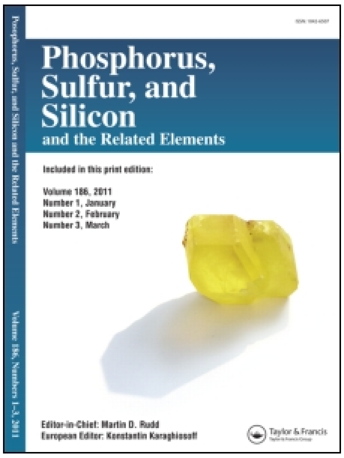

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SULFAMOYLATION OF ESTER ENOLATE ANIONS

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SULFAMOYLATION OF ESTER ENOLATE ANIONS

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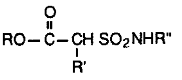
Stabilized carbanions such as the α-carbanions of carboxylic acid esters react with sulfamoyl chlorides by nucleophilic displacement at chlorine which results in chlorination of the carbanion. Thus direct sulfamoylation of these carbanions with sulfamoyl chlorides fails. Conversion of sulfamoyl chlorides to N-sulfonylamines followed by addition of carbanions at −78°C results in sulfamoylation of the carbanion. The method has not been successful with carbanions from diethyl acetamidomalonate and ethyl diphenylacetate.

Key words: Sulfamoylation; ester enolates; sulfonylamines; sulfamoylacetates; carbalkoxylation; sulfamoyl chlorides.

INTRODUCTION

For the synthesis of 1,2,4-thiadiazolin-3-one, 1,1-dioxides[1] we needed a facile preparation of alkyl α-(N-alkylsulfamoyl)acetates (**1**). The simple members of



$$\mathrm{RO{-}\overset{O}{\overset{\|}{C}}{-}\underset{R'}{\underset{|}{CH}}\,SO_2NHR''}$$

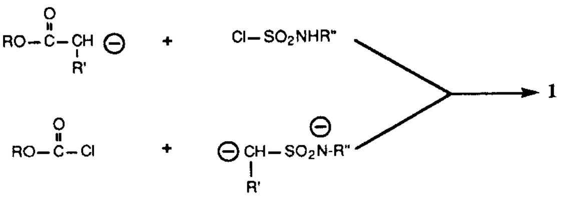
1

this series (**1**, R = H or CH_3) are easily prepared by the reaction of sodium bisulfite with α-halo esters followed by chlorination of the sulfonic acid and amination of the sulfonyl chloride.[2] This method is not satisfactory for the higher members of the series (**1**, R′ = phenyl).

This report describes the successful direct sulfamoylation of ester enolate anions.

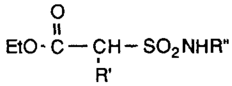
RESULTS AND DISCUSSION

Formation of **1** can be envisioned from either sulfamoylation of the α-carbanion of an ester or the carbalkoxylation of the α-carbanion of a sulfonamide (Scheme 1).



Scheme1

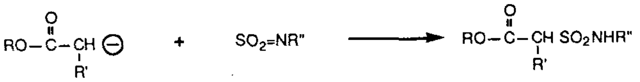
TABLE I
PROPERTIES AND YIELDS OF ETHYL α-SULFAMOYLACETATES



$EtO{\cdot}C(=O){-}CH(R'){-}SO_2NHR''$

R'	R"	M-P	Yield by Sulfamoylation	Yield by Carbethoxylation
H	t-Bu	oil	72%	
Phenyl	t-Bu	oil	25%	77%
Phenyl	H	96-99°C	20.5%	0%

We had previously attempted the direct sulfamoylation of α-carbanions of esters using sulfamoyl chlorides[3] and discovered as Kohler and MacDonald[4] had much earlier that at least in some cases sulfonyl chlorides undergo nucleophilic attack at chlorine to give chlorination of carbanions. Atkins and Burgess[5] described the electrophilic N-sulfonylamines (sulfonyl imides or sulfonyl imines[6]) which are generated by treating sulfamoyl chlorides with bases at low temperatures. Thus as shown in Scheme 2, we proposed that α-carbanions of esters would react with N-sulfonylamines to form sulfonamides.



Scheme2

We have completed the reaction shown in Scheme 2 using the α-carbanions from ethyl acetate and ethyl phenylacetate with N-*t*-butylsulfonylamine and sulfonylamine. The results are shown in Table I. The main competing reaction is self condensation of the esters. Although we have not attempted it, the use of *t*-butyl esters instead of ethyl esters should minimize this side reaction. This reaction was not successful with the anions from ethyl diphenylacetate and diethyl acetamidomalonate.

In order to make a comparison of the second method shown in Scheme 1 (carbalkoxylation) to sulfamoylation we have run the reaction between the dianion of N-*t*-butylbenzylsulfonamide and ethyl chloroformate. This procedure furnishes a better yield of a product which is easier to purify than the product from sulfamoylation of ethyl phenylacetate.

This procedure fails in the case where R″ is H and no C-carbethoxylated product was isolated.

EXPERIMENTAL SECTION

All melting points were taken on a Thomas Hoover melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin–Elmer model 283-B spectrophotometer. Nmr spectra were taken on a Varian model EM390 spectrometer using tetramethylsilane (TMS) as an internal standard. Gas chromatographic analyses were carried out on a Hewlett Packard Model 5720 A gas chromatograph using a 6-foot glass column with 3% OV-17 packing. Elemental analyses were performed by Atlantic Microlab, Inc., Atlanta, GA.

Ethyl α-(N-tert-Butylsulfamoyl)phenylacetate (carbethoxylation method). To a cold solution (−10°C) of 4.5 g (20 mmol) of N-(*t*-butyl)benzylsulfonamide in 40 mL of THF was added 23 mL (52.9 mmole) of 2.3 M n-butyllithium. As the butyllithium was added the solution changed to a light blue-green color and then to orange as the addition of the butyllithium was completed. The reaction mixture was stirred at −10°C for 1 hr. To this solution was added 5 mL (5.5 g, 50 mmole) of freshly distilled ethyl chloroformate. The reaction mixture was warmed to room temperature over 1 hr, poured onto ice, acidified with 10% HCl and extracted with ether (2 × 100 mL). The ether was dried over $CaCl_2$ and concentrated *in vacuo* to give 7 g of a viscous oil. This oil was chromatographed on Kieselgel® 60 (230–400) mesh) silica using 3:1 hexane/ethyl acetate for elution to afford 4.6 g (77%) of the desired sulfonamide as a viscous oil: GC. r_t (3.25 min., 200°C; 8.13 min., 175°C) ir. (neat) 3300 cm^{-1} (NH, 1730 cm^{-1} (CO), 1330 and 1140 cm^{-1} (SO_2); ^{1}HNMR ($CDCl_3$) δ 1.3 (m, 12^1H, $CH3$, t-C_4H_9), δ 4.3 (q, 2^1H, O-CH_2), δ 4.71 (br s, 1^1H, NH), δ 5.06 (s, 1^1H, SO_2-CH-CO), δ 7.00–7.73 (m, 5^1H, C_6H_5).

Anal. Calc. for $C_{13}H_{21}NO_4S$: C 56.17, H 7.07, N 4.68, S 10.68. Found: C 56.10, H 7.09, N 4.65, S 10.68.

Ethyl α-(N-tert-Butylsulfamoyl)phenylacetate (sulfamoylation). To a suspension of 3g (65 mmole) of 50% sodium hydride oil suspension in 100 mL of THF was added at room temperature 10g (61 mmole) of freshly distilled ethyl phenylacetate and the mixture was stirred for 3 hrs. This mixture was added to a solution of N-*t*-butylsulfonylamine (formed from 5 mL *t*-butylalcohol and 5 mL chlorosulfonyl isocyanate in the presence of 3.0 g (65 mmoles) 50% of NaH oil suspension in the presence of 150 mL of THF at −78°C). The reaction was warmed to room temperature, added to ice, acidified with 10% HCl and extracted with ether (1 × 100 mL). The ether was dried over $CaCl_2$ and concentrated *in vacuo* to obtain 21 g of an oil which was chromatographed two times on Kieselgel® 60 (230–400 mesh) silica using hexane (500 mL) followed by $CHCl_3$ (200 mL) for elution to afford 4.5 g (25.0%) of a clear-yellow oil. ^{1}NHMR, IR, GC are the same for this material as that obtained by carbethoxylation.

ACKNOWLEDGEMENT

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