An efficient synthesis of aryloxyacetic acid and arylthioacetic acid esters

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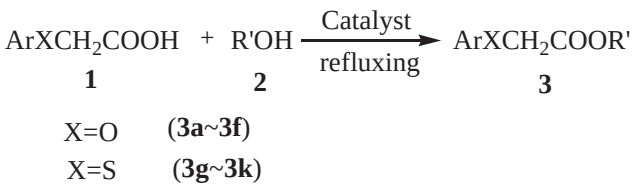
The esterification of the aryloxyacetic acid and arylthioacetic acid catalysed by silica sulfuric acid results aryloxyacetic acid and arylthioacetic acid ester in 83–94% yields respectively under mild reaction conditions.

Keywords: esterification, aryloxyacetate, arylthioacetate, synthesis, silica sulfuric acid

Aryloxyacetic acid and arylthioacetic acid esters are used as herbicides, plant regulators and insecticides. Recently, Wille et al have reported that a methyl aryloxyacetate can be used in the treatment of dermatitis.[1] These compounds are also intermediates in synthesis.[2,3] Various methods have been developed for their synthesis. Heating sodium phenoxide (mercaptide) with Et chloroacetate (or bromoacetate) in DMF[4-6] often affords unsatisfactory yields (24–83%).[6] Esterification catalysed by concentrated H_2SO_4[7-10] is an efficient method for the synthesis of aryloxyacetic acid and arylthioacetic acid ester, although decomposition by the concentrated H_2SO_4 can occur. In 1986, Bandgar *et al.* used a polymer-supported aryloxyacetic acid anion exchange resin to prepare the corresponding ester with a good yield.[11] However, the method took a long time (up to 4–15 h) and the preparation of the anion resin was very cumbersome. Consequently, alternative methods for the synthesis of aryloxyacetic and arylthioacetic acid esters under mild and environmentally friendly conditions have been developed.

Recently, silica gel-supported catalysts have been examined because they are stable, reusable, green and cheap.[12,13] Continuing our investigations in this area, we wish to report a rapid, efficient procedure for the synthesis of aryloxyacetic acid and arylthioacetic acid esters via esterification catalysed by silica sulfuric acid (Scheme 1)**.**

As shown in Table 1 and Scheme 1, aryloxyacetic acids (or arylthioacetic acids) (**1**) on treatment with alcohols (**2**) in the presence of silica sulfuric acid (Scheme 1), gave the corresponding esters in excellent yields in short period of time under mild conditions. For example, compound **3a** was obtained in 87% yields within 20 min in the presence of silica sulfuric acid. Whereas, in the classical method, [6] the yield of **3a** was only 52%, and in another method using anion exchange resin,[11] **3a** was obtained with 87% yield but over 6hr. In the reactions catalysed by conc. H_2SO_4 within 25min and $ClSO_3H$ within 30min, the yields of ethyl phenoxyacetate were 87% (**3a**[2]) and 85% (**3a**[3]) respectively, while ethyl phenoxyacteate can be obtained with 88% yield catalysed by silica sulfuric acid within 20min. Compared with literature, the main advantages of the present procedure are milder conditions, higher yield, short reaction period, less-pollution, and a reusable catalyst (the catalyst was used the third time without significant loss of activity **3a**[4]) and simple work-up.



Scheme 1

Mention must be made here that the reaction of phenoxyacetic acid or phenylthioacetic acid with alcohol can give excellent result, but when phenol replace alcohol, no ester (**3b**) was obtained under the same reaction condition.

Experimental

Boiling points were uncorrected. ^{1}H NMR spectra were obtained on a Bruker AVANCE (400MHz) spectrometer using TMS as internal standard and $CHCl_3$ as solvent. The products were characterised by comparison of their boiling points with literature values and the data of ^{1}H NMR.

Table 1 Esterification of the aryloxyacetic acid and arylthioacetic acid catalysed by silica sulfuric acid

Entry	R	R′	Time/min	Yields%	B.p./°C	
					Found	Reported
3a	C_6H_5	Et	20	88	137/20mm	137/19mm[6]
3a[1]	C_6H_5	Et	120	–		
3a[2]	C_6H_5	Et	25	87		
3a[3]	C_6H_5	Et	30	85		
3a[4]	C_6H_5	Et	25	85		
3b	C_6H_5	Ph	180	–		
3c	C_6H_5	Me	20	90	93–94/5mm	93–94/5mm[14]
3d	2-ClC_6H_4	Et	23	83	162–163.5/20mm	162/20mm[6]
3e	4-Cl C_6H_4	Et	25	83	178/24mm	178/24mm[6]
3f	2,4-$Cl_2C_6H_3$	Et	30	94	185–186/25mm	184.5–186/25mm[6]
3g	C_6H_5	Et	15	92	159–160/16mm	159–161/16mm[9]
3h	2-$CH_3C_6H_4$	Et	30	90	165–166/15mm	166/15mm[5]
3i	3- $CH_3C_6H_4$	Et	30	88	162/15mm	162/15mm[5]
3j	4- $CH_3C_6H_4$	Et	30	87	163–164/15mm	165/15mm[5]
3k	2- HOC_6H_4	Et	25	91	112–113/0.2mm	112–115/0.2mm[9]

3a[1] using SiO_2 as catalyst, **3a**[2] using conc. H_2SO_4 as catalyst, **3a**[3] using $ClSO_3H$ as catalyst, **3a**[4] using reused catalyst.

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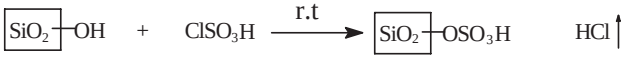
General procedure for preparation of catalyst silica sulfuric acid



A 500ml suction flask was used. It was equipped with a constant pressure dropping funnel containing of chlorosulfuric acid (23.3g, 0.2mol) and gas inlet tube for conducting of HCl gas over an absorbing solution Silica gel (60g) was placed in the flask. Chlorosulfuric acid was added dropwise over a period of 30 min at room temperature. The HCl gas was evolved from reaction vessel immediately. After the addition was completed, the mixture was shaken for 30 min. A white solid (H_2SO_4/SiO_2) 76.0g(~100%) was obtained.

General procedure for the preparation of aryloxyacetate and arylthioacetate

A mixture of the alcohol (**2**, 10.00mmol), aryloxyacetic acid (or arylthioacetic acid) (**1**, 5.00mmol), catalyst (200mg) and ether (4 ml) was heated for the period as indicated in the Table 1, the progress of the reaction was monitored by TLC. After the completion of the reaction, Et_2O (5ml) was added to the reaction mixture. The catalyst was filtered off and washed with Et_2O (2×5ml). The filtrate was washed with 5% $NaHCO_3$ (10 ml) and dried with $MgSO_4$. The solvent was evaporated under reduced pressure; the residue was separated by column chromatography on silica gel. Elution with petroleum ether or a mixture of petroleum ether and diethyl ether gave the products, which were identified by comparing their boiling point with literature and their ^{1}H NMR spectroscopic data.

3a: ^{1}H NMR δ: 6.92–7.30(5H, m, Ar–H), 4.64(2H, s, CH_2), 4.30(2H, q, *J*=7.0 Hz, CH_2), 1.33(3H, t, *J*=7.0Hz, CH_3).

3c: ^{1}H NMR δ: 6.80–7.27(5H, m, Ar–H), 4.61(2H, s, CH_2), 4.28(3H, s, CH_3).

3d: ^{1}H NMR δ: 6.89–7.35(4H, m, Ar–H), 4.64(2H, s, CH_2), 4.30(2H, q, *J*=7.2Hz, CH_2), 1.33(3H, t, *J*=7.2Hz, CH_3).

3e: ^{1}H NMR δ: 7.35(2H, d, *J*=8.6 Hz, Ar–H), 7.15(2H, d, *J*=8.6 Hz, Ar–H), 4.64(2H, s, CH_2), 4.30(2H, q, *J*=7.0Hz, CH_2), 1.33(3H, t, *J*=7.0Hz, CH_3).

3f: ^{1}H NMR δ: 8.02(1H, s, Ar–H), 6.95 (1H, d, *J*=8.4 Hz, Ar–H), 7.15(1H, d, *J*=8.4Hz, Ar–H), 4.64(2H, s, CH_2), 4.30(2H, q, *J*=7.1Hz, CH_2), 1.33(3H, t, *J*=7.1Hz, CH_3).

3g: ^{1}H NMR δ: 6.87–7.38(5H, m, Ar–H), 3.73(2H, s, CH_2), 4.30(2H, q, *J*=7.2Hz, CH_2), 1.33(3H, t, *J*=7.0Hz, CH_3).

3h: ^{1}H NMR δ: 6.87–7.19(4H, m, Ar–H), 3.70(2H, s, CH_2), 4.28(2H, q, *J*=7.0Hz, CH_2), 1.28 (3H, t, *J*=7.0Hz, CH_3), 2.41(3H, s, CH_3).

3i: ^{1}H NMR δ: 7.17(1H, s, Ar–H), 6.87–7.19(4H, m, Ar–H), 3.78(2H, s, CH_2), 4.17(2H, q, *J*=7.2Hz, CH_2), 1.24(3H, t, *J*=7.2Hz, CH_3), 2.37(3H, s, CH_3).

3j: ^{1}H NMR δ: 7.15(2H, d, *J*=8Hz, Ar–H), 6.95(2H, d, *J*=8Hz, Ar–H), 3.70(2H, s, CH_2), 4.31(2H, q, *J*=7.1Hz, CH_2), 1.30(3H, t, *J*=7.1Hz, CH_3), 2.35(3H, s, CH_3).

3k: ^{1}H NMR δ: 6.80–7.35(4H, m, Ar–H), 3.68(2H, s, CH_2), 4.30(2H, q, *J*=7.0Hz, CH_2), 1.33(3H, t, *J*=7.0Hz, CH_3), 5.71(1H, brs, OH).

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