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A CLAY CATALYZED METHOD FOR DIETHYL 2,2,2-TRICHLOROETHYLIDENEPROPANEDIOATE, AN EFFICIENT INTERMEDIATE FOR THE SYNTHESIS OF ENAMINO ESTERS

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Abstract: An improved high yielding procedure for diethyl 2,2,2-trichloroethylidenepropanedioate (**3**) using montmorillonite K-10 catalyst has been described. Various diethyl (substituted aminomethylene)propanedioates (**6a-j**) have been synthesised in excellent yields starting from propanedioate (**3**) *via* addition products (**5a-j**).

2,2,2-Trichloroethylidenepropanedioates are known for their insecticidal,[1] herbicidal[2] and fungicidal[3,4] activities. Diethyl 2,2,2-trichloroethylidenepropanedioate was originally prepared by the reaction of diethyl malonate with chloral in presence of conc. H_2SO_4 and acetic anhydride.[5] This trichloro compound has also been synthesised[3] in two steps by the condensation reaction of dimethyl malonate with chloral in presence of catalytic amount of diethylamine followed by dehydration of the aldol formed with conc. H_2SO_4 in over all yields of 60%. As

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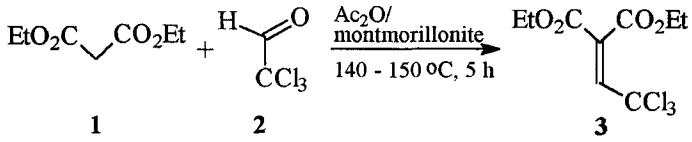
a part of our ongoing programme on the search for eco-friendly methods for the synthesis of organic intermediates using solid catalysts,[6] we were interested in developing a practical procedure for diethyl 2,2,2-trichloroethyledinepropane-dioate. We herein now report an efficient clay catalyzed method for the preparation of diethyl 2,2,2-trichloroethylidenepropanedioate and its conversion to various diethyl (substituted aminomethylene) propanedioates (enamino esters), key intermediates for quinolone antibiotics.[7,8]

Diethyl 2,2,2-trichloroethylidenepropanedioate (**3**) was obtained in almost quantitative yield by heating a mixture of diethyl malonate (**1**) and chloral (**2**) at 140-150°C in presence of montmorillonite K-10 and acetic anhydride for 5h (Scheme 1). This method not only offers substantial improvement in yield over the reported methods[3,5] but also replaces hazardous conc. H_2SO_4 with solid clay catalyst.

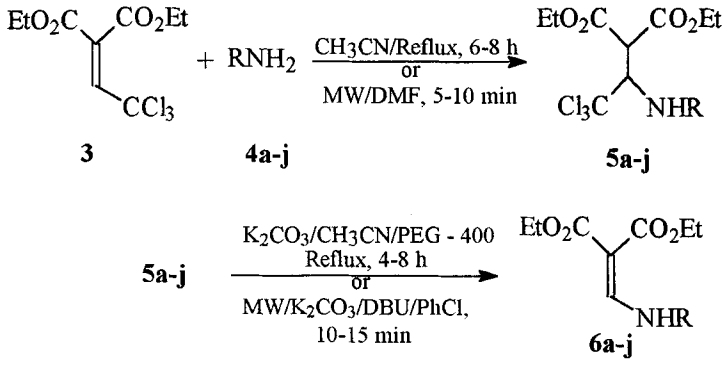
Scheme 1



1 **2** **3**

We envisioned that, diethyl 2,2,2-trichloroethylidinepropanedioate (**3**) will act as ethoxymethylene malonic acid ester (EMME) equivalent for the synthesis of enamino esters by the substitution of trichloromethyl group[9] with amino group *via*

Scheme 2



addition-elimination reaction sequence. The addition of various aromatic amines (**4a-f**) to propanedioate (**3**) in refluxing acetonitrile for 6-8 h offered diethyl 1-(arylamino)-2,2,2-trichloroethylpropanedioates (**5a-f**) in quantitative yields (Scheme 2). However, the addition of aliphatic amines (**4g-j**) to **3** was complete in just one hour (TLC) and gave quantitative yields of diethyl 1-(alkylamino)-2,2,2-trichloroethylpropanedioates (**5g-j**).

Base catalyzed elimination of trichloromethyl group was effected by refluxing a mixture of **5a-j**, K_2CO_3 and a catalytic amount of polyethylene glycol (PEG-400) in acetonitrile for 4-8 h to yield the desired diethyl [(aryl/alkylamino)-methylene]propanedioates (**6a-j**) in very high yields (Scheme 2, Table 1). The exclusive one-pot formation of eliminated product **6g-j** in very high yields was observed when 1.5 equivalent of alkyl amines (**4g-j**) were refluxed in acetonitrile with trichloro ester **3** for 1.5 h.

Table 1. Physical data for diethyl 1-(aryl/alkylamino)-2,2,2-trichloroethylpropanedioates (**5a-j**) and diethyl [(aryl/alkylamino)methylene]propanedioates (**6a-j**).

Compd **5** & **6**	R	Propanedioates **5**[a]		Propanedioates **6**[a]	
		m. p. (°C)	yield[b,c] (%)	m. p. (°C)	yield[b,c] (%)
a	C_6H_5-	41-42	90 (65)	49-50[8b]	82 (56)
b	3-ClC_6H_5-	43-45	91	49-50[8b]	80
c	4-ClC_6H_5-	57-58	90 (98)	79-80[10]	85 (57)
d	3-MeC_6H_5-	44-45	88 (78)	38-39[11]	85
e	4-$MeOC_6H_5$-	oil	80 (77)	38-39[8b]	82 (85)
f	3-Cl,4-FC_6H_4-	76-78	85	59-60[12]	70
g	Cyclohexyl-	oil	90	Oil[13]	85
h	Propyl-	oil	90	Oil[13]	80
i	Ethyl-	oil	91	Oil[13]	81
j	Benzyl-	oil	80	69-71[14]	87

[a] All the compounds were purified by column chromatography using EtOAc/pet. ether and all the solid compounds were crystallized from suitable solvents. [b] Isolated yield after column chromatography. [c] Figures in parenthesis represent yields obtained under microwave irradiation conditions.

The addition of amines (**4a,c-e**) to trichloro ester **3** to provide addition products **5a,c-e**, and subsequent elimination of trichloromethyl group of **5a,c,e** to afford corresponding enamino ester **6a,c,e**, were also realized by carrying out these reactions under microwave irradiation for 5-15 min (Table 1).

All the compounds (**6a-j**) were characterized by spectral analysis and their physical data were compared with the reported values.

In conclusion, we have described an efficient eco-friendly procedure for the preparation of diethyl 2,2,2-trichloroethylidenepropanedioate (**3**) using montmorillonite clay catalyst. We have further shown the application of **3** in the synthesis of diethyl [(arylamino)methylene]propanedioates (**6**) by replacement of trichloromethyl group with various aryl or alkyl amines *via* a two-step addition-elimination process, which is often carried out by a single-pot operation.

Experimental Section

A typical procedure for the synthesis of diethyl 2,2,2-trichloroethylidene-propanedioate (3). A mixture of diethyl malonate (**1**, 48 g, 0.30 mol), chloral (**2**, 54 g, 0.36 mol), acetic anhydride (40.8 g, 0.40 mol) and montmorillonite (KF-10, 2 g) was heated at 140 - 150 °C for 5 h. The acetic acid formed and excess acetic anhydride was removed by distillation under reduced pressure. The residue on fractional distillation gave 84.4 g (97%) of propanedioate (**3**), b. p. 115-120 °C/5 mm (lit.[4] 160-164 °C/22 mm). IR (neat) : 1740, 1260, 1230, 1100, 780 cm^{-1}. ^1H NMR ($CDCl_3$) : δ 1.33 (t, J = 6 Hz, 6H), 4.26 (q, J = 6 Hz, 4H), 7.20 (s, 1H).

Typical procedure for 5d. A mixture of *m*-toluidine (1.07 g, 10 mmol), ester **3** (2.89 g, 10 mmol), acetonitrile (15 ml) was refluxed for 6 h. The solvent was removed by distillation under reduced pressure and residue was purified by column chromatography (silica gel, 60-120 mesh, pet. ether:EtOAc, 8:2) to give 3.48 g (88%) of **5d** as a solid, m.p. 44-45 °C. IR (neat) : 3380, 1735, 1600 cm^{-1}. ^1H NMR ($CDCl_3$) : δ 1.10 - 1.45 (m, 6H), 2.25 (s, 3H), 4.00 - 4.45 (m, 4H), 5.27 (dd, J = 3 & 10 Hz, 1H), 5.45 (d, J = 10 Hz, 1H), 6.55 - 6.75 (m, 3H), 7.05 - 7.20 (m, 1H).

Typical procedure for the reaction carried out under microwave for 5e. A mixture of p-anisidine (**4e**, 1.23 g, 10 mmol), ester **3** (3.62 g, 12.5 mmol), DMF (3 ml) was irradiated in a domestic microwave oven (2450 MHz) operating at 60% power for 5 min. The reaction mixture was diluted with ethyl acetate (25 ml) and washed with water (2 x 25 ml) followed by brine (20 ml). The organic layer was dried over anhyd. sodium sulfate. It was then filtered and filtrate on concentration under reduced pressure gave 3.5 g of crude product, which was purified by column chromatography to give 3.17 g (77%) of pure **5e** as oil. IR (neat) : 3320, 1720, 1580 cm^{-1}. ^1H NMR ($CDCl_3$) : δ 1.20 - 1.30 (m, 6H), 3.72 (s, 3H), 4.10 - 4.20 (m, 5H), 5.13 (dd, J = 4 & 8.5 Hz, 1H), 6.75 (d, J = 9 Hz, 2H), 6.80 (d, J = 9 Hz, 2H).

Typical procedure for 6d. A mixture of **5d** (1.97 g, 5 mmol), K_2CO_3 (2.07 g, 15 mmol), PEG-400 (25 mg), acetonitrile (20 ml) was refluxed for 8 h. It was cooled to room temperature and solid was filtered off. The filtrate on removal of solvent by distillation gave crude product which was purified by column chromatography (silica gel, 60-120 mesh, pet. ether: EtOAc, 9:1) to give 1.17 g (85%)of pure **6d**, as low melting solid, m.p. 38-39 °C. IR (neat) : 3200, 1689, 1640, 1382, 1250, 1096 cm^{-1}. ^1H NMR ($CDCl_3$) : δ 1.10 - 1.50 (m, 6H), 2.4 (s, 3H), 4.12 - 4.55 (m, 4H), 6.91 - 7.33 (m, 4H), 8.54 (d, J = 16 Hz, 1H), 11.05 (bd, 1H).

Typical procedure for the reaction carried out under microwave for 6e. A mixture of **5e** (0.5 g, 1.2 mmol), K_2CO_3 (1.12 g), DBU (50 mg) and chlorobenzene (1.5 ml) was irradiated in a domestic microwave oven (2450 MHz) operating at 60% power for 15 min. The reaction mixture was diluted with ethyl

acetate (25 ml) and washed with water (2 x 25 ml) followed by brine (20 ml). The organic layer was dried over anhyd. sodium sulfate. It was then filtered and filtrate on concentration under reduced pressure gave 0.35 g of crude product, which was purified by column chromatography to give 0.301 g (85%) of pure **6e** as oil, which solidified on standing, m.p. 38-39 °C. IR (neat) : 3200, 1680, 1660 cm^{-1}. ^1H NMR ($CDCl_3$) : δ 1.22 - 1.40 (m, 6H), 3.81 (s, 3H), 4.20 - 4.44 (m, 4H), 6.93 (d, J = 8 Hz, 2H), 7.12 (d, J = 8 Hz, 2H), 8.4 (d, J = 13 hz, 1H), 11.00 (d, J = 13 Hz, 1H).

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