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A FACILE PHASE TRANSFER CATALYZED MICHAEL ADDITION OF ISOPROPYL 4-CHLOROBENZENESULFONYL ACETATE TO α, β-UNSATURATED ESTERS

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Abstract: The Michael addition of isopropyl 4-chlorobenzenesulfonyl acetate to α, β-unsaturated esters was studied under PTC conditions. The method has the advantage of mild reaction conditions and high yield.

The application of sulfones in modern organic synthesis is one of the most attractive subjects of current research interests[1-3]. Arylsulfonyl groups are easily eliminated[4-5] or reductively replaced[6-7] and thus they are useful temporary activating groups for alkylation, acylation and addition reactions[1,4-7]. The conjugate addition of a sulfone anion to electrophilic olefins is

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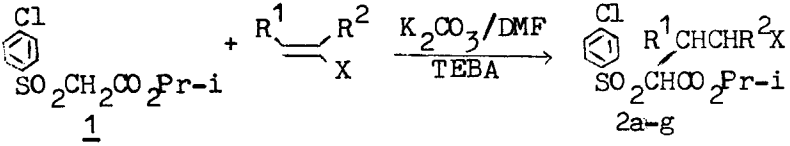
synthetically important for effecting carbon-carbon bond formation[4, 8-9].

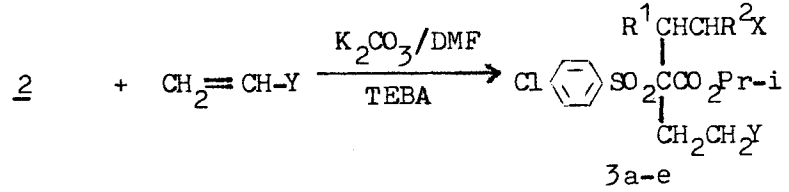
In the course of our investigations on sulfur-containing carbanions, we have reported a facile alkylation of α-arylsulfonylacetate under the solid-liquid PTC conditions[10]. In this paper we wish to describe a new type Michael addition of isopropyl 4-chlorobenzenesulfonyl acetate 1 to α, β-unsaturated esters.

Our procedure involves initially formation of the sulfur-containing carbanion from α-arylsulfonylacetate 1 with potassium carbonate under PTC conditions and then *in situ* reaction with the α, β-unsaturated esters at 40-60℃ (Scheme 1). The progress of the reaction was monitored by TLC. The addition of 1 to acrylate or itaconate proceeded smoothly and excellent yields were obtained for products 2a-d (89-95%). An increase in the bulk of β-substituting groups in the esters seems to result in a decrease of yields of 2e-g (56-85%). On the other hand, the monoaddition product can directly react with another active α, β-unsaturated ester (CH_2=CH-Y, Y=CO_2CH_3, CO_2Et or acrylonitrile) in one-pot to give the double addition compounds (Scheme 2). The scope of the reaction is illustrated in Table 1.

We believe the route described in this paper represents a significant improvement in the conjugate addition of a α-sulfonylcarbanion to α, β-unsaturated esters by contrast with previously reported procedure which is frequently carried out in the presence of strong bases.



Scheme 1



Scheme 2

TABLE 1

Product No.	R1	R2	X	Y	Time (hr.)	Yield (%)
2a	H	CH_3	CO_2CH_3	-	2.0	89
2b	H	CH_2CO_2Et	CO_2Et	-	1.5	90
2c	H	$CH_2CO_2Pr\text{-}i$	$CO_2Pr\text{-}i$	-	2.0	95
2d	H	$CH_2CO_2Bu\text{-}i$	$CO_2Bu\text{-}i$	-	1.5	92
2e	CH_3	H	$CO_2Pr\text{-}i$	-	3.0	85
2f	CO_2CH_3	CO_2CH_3	H	-	3.5	74
2g	$CO_2Pr\text{-}i$	$CO_2Pr\text{-}i$	H	-	4.0	56
3a	H	CH_3	CO_2CH_3	CO_2Et	2 + 2	80
3b	H	CH_3	CO_2CH_3	CN	2 + 2	55
3c	H	$CH_2CO_2Bu\text{-}i$	$CO_2Bu\text{-}i$	CO_2CH_3	1.5+ 3	56
3d	H	H	CO_2Et	CO_2Et	2.0	92
3e	H	H	CO_2CH_3	CO_2CH_3	3.3	81

The reactions were carried out at temperature of 40°C, except for 2g and 3d at 50°C and for 2c at 60°C.

Experimental

General: Melting points were taken on a Yanaco MP-S2 melting point apparatus and were uncorrected. Proton NMR spectra were recorded on a JEOL PMX-60 SI spectrometer, using TMS as an internal standard in CCl_4. Chemical shifts are given in ppm. MS spectra and IR spectra were obtained using a VG ZAB-HS and a NICOLET 170SX spectrophotometer respectively. Elemental analyses were performed on a Perkin-Elmer 240C element analytical instrument.

2a (General procedure)

To a well stirred mixture of 1 (1.11g, 4mmol), anhydrous potassium carbonate (0.83g, 6mmol) and TEBA (0.07g, 0.3mmol) in 5mL of DMF at 40℃, methyl methacrylate (0.50g, 5mmol) was added dropwise. The reaction mixture was stirred and monitored by TLC (petroleum ether / ethyl acetate=3/1). When starting material had been consumed, the reaction mixture was poured into water and neutralized with 1M HCl. After the extraction of the mixture with CH_2Cl_2 (15mL×3), the combined organic extracts were washed with water (10mL×2) and then dried (Na_2SO_4). The solvent was removed in vacuo and the residue was chromatographed on silica gel using 1:3 ethyl acetate/petroleum ether (60- 90℃) to give the product 2a as a viscous oil (1.34g, 89%).

3a (General procedure)

A stired suspersion of 1 (1.11g, 4mmol), anhydrous potassium carbonate (0.83g, 6mmol), TEBA (0.07g, 0.3mmol) and methyl methacrylate (0.50g, 5mmol) in 5mL of DMF was heated at 40℃ for 2hr. Then, ethyl acrylate (0.50g, 5mmol) was added, and the mixture was continuously reacted for

2hr. After work up and purification as decribed for 2a, 1.62g(80%) of the title compound was obtained as a yellowish viscous oil.

Spectral data of compounds 2a-g and 3a-e

2a IR (KBr): 1736, 1327, 1152cm^{-1}; NMR (CCl_4) δ 8.06 (2H, d, J=9.2Hz, ArH), 7.74 (2H, d, J=9.2Hz, ArH), 5.11 (1H, m, CO_2CH), 4.04 (1H, m, SO_2CH), 3.64 (3H, s, CO_2CH_3), 2.25 (3H, m, CH_2CH), 1.00-1.40 (9H, m, $3CH_3$); MS (m/z, %, FAB) 377 (M^++1, 11.5); Anal. Calcd. for $C_{16}H_{21}ClO_8S$: C 51.00 H 5.62 Found C 51.28 H 5.67.

2b IR (KBr): 1735, 1327, 1153cm^{-1}; NMR (CCl_4) δ 8.08 (2H, d, J=9.2Hz, ArH), 7.76 (2H, d, J=9.2Hz, ArH), 5.08 (1H, m, CO_2CH), 4.48-3.97 (5H, m, $2CO_2CH_2$, SO_2CH), 3.17-2.00 (5H, m, CH_2CHCH_2), 1.47-1.07 (12H, m, $4CH_3$); MS (m/z, %, FAB) 463 (M^++1, 10.5); Anal. Calcd. for $C_{20}H_{27}ClO_8S$: C 51.89 H 5.88 Found C 51.95 H 5.87.

2c IR (KBr): 1733, 1328, 1152cm^{-1}; NMR (CCl_4) δ 8.05 (2H, d, J=9.2Hz, ArH), 7.73 (2H, d, J=9.2Hz, ArH), 5.13 (3H, m, $3CO_2CH$), 4.16 (1H, m, SO_2CH), 3.64-2.02 (5H, m, CH_2CHCH_2), 1.10-1.01 (18H, m, $6CH_3$); MS (m/z, %, FAB) 491 (M^++1, 0.9); Anal. Calcd. for $C_{22}H_{31}ClO_8S$: C 53.82 H 6.36 Found: C 53.40 H 6.27.

2d IR (KBr): 1737, 1328, 1153cm^{-1}; NMR (CCl_4) δ 8.10 (2H, d, J=9.2Hz, ArH), 7.78 (2H, d, J=9.2Hz, ArH), 5.12 (1H, m, CO_2CH), 4.35-3.91 (5H, m, $2CO_2CH_2$, SO_2CH), 3.21-1.58 (7H, m, CH_2CHCH_2, 2CH), 1.44-0.84 (18H, m, $6CH_3$); MS (m/z, %, FAB) 519 (M^++1, 1.0); Anal. Calcd. for $C_{24}H_{35}ClO_8S$: C 55.54 H 6.80 Found C 55.50 H 6.81.

2e IR (KBr): 1731, 1326, 1150cm^{-1}; NMR (CCl_4) δ 8.17 (2H, d, J=9.2Hz, ArH), 7.83 (2H, d, J=9.2Hz, ArH), 5.11 (2H, m, J=6.0Hz, $2CO_2CH$), 4.25 (1H, m, SO_2CH), 3.07-2.13 (3H, m, $CHCH_2$), 1.50-0.99 (15H, m, $5CH_3$); MS (m/z, %, FAB) 405 (M^++1, 7.6); Anal. Calcd. for $C_{18}H_{25}ClO_6S$: C 53.39 H 6.22 Found: C 53.37 H 6.25.

2f m.p. 111-112. IR (KBr): 1737, 1322, 1145cm^{-1}; NMR (CC14) δ 7.56 (2H, d, J=9.2Hz, ArH), 7.21 (2H, d, J=9.2Hz, ArH), 4.63-3.97 (2H, m, $CHCO_2CH$), 3.40 (6H, s, $2CO_2CH_3$), 3.00-2.43 (3H, m, $CHCH_2$), 1.23-0.53 (6H, m, $2CH_3$); MS (m/z, %, FAB) 421 (M^++1, 23.1); Anal. Calcd. for $C_{17}H_{21}ClO_8S$: C 48.52 H 5.03 Found: C 48.71 H 5.04.

2g IR (KBr): 1733, 1328, 1149cm^{-1}; NMR (CCl_4) δ 7.85 (2H, d, J=9.2Hz, ArH), 7.60 (2H, d, J=9.2Hz, ArH), 5.20-4.63 (3H, m, $3CO_2CH$), 4.01 (1H, m, SO_2CH), 3.23-2.66 (3H, m, $CHCH_2$), 1.58-0.92 (18H, m, $6CH_3$); MS (m/z, %, FAB) 477 (M^++1, 21.8); Anal. Calcd. for $C_{21}H_{29}ClO_8S$: C 52.88 H 6.13 Found: C 53.13 H 6.10.

3a IR (KBr): 1735, 1319, 1145cm^{-1}; NMR (CC14) δ 8.01 (2H, d, J=9.6Hz, ArH), 7.70 (2H, d, J=9.6Hz, ArH), 5.04 (1H, m, CO_2CH), 4.22 (2H, q, J=7.4Hz, CO_2CH_2), 3.68 (3H, s, CO_2CH_3), 3.26-1.65 (7H, m, CH_2CH, CH_2CH_2), 1.52-0.99 (12H, m, $4CH_3$); MS (m/z, %, FAB) 477 (M^++1, 3.2); Anal. Calcd. for $C_{21}H_{29}ClO_8S$: C 52.88 H 6.13 Found: C 53.29 H 6.00.

3b IR (KBr): 2250, 1733, 1317, 1145cm^{-1}; NMR (CCl_4) δ 8.04 (2H, d, J=9.6Hz, ArH), 7.76 (2H, d, J=9.6Hz, ArH), 5.09 (1H, m, J=6.4Hz, CO_2CH), 3.74 (3H, s, CO_2CH_3), 3.13-1.75 (7H, m, CH_2CH, CH_2CH_2), 1.52-1.03 (9H, m, $3CH_3$); MS (m/z, %, FAB) 430 (M^++1, 1.9); Anal. Calcd. for $C_{19}H_{24}ClNO_6S$: C 53.08 H 5.63 N 3.26 Found: C 52.72 H 5.62 N 3.14.

3c IR(KBr): 1737, 1320, 1147cm^{-1}; NMR(CCl_4) δ 8.05 (2H, d, J= 9.0Hz, ArH), 7.77 (2H, d, J=9.0Hz, ArH), 5.10 (1H, m, J= 6.4Hz, CO_2CH), 4.00 (4H, d, J=6.4Hz, $2CO_2CH_2$), 3.80 (3H, s, OCH_3), 3.40-1.70 (11H, m, CH_2CHCH_2, 2CH, CH_2CH_2), 1.25 (6H, d, J=6.4Hz, $2CH_3$), 0.97 (12H, d, J=6.4Hz, $4CH_3$); MS (m/z, %, FAB) 605 (M^++1, 1.1); Anal. Calcd. for $C_{28}H_{41}ClO_{10}S$: C 55.58 H 6.83 Found C 55.73 H 6.75.

3d IR(KBr): 1735, 1319, 1146cm^{-1}; NMR(CCl_4) δ 7.81 (2H, d, J= 8.0Hz, ArH), 7.54 (2H, d, J=8.0Hz, ArH), 4.95 (1H, m, J=6.4Hz, CO_2CH), 4.09 (4H, q, J=6.8Hz, $2CO_2CH_2$), 2.74-2.21 (8H, m, $2CH_2CH_2$), 1.54-1.08 (12H, m, $4CH_3$); MS (m/z, %, FAB) 477 (M^++1, 0.5); Anal. Calcd. for $C_{21}H_{29}ClO_8S$: C 52.88 H 6.13 Found: C 52.64 H 6.59.

3e m.p. 72-73.5 IR(KBr): 1733, 1317, 1146cm^{-1}; NMR(CCl_4) δ 7.82 (2H, d, J=8.2Hz, ArH), 7.52 (2H, d, J=8.2Hz, ArH), 4.97 (1H, m, J =6.4Hz, CO_2CH), 3.66 (6H, s, $2CO_2CH_3$), 2.74-2.23 (8H, m, $2CH_2CH_2$), 1.23 (6H, d, J=6.4Hz, $2CH_3$); MS (m/z, %, FAB) 449 (M^++1, 12.2); Anal Calcd. for $C_{19}H_{25}ClO_8S$: C 50.84 H 5.61 Found: C 51.15 H 5.98.

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