SHORT PAPER

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Microwave assisted hydrolysis of Meldrum's acid derivatives and decarboxylation of derived malonic acids[†‡]

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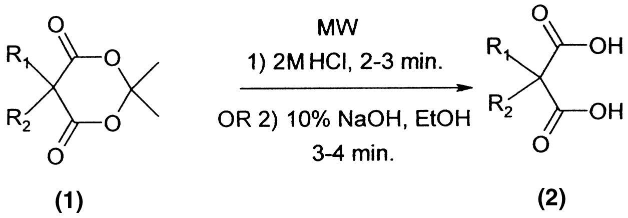
Microwave induced hydrolysis of alkyl Medrum's acids and decarboxylation of derived malonic acids using poly-4-vinylpyridine as a catalyst gives high yields of carboxylic acids in a short time.

Keywords: Meldrum's acid, decarboxylation, malonic acid

The application of microwaves has acquired much importance in organic transformations[1a-g]. Meldrum's acid has the distinction of being a versatile reagent in organic synthesis.[2,3] Hydrolysis of mono- and bis-alkylated Meldrum's acids gives the corresponding malonic acids which on decarboxylation with pyridine yield mono-carboxylic acids. Monoalkyl Meldrum's acids resist alkaline hydrolysis due to their conversion into enolate anions and bisalkyl Meldrum's acids require long reaction times for hydrolysis.[4] Hydrolysis and decarboxylation of monoalkyl Meldrum's acids by conventional heating with conc. hydrochloric acid requires two days.[5] Mane and co-workers[6] have reported the hydrolysis and decarboxylation of alkyl Meldrum's acids using pyridine–water or pyridine–D_2O in 3h. There are reports about the use of microwaves for hydrolysis and decarboxylation such as that of indole-2-carboxylic acid with quinoline and at 190°C in water in an autoclave.[7] Microwave assisted decarboxylation of malonic acids during Knovenagel condensation[8] using zinc chloride has been reported. Some recent applications of Meldrum's acid include Knovenagel condensations using proline,[9] solid support,[10] KF-alumina,[11] without catalyst in water,[12] and without catalyst in DMF.[13] Trimolecular condensation of indole, parafarmaldehyde and Meldrum's acid under microwave irradiation has been reported.[14] Our interest[6,15a-f] in the applications of Meldrum's acid prompted us to explore the possibility of using microwaves for the hydrolysis and decarboxylation of Meldrum's acids. The hydrolysis involves a dipolar transition state[1g] the formation of which is expected to be facilitated by microwaves. We report here a very simple and efficient hydrolysis of alkylated Meldrum's acids **(1)** and the decarboxylation of the derived malonic acids using microwave irradiation. The alkyl Meldrum's acids undergo hydrolysis with 2M hydrochloric acid in a short time, compared to the reported methods, to yield the corresponding malonic acids **(2)** (Scheme 1, Table 1). The aryl Meldrum's acids were hydrolysed with 10% sodium hydroxide in ethanol. The details of microwave irradiation time, yield of the product and observed physical constants are given in Table 1.

The derived malonic acids **(2)** were decarboxylated using poly-4-vinyl pyridine as a catalyst in DMF as solvent under microwave irradiation in a short time with high yields to give monocarboxylic acids **(3)** (Scheme 2 and Table 2). The advantages of this method are that the decarboxylation of malonic acids can be carried out at a lower temperature, it avoids use of pyridine and the catalyst can be easily removed just by filtration and recycled.



Scheme 1

Table 1 Hydrolysis of alkyl Meldrum's acids

Derived malonic acid, **2**[a]	Substituents R[1]	R[2]	MW irradiation time/s x pulse medium power	Yield /%	M.p./°C (Lit./°C)
a	n-C_3H_7	H	30 × 6 = 3 min	90	93(93)[16]
b	$(CH_3)_2CH$	H	30 × 4 = 2 min	91	78(78)[17]
c	C_3H_5	H	30 × 4 = 2 min	97	107(105)[17]
d	n-C_4H_9	H	30 × 6 = 3 min	95	105(105)[16]
e	CH_3	CH_3	30 × 4 = 2 min	96	194(195)[18]
f	C_2H_5	C_2H_5	30 × 4 = 2 min	94	123(125)[19]
g	n-C_3H_7	n-C_3H_7	30 × 4 = 2 min	95	159(161)[20]
h[b]	n-C_4H_9	n-C_4H_9	30 × 6 = 3 min	94	93(.......)
i	Ph-CH_2	H	30 × 6 = 3 min	95	120(120)[17]
j	Ph-CH_2	Ph-CH_2	30 × 8 = 4 min	92	176(175)[17]

[a] a to h = hydrolysis by 2 N HCl; i and j = Hydrolysis by 10% NaOH.
[b] Tentative structural assignment – the absence of analytical data.

Experimental

Reactions were carried out in a Sharp convection microwave oven model No. R-880 B. NMR spectra were recorded on Bruker 300 FNMR Spectrometer 300 MHz instrument and chemical shifts are in δ. The IR spectra were recorded on a PERKIN ELMER-FT-IR or a PERKIN ELMER-783 and peak positions are in wavenumbers (cm^{-1}). M.p.'s are uncorrected.

General procedure for the hydrolysis of alkyl Meldrum's acids with 2M HCl to give (**2a** to **h**): A mixture of Meldrum's acid (0.5 g) and 2 M hydrochloric acid (2 ml) was stirred well with a Teflon coated magnetic needle using a magnetic stirrer. It was then exposed to microwave irradiation for 30 s at low power. The flask was removed from oven, the mixture stirred well and cooled. The MW pulse, stirring and cooling were repeated as required and described in Table 1.

The compounds were extracted with ether and the ether layer was washed with water and dried over anhydrous sodium sulfate. Removal of the ether gave the pure malonic acids.

Allylmalonic acid (**2c**) : IR: 3600–2900, 1705, 1646 cm^{-1}, PMR ($CDCl_3$): 2.69 (2H, *t*, J = 6.5Hz, methylene-H), 3.55 (1H, *t*, J = 6.5Hz, methine-H), 5.11-5.20 (2H, *m*, vinylic-H). 5.73-5.87 (1H, *m*, vinylic-H), 11.35 (2H, *bs*, 2 × COOH).

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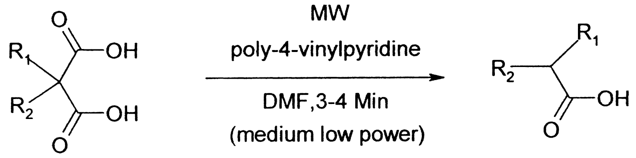
[†] This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*
[‡](Dedicated to the memory of the late Dr Nitiraj R. Mane.)



(2) (3)

Scheme 2

Table 2 Decarboxylation of malonic acids

Derived malonic acid, **2**[a]	Substituents R^1	R^2	MW irradiation time/s x pulse medium power	Yield /%	B.p./°C (Lit./°C)
a	n-C_3H_7	H	45 × 4 = 3 min	98	182(185)[16]
b	$(CH_3)_2CH$	H	30 × 8 = 4 min	84	174(175-177)[17]
c	C_3H_5	H	30 × 8 = 4 min	96	187(189-190)[16]
d	n-C_4H_9	H	30 × 6 = 3 min	94	202(202-203)[16]
e	CH_3	CH_3	30 × 6 = 3 min	91	152(153-154)[16]
f	C_2H_5	C_2H_5	30 × 6 = 3 min	93	192(198)[17]
g	n-C_3H_7	n-C_3H_7	30 × 6 = 3 min	88	226(228)[17]
h[a]	n-C_4H_9	n-C_4H_9	30 × 6 = 3 min	94	175
i	Ph-CH_2	H	30 × 6 = 3 min	94	*49(49)*[16b]
j	Ph-CH_2	Ph-CH_2	30 × 8 = 4 min	92	*163(165)*[17b]

[a] Tentative structural assignment in the absence of analytical data.

[b] Italic numbers indicate m.p.

Dimethylmalonic acid (**2e**): IR: 3600–2900 (broad), 1715 cm^{-1}. PMR ($CDCl_3$): 1.40 (6H, *s*, 2 × CH_3), 10.59 (2H, *bs*, 2 × COOH).

Diethylmalonic acid (**2f**): IR: 3600–2900 (broad) 1702 cm^{-1}, PMR ($CDCl_3$): 0.93 (6H, *t*, *J* = 7 Hz, 2 x CH_3). 1.99 (4H, *q*, *J* = 7 Hz, methylene-H), 10.5 (2H, *bs*, 2 x COOH).

Di-*n*-propylmalonic acid (**2g**) I.R.: 3600–2900 (broad), 1703 cm^{-1}, PMR ($CDCl_3$): 0.93 (6H, *t*, *J* = 7 Hz, 2 × CH_3), 1.26 (4H, sextet, *J* = 7 Hz, methylene – H), 1.94 (4H, *t*, *J* = 7 Hz, methylene-H), 11.0 (2H, *bs* 2 × COOH).

Ethyl malonic acid (**2**) $R_1 = C_2H_5$, R_2 = H); I.R. :3600–2900, 1712 cm^{-1}, PMR ($CDCl_3$) : 1.46 (3H, *t*, *J* = 7Hz, CH_3), 2.01 (2H, apparent quintet, -CH_2-), 3.39 (1H ,*t*, *J* = 7Hz, -CH), 10.5 (2H, *bs*, COOH).

General procedure for the hydrolysis of Meldrum's acids with aqueous NaOH to give (**2i** and **j**): A mixture of Meldrum's acid (0.5 g), 10% NaOH (3 ml) and ethanol (5ml) was stirred with a Teflon coated magnetic needle. It was then exposed to MW irradiation for 30 seconds at low power. The MW pulse, stirring and cooling was repeated as required and described in Table 1. The ethanol was removed and the aqueous layer was washed with ether. The aqueous layer was acidified and extracted with ether. The ether layer was washed with water and dried over anhydrous sodium sulfate. Removal of ether gave the crude product which was recrystallised from ethanol. The products were characterised by comparison of literature data. Spectral data of (**2i** and **j**) are given below.

Benzylmalonic acid (**2i**): IR:3600–2900,1730,1602cm^{-1}, PMR ($CDCl_3$): 3.2 (2H, *d*,*J*=7Hz, methylene-H), 3.75 (1H, *t*, *J*=7 Hz, methine-H), 7.19–7.32 (5H, *m*, Ar-H), 8.8 (2H, *bs*, 2 x COOH).

Dibenzylmalonic acid (**2j**): I.R: 3600–2900, 1732, 1603cm^{-1}, PMR ($CDCl_3$): 3.46 (4H, *s*, methylene-H), 7.23 (10H, *m*,Ar-H), 8.97 (2H, *bs*, 2 x COOH).

General procedure for the decarboxylation of malonic acids (**2a–j**) *to give monocarboxylic acids* (**3a–j**): In a 100 ml corning R.B. flask, malonic acid derivative (**2a–j**) (300 mg), poly-4-vinylpyridine (0.5 g) and dry DMF (2 ml) as solvent were placed and well mixed by stirring with the help of Teflon coated magnetic needle. The R.B. flask was exposed to MW irradiation. The exposure pulse time was 30 to 45 seconds at a medium power. The temperature measured immediately after MW exposure was in the range 90–100°C. The application of pulse was repeated as required and described in the Table 2.

The reaction mixture was cooled and ether (10 ml) was added and then it was filtered to remove the polymer. The R.B. flask and the polymer were washed with ether. The ether extract was washed with water and dried over anhydrous sodium sulfate. Removal of the ether furnished the acids in pure form. The products were characterised by comparison with literature data. The spectral data of some compounds is given below.

Pent-4-enoic acid (**3c**): IR: 3600–2900, 1713, 1643 cm^{-1}, PMR ($CDCl_3$): 2.29–2.36 (4H, *m*, methylene-H), 4.93–5.03 (2H, *m*, vinylic-H), 5.69–5.79 (1H, *m*, vinylic-H), 10.19 (1H, *bs*,-COOH).

Hexanoic acid (**3d**) : IR: 3600–2900, 1711, 1462 cm^{-1}, PMR ($CDCl_3$) : 0.91 (3H, *t*, *J=6.5 Hz*), 1.25-1.33 (4H, *m*, methylene –H),1.64 (2H, apparent quintet, *J* = 6.5 Hz, β-methylene to keto group), 2.35 (2H, *t*, *J* =6.5 Hz, α-methylene to keto group), 9.66 (1H, *bs*, -COOH).

3-Phenylpropanoic acid (**3i**) : IR:3600–2900, 1710, 1604cm^{-1}, PMR: ($CDCl_3$) : 2.69 (2H, *t*, *J* = 7 Hz, CH_2-CO-), 2.96 (2H, *t*, *J* = 7 Hz, Ph-CH_2), 7.20-7.32 (5H, *m*, Ar-H),11.15 (1H, *bs*,- COOH).

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