounts of methyl nitroacetate and activated olefin and 10% of the polymer were used. b) All reactions were performed at reflux temperature. c) Unless otherwise indicated yields refer to pure isolated compounds. d) Yields determined by G.L.C. analysis. e) These new compounds have satisfactory spectral data in agreement with the assigned structure. f) These reactions can be also performed with comparable yields by stirring a mixture of Amberlite IRA 400 ( $\text{OH}^-$ ) resin (10%) with methyl nitroacetate and the activated olefins.

those reported in the literature for other more conventional procedures. Specifically, in the reaction of methyl bromoacetate with methyl nitroacetate, in basic conditions and in dipolar solvents, dimethyl  $\alpha$ -nitrosuccinate has been prepared in poor yields ( $\sim 23\%$ )<sup>2</sup> while our method permits to obtain it in reasonably higher yields (54%). Higher yields of dimethyl  $\alpha$ -nitroglutarate with respect to those reported (45%<sup>2</sup> and 5.4%<sup>3</sup>) have also been obtained both in the substitution and in the addition reactions. Moreover, while significant amounts of dialkylated by-products have been found by following other procedures<sup>2,4</sup>, in our reactions these by-products are obtained in lower amounts ( $\sim 10\%$ , GC) in all cases, except for entry 8 (23%). In conclusion, taking also into account the advantages of mild reaction conditions and simplified work-up procedures, it appears that the polymer-supported carbanion 1 can be considered an useful reagent with a promising synthetic potential.

To prepare the reagent 1 a solution of methyl nitroacetate<sup>8</sup> (25 g) in methylene chloride (75 ml) is slowly passed, six-seven times, through a column filled with the Amberlite IRA 400 ( $\text{OH}^-$ ) (50 g), previously washed with the same solvent. The new polymeric material is washed with methylene chloride and dried under vacuum. From the amount of methyl nitroacetate recovered unchanged, the exchange capacity of our resin was estimated to be in the range 2.2 - 2.5 mmol/g. Similar values were also obtained by treating the resin with dilute HCl and extracting with methylene chloride the methyl nitroacetate produced.

In a typical reaction polymer-supported reagent 1 (8 g, 18.4 mmol) and methyl 3-bromopropionate (1.53 g, 9.2 mmol) are stirred in refluxing methylene chloride (40 ml). After reaction completion (G.L.C. analysis), the resin is filtered off and washed with methylene chloride and with dilute HCl. The acid is extracted with the same solvent and the combined organic layers are dried over  $\text{Na}_2\text{SO}_4$  and evaporated to give dimethyl  $\alpha$ -nitroglutarate<sup>2</sup> as an oil which is purified by distillation (1.31 g, 70% yield). The same product was obtained in 75% yield by Michael addition of methyl nitroacetate to methyl acrylate (entry 7), using equimolecular amounts of the two esters and 10% of the polymer 1.

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