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A survey of mono- or bis-decarboxylation of β-methyl polyethylenic-malonic acids

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Abstract—Diverse experimental conditions, leading to mono- or bis-decarboxylation of β-methyl polyethylenic-malonic acids, were examined. A clean and easy bis-decarboxylation was reported.

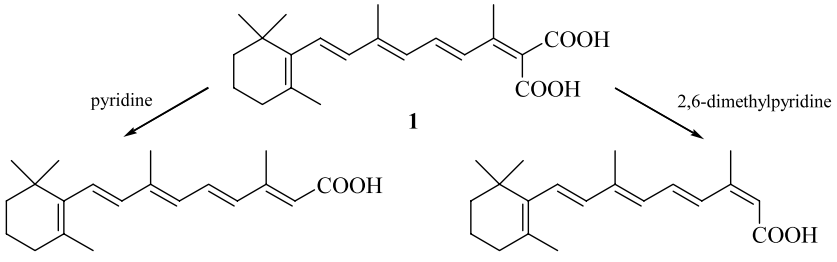
Mono-decarboxylation of malonic acids is well documented and its kinetics in various solvents reported.[1] This reaction has been described as catalyzed by copper(I)[2] or copper(II) complexes,[3] was performed in polar solvents,[4] or neutral solvents,[5] and was carried out by microwave heating.[6] A recent report showed that mono-decarboxylation in the presence of Cu(I) could not be considered as catalyzed, but was base-dependent.[7]

We have previously reported that the base-catalyzed decarboxylation of ethylenic diacids **1** produced stereoselectively *E* or *Z* monoacids[8,9] (Scheme 1).

However, it was well-known that bis-decarboxylation of malonic acids requires drastic conditions such as reflux in quinoline,[10] in quinoline with copper powder,[11] in *N*,*N*-dimethylaniline.[12] Consequently, the olefins were obtained as by-products and the yields were low to very low.

We report herein a smooth method, leading to suitable yields of the bis-decarboxylation of diacids **1a**,**b**, which were synthesized by a Stobbe-like condensation of the corresponding aldehyde with methyl isopropylidenemalonate[8,9] (Scheme 2).

It was found that bis-decarboxylation occurred suitably in benzene at reflux with triethylamine (47 and 64%), and was less efficient with DABCO (15 and 32%). The non-polar olefin was easily purified by column chromatography (SiO_2/CH_2Cl_2). This reaction was accompanied by the corresponding **3** and **4** monoacids (Scheme 3). Reflux in benzene, benzene/$Ba(OH)_2$ or AcOH/AcONa led regioselectively to high yields of *all E* monoacids **3a**,**b**. Triethylamine and 2,6-dimethylpyridine led quantitatively or regioselectively to the 1*Z* monoacids **4a**,**b** (Scheme 3). The choice of benzene as solvent for the production of the olefin appeared important.



Scheme 1.

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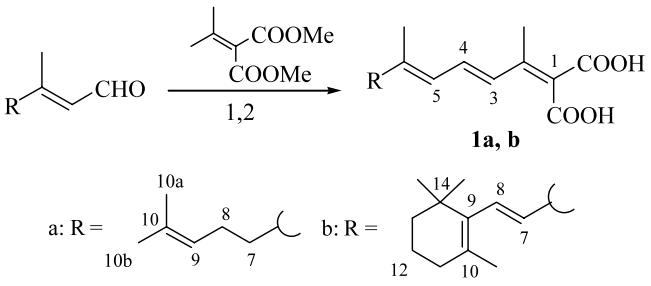
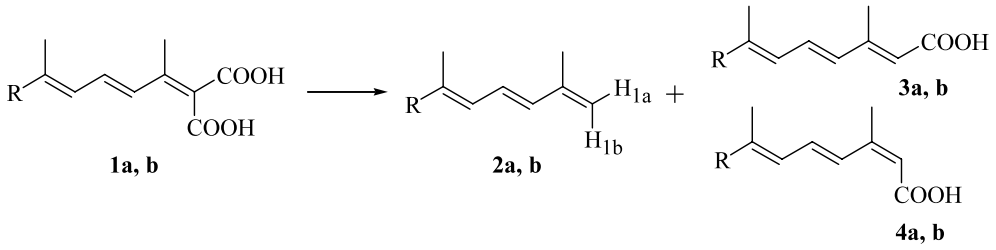


Scheme 2. *Reagents*: (1) MeOK; (2) KOH/MeOH/H_2O.

These results are summarized in Table 1.

In these series, no intermediate in the decarboxylation have been observed, as in the aromatic di- or triethylenic malonic acids.

In this latter series (**1c**,**d**), we have isolated a carboxylic α-ethylenic-δ-lactone **5c** (besides the corresponding δ-lactone **6c**), which has been previously suggested as an intermediary in the decarboxylation of β-methyl ethylenic malonic acid.[13] According to Corey,[14] this

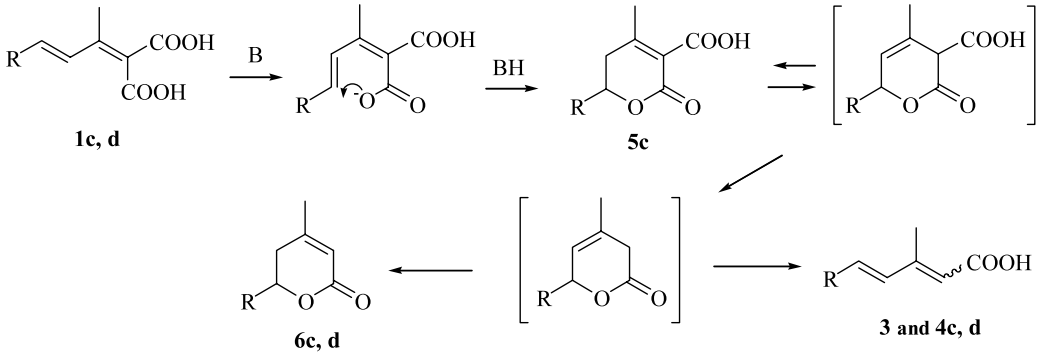


Scheme 3.

Table 1.

1			Reflux (h)	2	3	4
a	Benzene		0.5	Traces	79	21
b	–	–	–		75	25
a	Benzene	DABCO	0.8	15	10	75
b	–	–	–	32	Traces	68
a	Benzene	$Ba(OH)_2$	0.5		81	19
b	–	–	–		80	20
a	Benzene	Et_3N	0.3	47	8	45
b	–	–	–	64	6	30
a	Benzene	quinoline	1.5		24	76
b	–	–	0.8	Traces	58	42
a	2,6-Dimethylpyridine		0.3	Traces	Traces	100
b		–	–			100
a	Piperidine		1.3		36	64
b		–	1		61	39
a	Et_3N		0.3	Traces	Traces	100
b		–	–		20	80
a	AcOH	AcONa, cat.	0.8		72	28
b	–	–	0.3	Traces	75	25

In benzene, 8 equiv. of base were used. % are calcd for **2**+**3**+**4** = 100.

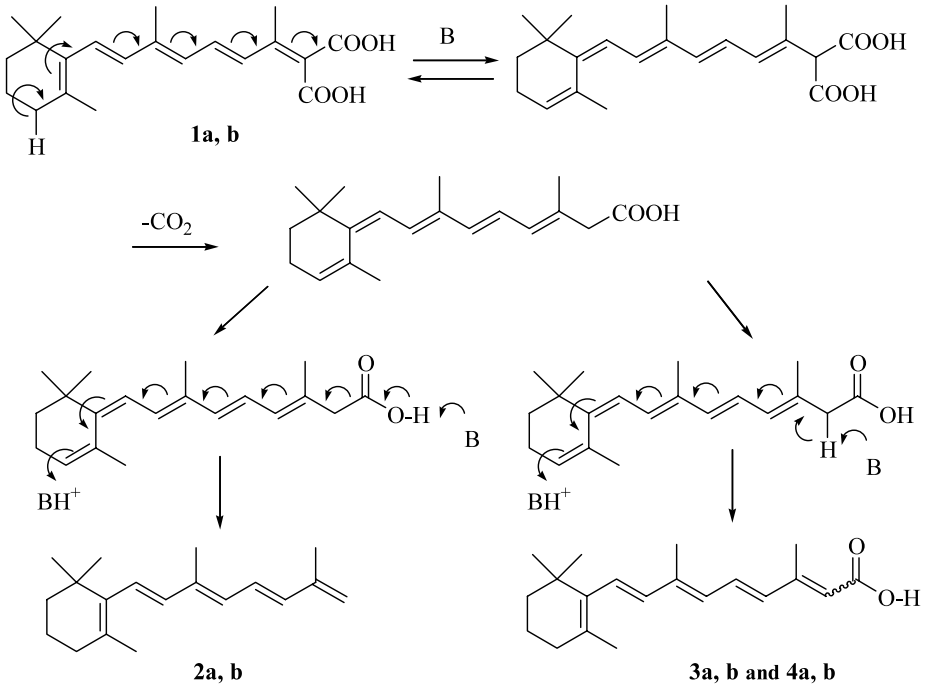


Scheme 4. *Reagents*: (c) R = C_6H_5-; (d) R = C_6H_5-CH=CH-.

decarboxylation requires a previous isomerization to the β-ethylenic-δ-lactone (Scheme 4). In our experimental conditions, the β-ethylenic-δ-lactone (in brackets in Scheme 4) has not been observed and was isomerized to the more stable lactone **6** (in this case). We have established that the heating of compound **5c** in benzene/Et_3N for 30 min led to a mixture of lactone **6** and acid **4**).[15]

The fact that no lactone could be detected in series **1a**,**b** could be explained by an alternative mechanistic pathway, not possible in series **1c**,**d**. This proposal may perhaps explain the easy formation of compounds **2a**,**b** and **3a**,**b** and **4a**,**b** (Scheme 5).

These results are summarized in Table 2.



Scheme 5.

Table 2.

1			Reflux (h)	2	3	4	5	6
c	C_6H_6		0.5	11	Traces	60	22	7
d*	–		1		6	3		
c	C_6H_6	Et_3N	0.5	5	Traces	67		28
d	–	–	1		Traces	67		33
c	Et_3N		0.5	8	3	46		43
d	-		1.5	Traces	14	41		45
c	DME	Et_3N	1		5	75		20
d	–	–	1.2			75		25
c	C_6H_6	DABCO	0.8		5	50		45
d	–	–	–			66		34
c	C_6H_6	Quinoline	1.5	14	6	77		3
d	–	–	2.5		22	78		
c	C_6H_6	$Ba(OH)_2$	0.5			56	44	
d*	–	–	0.8		7	7		12
c	C_6H_6	Pyridine	0.5	3	1	85		11
d	–	–	–		13	76		11
c	Piperidine		0.5		Traces	55	45	
d	–		1	3	43	54		
c	AcOH/AcONa, cat		1.8	38		47		15
d	–		–	17	56	27		

In benzene, 8 equiv. of base were used. % are calcd for **2**+**3**+**4**+**5**+**6**=100.
* Recovered diacid→100%.

Acknowledgements

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15. *Standard procedure:* After treating of 10 mmol of diacid (see tables), the solvent was removed in vacuo and the oily mixture was extracted with Et_2O. The acids **3**, **4** and **5** were extracted with a saturated $NaHCO_3$ solution. The neutral organic layer, constituted of compounds **2** and **6** was washed with water, dried over $MgSO_4$ and the solvent removed in vacuo. Purification by chromatography on silica gel, using dichloromethane as eluent, yielded the decarboxylated compound **2** or the lactone **6**.

2a: colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): 6.44 (dd, 1H, $J=15.3$, $J=10.8$, H_4); 6.26 (d, 1H, $J=10.8$, H_5); 5.12 (m, 1H, H_9); 4.97 (m, 2H, H_{1a}+H_{1b}); 2.13 (s, 4H, 7-CH_2 and 8-CH_2); 1.92 (s, 3H, 6-CH_3); 1.82 (s, 3H, 2-CH_3); 1.71 (s, 3H, 10b-CH_3); 1.63 (s, 3H, 10a-CH_3). ^{13}C NMR (CH): 133.6, C_3; 126.0, C_4; 124.3, C_5; 122.2, C_9 (CH_2): 115.9, C_1; 40,5, C_7; 27.0, C_8 (CH_3) 26.1, C_{10b}; 19.0, C_2; 18.1, C_{10a}; 17.2, C_6.

2b: colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): 6.59 (dd, 1H, $J=15.2$, $J=11.3$, H_4); 6.36 (d, 1H, $J=15.2$, H_3); 6.15 (2d, 2H, $J=15.2$, H_8, $J=11.3$, H_5); 6.13 (d, 1H, $J=15.2$, H_7); 5.02 and 5.00 (2s, H_{1a}+H_{1b}). ^{13}C NMR (CH): 138.1, C_7; 135.5, C_3; 130.4, C_5; 127.1, C_{10}; 126.1, C_4; (CH_2): 116.8, C_1; 40.0, C_{13}; 33.5, C_{11}; 19.7, C_{12} (CH_3) 29.4, C_{14}; 22.1, C_{10}; 19.1, C_2; 13.1, C_6.

5c: colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): 7.30 (m, 5H, Ar); 5.46 (d, 1H, $J=12.3$, H_7); 3.04 (dd, 1H, $J=18.9$, $J=12.3$, H_8); 2.82 (d, 1H, $J=18.9$, $H_{8'}$); 2.58 (s, 3H, 9-CH_3).

5d: colourless oil. ^{1}H NMR ($CDCl_3$): 7.29 (m, 5H, Ar); 5.90 (s, 1H, H_{10}); 5.40 (dd, 1H, $J=12.0$, $J=4.0$, H_7); 2.64 (dd, 1H, $J=17.9$, $J=12.0$, H_8); 2.45 (dd, 1H, $J=17.9$ $J=4.0$, $H_{8'}$); 2.02 5s, 3H, 9-CH_3).

6d: colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): 7.31 (m, 5H, Ar); 6.73 (d, 1H, $J=16.0$, H_7); 6.27 (dd, 1H, $J=16.0$, $J=6.2$, H_8); 5.87 (s, 1H, H_{12}); 5.06 (m, 1H, $J=10.7$, $J=5.6$, $J=5.2$, H_9); 2.52 (dd, 1H, $J=17.8$, $J=10.7$, H_{10}); 2.14 (dd, 1H, $J=17.8$, $J=4.2$, $H_{10'}$); 2.02 (s, 3H, 11-CH_3).