The Reaction of Carboxylic Acids with Conjugated Olefins Using Sodium Naphthalenide in the Presence of *N,N,N',N'*-Tetramethylethylenediamine

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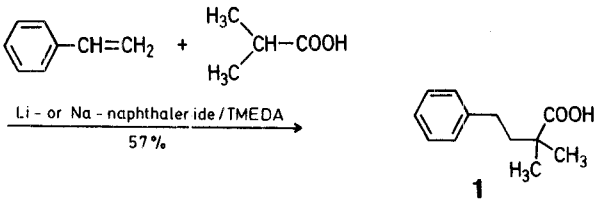
Earlier, we have studied the reaction of electrophiles with lithium α-lithiocarboxylates produced from carboxylic acids and lithium naphthalenide* in the presence of diethylamine[1,2,3]. In the metallation of carboxylic acids using lithium naphthalenide, the presence of diethylamine was essential[1,3]. However, diethylamine tends to react with conjugated olefins under the above mentioned reaction conditions[4]. Recently, Crimmins and Rather reported the metallation of ethylbenzene with pentylsodium in the presence of *N,N,N',N'*-tetramethylethylenediamine (TMEDA)[5]. Thus, TMEDA appears to be an excellent activating agent for the metallation of organic compounds.

We now report the reaction of carboxylic acids with conjugated olefins using sodium or lithium naphthalenide in the presence of TMEDA. When styrene is added slowly to a mixture of sodium naphthalenide, TMEDA, and 2-methylpropanoic acid in tetrahydrofuran, 2,2-dimethyl-4-phenylbutanoic acid (**1**) is obtained in 57% yield. In the absence of TMEDA, **1** is not obtained. The use of diethylamine instead of TMEDA gives unsatisfactory results.



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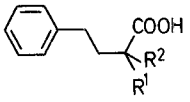
The alkylation with styrene was also carried out with other alkanoic acids (see Table).

We also extended the reaction to conjugated olefins other than styrene. Thus, the reaction of 2-methylpropanoic acid with isoprene or myrcene afforded 2,2,5-trimethyl-4-hexenoic acid (**2**; 66%) and 2,2,5,9-tetramethyl-4,8-decadienoic acid (**3**; 33%), respectively.

Table. 4-Phenylbutanoic Acids from Alkanoic Acids and Styrene[a]



R^1	R^2	Yield [%] with Na	Yield [%] with Li	b.p./torr	Molecular formula[b]	I.R. (KBr) ν_{max} [cm^{-1}]	^{1}H-N.M.R. (CCl_4) δ [ppm]
H	H	5	7	78–79°/4	$C_{10}H_{12}O_2$ (164.2)	3000, 1700, 745, 700	1.6 ~ 2.0 (m, 2H, Ar—CH_2—CH_2); 2.3 (m, 2H, CH_2—COOH); 2.6 (m, 2H, Ar—CH_2—CH_2); 7.15 (s, 5H_{arom}); 10.2 (s, 1H, COOH)
CH_3	H	11	29	105–107°/5	$C_{11}H_{14}O_2$ (178.2)	3000, 1700, 745, 695	1.2 (d, 3H, J = 7 Hz, CH—CH_3); 1.9 (m, 2H, Ar—CH_2—CH_2); 2.3 (m, 1H, CH—COOH); 2.6 (m, 2H, Ar—CH_2—CH_2); 7.2 (s, 5H_{arom}); 11.45 (s, 1H, COOH)
C_2H_5	H	15	25	120–123°/6	$C_{12}H_{16}O_2$ (192.3)	3000, 1700, 745, 695	0.95 (t, 3H, J = 6 Hz, CH_2—CH_3); 1.3 ~ 2.0 (m, 4H, Ar—CH_2—CH_2, CH_2—CH_3); 2.2 (m, 1H, CH—COOH); 2.6 (m, 2H, Ar—CH_2—CH_2); 7.15 (s, 5H_{arom}); 11.35 (s, 1H, COOH)
CH_3	CH_3	57	46	107–109°/3	$C_{12}H_{16}O_2$ (192.3)	see procedure	
n-C_3H_7	H	16	32	116–118°/2.5	$C_{13}H_{18}O_2$ (206.3)	3000, 1700, 745, 700	0.9 (t, 3H, J = 6 Hz, CH_2—CH_3); 1.2–1.9 (m, 6H, Ar—CH_2—CH_2, CH_2—CH_2—CH_3); 2.2 (m, 1H, CH—COOH); 2.6 (m, 2H, Ar—CH_2—CH_2); 7.15 (s, 5H_{arom}); 11.8 (s, 1H, COOH)
i-C_3H_7	H	16	20	122–124°/2	$C_{13}H_{18}O_2$ (206.3)	3000, 1700, 745, 695	0.95 [d, 6H, J = 6 Hz, $CH(CH_3)_2$]; 1.6–2.2 [m, 4H, CH—$CH(CH_3)_2$, Ar—CH_2—CH_2]; 2.6 (m, 2H, Ar—CH_2—CH_2); 7.15 (s, 5H_{arom}); 10.9 (s, 1H, COOH)
n-C_4H_9	H	21	35	126–129°/2	$C_{14}H_{20}O_2$ (220.3)	3000, 1700, 745, 695	0.9 (t, 3H, J = 6 Hz, CH_2—CH_3); 1.3–2.1 [m, 8H, Ar—CH_2—CH_2, $(CH_2)_3$—CH_3]; 2.2 (m, 1H, CH—COOH); 2.65 (m, 2H, Ar—CH_2—CH_2); 7.2 (s, 5H_{arom}); 10.8 (s, 1H, COOH)

[a] Reaction conditions: Sodium metal (0.2 mol), naphthalene (0.1 mol), TMEDA (0.2 mol), styrene (0.1 mol), carboxylic acid (0.1 mol).
[b] The microanalyses were in satisfactory agreement with the calculated values: C, ±0.5%; H, ±0.5%.

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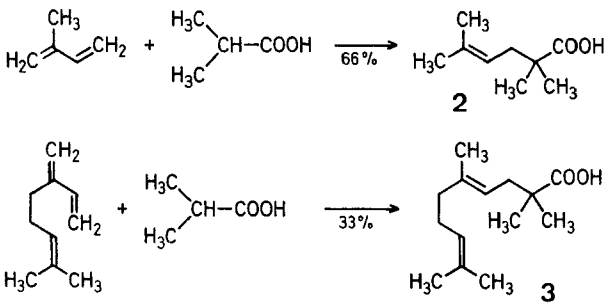

2,2-Dimethyl-4-phenylbutanoic Acid (1); Typical Procedure:
Sliced sodium (4.6 g, 0.2 mol) is added to a mixture of naphthalene (12.8 g, 0.1 mol), TMEDA (23.2 g, 0.2 mol), and purified tetrahydrofuran (200 ml), and the mixture is stirred at room temperature under dry nitrogen. After 1 h, a solution of 2-methylpropanoic acid (8.8 g, 0.1 mol) in tetrahydrofuran (50 ml) is gradually added and stirring is continued for 2 h at room temperature. Then, styrene (10.4 g, 0.1 mol) is added over a period of 1 h, the mixture is refluxed for an additional 8 h, and allowed to stand overnight. It is then decomposed with methanol, and the insoluble matter is dissolved in water (100 ml). To this solution, 10% aqueous sodium hydroxide (100 ml) is added, the mixture is extracted with diisopropyl ether (2 × 150 ml) to remove the non-acidic material, the remaining solution is acidified with conc. hydrochloric acid, and extracted with diisopropyl ether (3 × 150 ml). The latter extract is washed with water and dried with sodium sulfate. The solvent is distilled off and the residual mixture distilled at reduced pressure to give 2-methylpropanoic acid (2.1 g; b.p. 61–65°/26 torr) as a forerun, and 2,2-dimethyl-4-phenylbutanoic acid (**1**); yield: 10.9 g (57 %); b.p. 107–109°/3 torr; m.p. 97–98°.

$C_{12}H_{16}O_2$	calc.	C 74.97	H 8.39
(192.3)	found	74.69	8.37

M.S.: $m/e = 192$ (M^+).

I.R. (KBr): $\nu_{max} = 3100, 1700, 745, 690\ cm^{-1}$.

^{1}H-N.M.R. (CCl_4): $\delta = 1.3$ (s, 6H, $2CH_3$); 1.7–2.0 (m, 2H, Ar—CH_2—CH_2); 2.5–2.8 (m, 2H, Ar—CH_2—CH_2—); 7.15 (s, 5H_{arom}); 12.25 ppm (s, 1H, —COOH).

2,2,5-Trimethyl-4-hexenoic Acid (2):
From sodium (4.6 g, 0.2 mol), naphthalene (12.8 g, 0.1 mol), TMEDA (23.2 g, 0.2 mol), 2-methylpropanoic acid (8.8 g, 0.1 mol), and isoprene (6.8 g, 0.1 mol); yield: 10.3 g (66 %); b.p. 83–85°/2 torr.

[When the reaction was carried out with lithium in place of sodium the yield of **2** was 41 %].

$C_9H_{16}O_2$	calc.	C 69.19	H 10.32
(156.2)	found	69.30	10.35

M.S.: $m/e = 156$ (M^+).

I.R. (film): $\nu_{max} = 3000, 1700, 1670, 875\ cm^{-1}$.

^{1}H-N.M.R. (CCl_4): $\delta = 1.15$ (s, 6H, 2 2-CH_3); 1.6 (s, 3H, H_3C—C=C); 1.7 (s, 3H, H_3C—C=C); 2.2 (d, 2H, $J = 7$ Hz, C=CH—CH_2—); 5.1 (t, 1H, $J = 7$ Hz, C=CH—CH_2); 12.1 ppm (s, 1H, —COOH).

2,2,5,9-Tetramethyl-4,8-decadienoic Acid (3):
From sodium (4.6 g, 0.2 mol), naphthalene (12.8 g, 0.1 mol), TMEDA (23.2 g, 0.2 mol), 2-methylpropanoic acid (8.8 g, 0.1 mol), and myrcene (13.6 g, 0.1 mol); yield: 7.4 g (33 %); b.p. 146–148°/3 torr.

[When the reaction was carried out with lithium in place of sodium the yield of **3** was 28 %].

$C_{14}H_{24}O_2$	calc.	C 74.95	H 10.78
(224.3)	found	74.81	10.74

M.S.: $m/e = 224$ (M^+).

I.R. (film): $\nu_{max} = 3000, 1700, 1670, 880\ cm^{-1}$.

^{1}H-N.M.R. (CCl_4): $\delta = 1.2$ (s, 6H, 2 2-CH_3); 1.65, 1.7 (s, 9H, 3 H_3C—C=C); 2.05 (m, 4H, C=C—CH_2—CH_2—C=C); 2.25 (d, 2H, $J = 7$ Hz, CH_2—CH=C); 5.2 (m, 2H, 2CH=C); 12.1 ppm (s, 1H, —COOH).

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* Lithium naphthalenide, $[C_{10}H_8]^{\ominus}\cdot\ Li^{\oplus}$, an anion radical, should not be mistaken for naphthyllithium, $C_{10}H_7Li$.

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