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STUDIES IN METAL-AMMONIA REDUCTION—5[1]
REDUCTION AND REDUCTIVE METHYLATION OF SOME NAPHTHOIC ACIDS[2]

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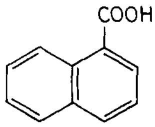
Abstract—Birch reduction and reductive methylations of some substituted naphthoic acids have been examined. The factors influencing the mechanism of reduction process have been discussed. Some of the reduced naphthoic acids are useful synthons for synthesis.

Metal-ammonia reduction of 1- and 2-naphthoic acids has been extensively studied.[3–13] Thus reduction of 1-naphthoic acid[3] affords 3,4-dihydro-1-naphthoic acid while reduction of 2-naphthoic acid yields the corresponding 1,2,3,4-tetrahydro-2-naphthoic acid.[9] Slobbe[8] reported that 2-naphthoic acids can be reduced under controlled conditions to give mainly the dihydro acids along with varying amounts of tetrahydro acids. We have shown recently that reduction of 1-acetylnaphthalene gives the 1-acetyl-3,4-dihydro-naphthalene while that of 2-acetylnaphthalene affords 2-acetyl-1,2,3,4-tetrahydronaphthalene.[14] However, reduction of 2-acetylnaphthalene in the presence of anhydrous ferric chloride afforded exclusively 2-acetyl-1,4-dihydronaphthalene. In view of these observations and our interest in the reduction of aromatic compounds having electron sinks, we reinvestigated the reduction and reductive methylation of 1- and 2-naphthoic acids and the results are reported in this paper.

Reduction and reductive methylation of 1-*naphthoic acids*

1-Naphthoic acid **1** underwent smooth reduction with lithium in ammonia to yield the expected 1,4-dihydronaphthoic acid **2** in excellent yield. 4-Methoxy-1-naphthoic acid **3** on reduction give the compound **2** with complete loss of the OMe group. Reduction of naphthoic acids with other metals (Na, K) either in the presence or absence of anhydrous ferric chloride did not change the product composition.

Reduction methylation of 1-naphthoic acid **1** gave the expected product **4** in good yield. Reductive methylation of the acid **3** gave a mixture of **4** and its dimethyl derivative **5** in the ratio of 7 : 3. The results of reduction and reductive methylation of 1-naphthoic acids are in agreement with those reported in the literature and are indicated in Table 1. The mechanism of reduction of 1-naphthoic acids with metal-ammonia reagents closely resembles that of benzoic acid or its methoxy derivatives. Addition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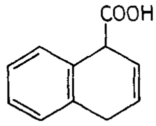
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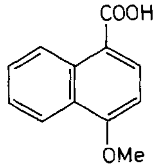
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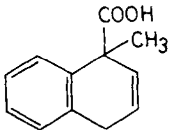
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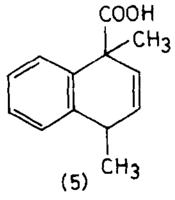
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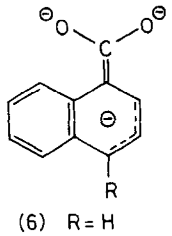

(6) R = H
(7) R = OMe

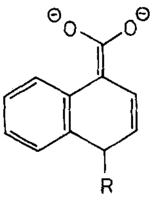

(8) R=H
(9) R=OMe

Table 1. Reductions and reductive methylations of 1-naphthoic acid 1 and 4-methyl-1-naphthoic acid 3 with metals (3 mol. equiv./mole of substrate)[a].

Substrate	Metal[b]	Quenching agent	Product (s) and yield (%)
(1)	Li	NH_4Cl	[2 (90)]
(3)	Li	NH_4Cl	[2 (75)]
(1)	Li	MeI	[4 (85)]
(3)	Li	MeI	[4 (56) + 5 (24)]

[a] 10 mmol in 20 ml THF and 100 ml liquid ammonia

[b] No significant change in either product composition or yield, was observed with sodium or potassium

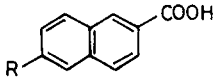
of two electrons to the acid **1** results in the anion **6** which on protonation at the *para* position gives the dienolate anion **8**. The anion **8** is resistant to further reduction and on protonation at the α-carbon yield the acid **2**. The alternative protonation of the dienolate anion **8** at γ-C is unlikely due to the lower charge density compared to α-C. Methylation of the dienolate anion **8** affords the product **4**. The intermediate dienolate anion **9** from 4-methoxy-1-naphthoic acid undergoes hydrogenolysis to give the anion **8** which is either protonated to the acid **2** or methylated to the acid **4**. The formation of acid **5** is due to further alkylation of acid **4** by the base (NH_2^-).

Reduction and reductive methylations of 2-naphthoic acids

Metal-ammonia reduction of 2-naphthoic acid **10** with 5 equiv metal/mole afforded the 1,2,3,4-tetrahydro-2-naphthoic acid **11** in good yield. However, reduction of the acid **10** in the presence of anhydrous ferric chloride gave exclusively the 1,4-dihydro-2-naphthoic acid **12**, while reduction with 3 equiv metal/mole gave a mixture containing the acid **12** and starting material. Reduction of 1-methoxy-2-naphthoic acid **13** gave the acid **11** with complete loss of the OMe group while reduction in the presence of anhydrous ferric chloride gave a mixture of compounds **10** and **12**. Reduction of the acid **13** with 3 equiv metal/mol gave a mixture of acids **10**, **11** and **12**. Reduction of 3-methoxy-2-naphthoic acid **14** gave 1,2,3,4-tetrahydro-2-naphthoic acid **11** with complete loss of OMe group while reduction in the presence of anhydrous ferric chloride gave 3-methoxy-1, 2-dihydro-2-naphthoic acid **15**. The dihydro acid **15** is unstable and gave β-tetralone on hydrolysis. Reduction of the acid **14** with 3 mol equiv of metal afforded a mixture of acids **11** and **15**. Reduction of 4-methoxy-2-naphthoic acid **16** gave the acid **11** with complete loss of OMe group. Reduction with 3 equiv metal followed by hydrolysis gave a mixture of the dihydro- **16** and the tetrahydro-acids **11**, while reduction in the presence of anhydrous ferric chloride followed by hydrolysis gave the keto acid **26** in excellent yield. Reduction of 6-methoxy-2-naphthoic acid **17** gave the acid **18**, while with 3 equiv of metal, a mixture of acid **17** and 6-methoxy-1,2-dihydro-2-naphthoic acid **19** was obtained. However, the acid **19** was obtained in good yield from the reduction of the acid **17** in the presence of anhydrous ferric chloride.

Reductive methylation of 2-naphthoic acid with 5 equiv. metal gave 2-methyl-1,2,3,4-tetrahydro-2-naphthoic acid **20**, while with 3 equiv metal a mixture of 2-methyl-1,2-dihydro-2-naphthoic acid **21** and the acid **11** was obtained. However, reductive methylation in the presence of anhydrous ferric chloride gave the acid **21** as the sole product in excellent yield. Reductive methylation of 1-methoxy-2-naphthoic acid **13** gave a mixture of acids **20** and **11**, while with 3 equiv metal gave a mixture of the acids **10**, **11** and **21**. However, reductive methylation in the presence of anhydrous ferric chloride gave the acids **10** and **21** with the total loss of the OMe group. Reductive methylation of 3-methoxy-2-naphthoic acid **14** gave a mixture of **11** and **20**, while with 3 equiv of metal gave a mixture of **11** and 3-methoxy-2-methyl-1,2-dihydro-2-naphthoic acid **22**. However, reductive methylation in the presence of anhydrous ferric chloride gave the acid **22** exclusively. Reductive methylation of 4-methoxy-2-naphthoic acid **16** gave a mixture of **11** and **20** with complete loss of OMe, while reductive methylation of **16** in the presence of anhydrous ferric chloride gave **23** exclusively without loss of OMe. The results of reductive methylation of 6-methoxy-2-naphthoic acid **17** were similar to that of 2-naphthoic acid and the details are presented in Table 3. Similar results were obtained in the reductions with Na or K metal.

The mechanism of reduction of 2-naphthoic acids involve the addition of two electrons to yield the anion **27** which on protonation at 1-position yields the anion **28**. Further electron addition to the anion **28** followed by protonation affords the dianion **29** which yields the products either on protonation (NH_4Cl) or methylation (MeI). In these cases, it appears that the protonation is effected by the thermodynamic control while the methylation is governed by the kinetic control. The anion **30** obtained from 1-methoxy-2-naphthoic acid **13** on protonation gives the anion **31**, which rapidly eliminates methoxide to give 2-naphthoate ion **21** and accounts for



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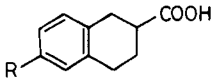
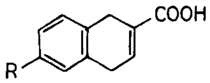
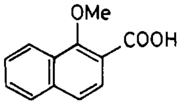


(11) R= H
(18) R= OMe



(12) R= H
(19) R= OMe



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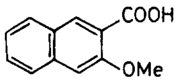

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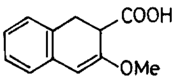

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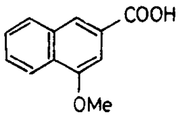

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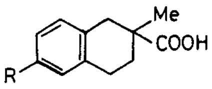
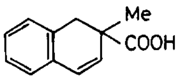
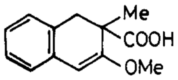


(20) R= H
(24) R= OMe



(21) R= H
(25) R= OMe



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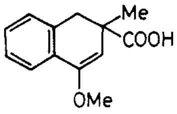

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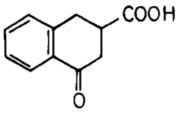

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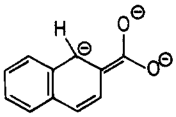

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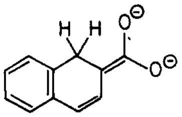

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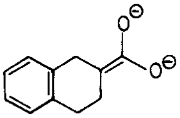

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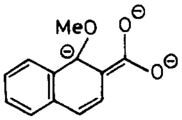

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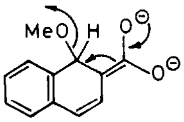

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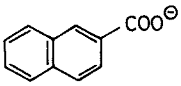

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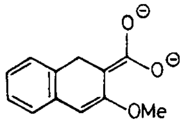

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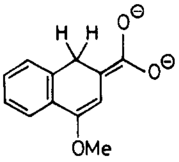

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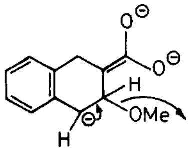

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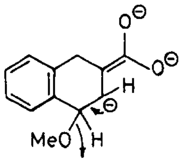

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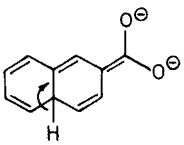

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Table 2. Reductions of 2-naphthoic acid **10**, 1-methoxy-2-naphthoic acid **13**, 3-methoxy-2-naphthoic acid **14**, 4-methoxy-2-naphthoic acid **16** and 6-methoxy-2-naphthoic acid **17**[a]

Substrate	Metal[b]	Quenching agent	Additive	Product(s) & yield (%)
(10)	Li(5)	NH_4Cl	-	[11 (90)]
	Li(5)	NH_4Cl	$FeCl_3$	[12 (75)]
	Li(3)	NH_4Cl	-	[11 (20) + 12 (75)]
(13)	Li(5)	NH_4Cl	-	[11 (75)]
	Li(5)	NH_4Cl	$FeCl_3$	[11 (15) + 10 (10) + 12 (40)]
	Li(3)	NH_4Cl	-	[11 (10) + 12 (60)]
(14)	Li(5)	NH_4Cl	-	[11 (85)]
	Li(5)	NH_4Cl	$FeCl_3$	[15 (80)]
	Li(3)	NH_4Cl	-	[15 (65) + 11 (25)]
(16)	Li(5)	NH_4Cl	-	[11 (80)]
	Li(5)	NH_4Cl	$FeCl_3$	[37 (80)]
	Li(3)	NH_4Cl	-	[11 (80)]
(17)	Li(5)	NH_4Cl	-	[18 (95)]
	Li(5)	NH_4Cl	$FeCl_3$	[19 (80)]
	Li(3)	NH Cl	-	[18 (15) + 17 (10) + 19 (40)]

[a] 10 mmol in 20 ml THF and 100 ml liquid ammonia

[b] No significant change in either product composition or yield, was observed with sodium or potassium

the formation of 2-naphthoic acid during reduction. Similarly the intermediates **33** and **34** obtained from the electron addition followed by *ortho* protonation yield **35** and **36** which undergo elimination of methoxide. The observed reduction of 2-naphthoic acids to the dihydroderivatives with alkali metals in the presence of anhydrous ferric chloride is a clear indication of the prevention of the competing processes which lead to further reduced products. The alternative mechanism proposed by Eliel[9] involving the initial protonation in *para* position yielding the intermediate **37** followed by rapid equilibration to the enolate anion appeared to be untenable. However, the *ortho* protonation appears to be more likely than the *para* since the latter destroys the aromaticity of the adjacent ring and the observed results are consistent with initial *ortho* protonation.

Our results clearly demonstrate that the reduction of 2-naphthoic acids with metal-ammonia solution can be controlled to yield either the dihydro- or the tetrahydro compounds unlike the Slobbe's observations. Further it is significant to note that the methoxyl group is retained during the reduction and reductive methylation of 4-methoxy-2-naphthoic acid, when anhydrous ferric chloride is used. The products obtained during the reduction and reductive methylation of 2-naphthoic acids, which are otherwise difficult to prepare can be used as substrates in the steroid and terpenoid synthesis and their utility will be discussed elsewhere.[15]

EXPERIMENTAL

M.ps are uncorrected. IR spectra of liquids were measured as thin films and of solids in nujol mull on a Perkin–Elmer infracord or a Model 237 spectrometer. PMR spectra (Chemical shifts in ppm from TMS) were recorded in $CDCl_3$ soln on a varian T-60 (60 MHz) spectrometer. THF was distilled over LAH and liquid ammonia was distilled over Na before use and reductions were done at −33°.

General procedure for reduction of naphthoic acids. To a well stirred soln of the substrate (10 mmol) in ammonia (100 ml) and THF or ether (20 ml), appropriate quantity of the alkali metal was added in portions. After 30 min the reaction was quenched by adding solid NH_4Cl. Ammonia was evaporated off. Water was added and acidified with 6NHCl with cooling. The ppt was extracted with ether several times, the combined organic extract was washed till neutral, dried over $NaSo_4$. The solvent was evaporated and the residue was purified by recrystallisation.

General procedure for reductive methylation of naphthoic acids. Appropriate quantity of the alkali metal was added in portions to a well stirred soln of the substrate (10 mmol) in THF or ether (20 ml) and ammonia (100 ml) and the resultant deep blue soln was stirred for 30 min. A soln of MeI in ether was added until the blue colour of the soln was discharged. Ammonia was

Table 3. Reductive methylations of 2-naphthoic acid **10**, 1-methoxy-2-naphthoic acid **13**, 3-methoxy-2-naphthoic acid **14**, 4-methoxy-2-naphthoic acid **16** and 6-methoxy-2-naphthoic acid **17**[a]

Substrate	Metal[b]	Quenching agent	Additive	Product(s) & Yield (%)
(10)	Li(5)	MeI	-	[11 (25) + 20 (65)]
	Li(5)	MeI	$FeCl_3$	[21 (75)]
	Li(3)	MeI	-	[11 (20) + 21 (70)]
(13)	Li(5)	MeI	-	[11 (25) + 20 (50)]
	Li(5)	MeI	$FeCl_3$	[10 (10) + 21 (60)]
	Li(3)	MeI	-	[11 (15) + 10 (10) + 21 (40)]
(14)	Li(5)	MeI	-	[11 (25) + 20 (55)]
	Li(5)	MeI	$FeCl_3$	[22 (75)]
	Li(3)	MeI	-	[11 (25) + 22 (65)]
(16)	Li(5)	MeI	-	[11 (24) + 20 (60)]
	Li(5)	MeI	$FeCl_3$	[23 (78)]
	Li(3)	MeI	-	[23 (65) + 11 (22)]
(17)	Li(5)	MeI	-	[18 (25) + 24 (70)]
	Li(5)	MeI	-	[25 (80)]
	Li(3)	MeI	-	[18 (25) + 25 (70)]

[a] 10 mmol in 20 ml THF and 100 ml liquid ammonia

[b] No significant change in either product composition or yield, was observed with sodium or potassium

allowed to evaporate, water was added and acidified with 6N Hcl with cooling. The ppt was extracted with ether and worked up as described before.

1,4-*Dihydro-1-naphthoic acid* **2**[3], m.p. 74°; ν_{max} 1700, 1600 and 1500 cm^{-1}; δ 3.4 (2 H, *dd*, benzylic), 4.4 (1 H, q, methine), 6.2 (2 H, m, vinylic), 7.3 (4 H, s, ArH) (Found: C, 75.7; H, 5.9; $C_{11}H_{10}O_2$ requires: C, 75.8 and H, 5.8%).

1,2,3,4-*Tetrahydro-2-naphthoic acid* **11**[9], m.p. 95–96°; ν_{max} 1700, 1600 and 1490 cm^{-1}; δ 1.8–2.2 (7 H, m, methylenes and methines), 7.2 (4 H, s, ArH) (Found: C, 74.7; H, 6.5; $C_{11}H_{12}O_2$ requires: C, 75.0 and H, 6.9%).

1,4-*Dihydro-2-naphthoic acid*[10] **12**, m.p. 154–55°; ν_{max} 1670 and 1590 cm^{-1}; δ 3.7 (4 H, bs, allylic-benzylic), 7.3 (4 H, bs, ArH), 7.4 (1 H, t, vinylic) (Found: C, 75.8; H, 6.0; $C_{11}H_{10}O_2$ requires: C, 75.8 and H, 5.8%).

3-*Methoxy-1,2-dihydro-2-naphthoic acid* **15**. Rapidly decomposing material, ν_{max} 1710, 1680, 1660, 1600 and 1500 cm^{-1}; δ 2.4–3.2 (3 H, m, benzylic and methine), 3.7 (3 H, s, OCH_3), 5.6 (1 H, s, vinyl), 7.72 (4 H, bs, ArH).

4-*Keto-1,2,3,4-tetrahydro-2-naphthoic acid*[11] **37**, m.p. 142°; ν_{max} 1710, 1680 and 1600 cm^{-1}; δ 3.09–3.36 (4 H, m, benzylic and methylene), 7.23–7.81 (3 H, m, ArH), 8.13–8.27 (1 H, m, *Peri* proton).

6-*Methoxy-1,2,3,4-tetrahydro-2-naphthoic acid* **18**, m.p. 150°; ν_{max} 1710, 1600 and 1500 cm^{-1}; δ 1.8–3.2 (7 H, m, methylene and methine), 4.0 (3 H, s, OCH_3), 6.7–7.2 (3 H, m, ArH) (Found: C, 69.7; H, 6.8; $C_{12}H_{14}O_3$ requires: C, 69.7 and H, 6.85%).

1-*Methyl-1,4-dihydro-1-naphthoic acid* **4**[13], m.p. 115°; ν_{max} 1700, 1600 and 1500 cm^{-1}; δ 1.6 (3 H, s, $-CH_3$), 3.42 (2 H, bs, benzylic), 5.9–6.1 (2 H, m, olefinic), 7.2 (4 H, s, ArH) (Found: C, 76.5; H, 6.9; $C_{12}H_{12}O_2$ requires: C, 76.6 and H, 6.4%).

1,4-*Dimethyl-1,4-dihydro-1-naphthoic acid*[8] **5**, m.p. 128–30°; ν_{max} 1700, 1600 and 1480 cm^{-1}; δ 1.3 (3 H, d, C_4–CH_3), 1.6 (3 H, s, C_1–CH_3), 3.7 (1 H, m, methine), 5.9–61. (2 H, m, olefinic), 7.1 (4 H, s, ArH) (Found: C, 77.3; H, 6.8; $C_{13}H_{14}O_2$ requires: C, 77.2 and H, 7.0%).

2-*Methyl-1,2,3,4-tetrahydro-2-naphthoic acid* **20**, m.p. 78–80°; ν_{max} 1690 and 1660 cm^{-1}; δ 1.4 (3 H, s, CH_3). 1.8–3.3 (6 H, m, methylenes), 7.1 (4 H, bs, ArH) (Found: C, 75.4; H, 7.5; $C_{12}H_{14}O_2$ requires: C, 75.8 and H, 7.4%).

2-*Methyl-1,2-dihydro-2-naphthoic acid* **21**, m.p. 72°; ν_{max} 1690 and 1660 cm^{-1}; δ 1.3 (3 H, s, CH_3), 2.9 (1 H, d, benzylic), 3.4 (1 H, d, benzylic), 6.2 (1 H, d, vinylic), 6.6 (1 H, d, vinylic), 7.2 (4 H, bs, ArH) (Found: C, 76.5; H, 6.8; $C_{12}H_{12}O_2$ requires: C, 76.6 and H, 6.4%).

3-*Methoxy-2-1,2-dihydro-2-naphthoic acid* **22**, m.p. 124–125°; ν_{max} 1710, 1660, 1680, 1600 and 1510 cm^{-1}; δ 1.20 (3 H, s, CH_3), 2.80 (1 H, d, benzylic), 3.30 (d, 1 H, benzylic), 3.70 (3 H, s, OCH_3), 5.7 (1 H, s, vinylic), 7.72 (4 H, bs, ArH) (Found: C, 71.34; H, 6.8; $C_{13}H_{14}O_3$ requires: C, 71.54 and H, 6.5%).

4-*Methoxy-2-methyl-1,2-dihydro-2-naphthoic acid* **23**, m.p. 118; ν_{max} 1700, 1660, 1640, 1600 and 1510 cm^{-1}; δ 1.2 (3 H, s, CH_3), 2.9 (1 H, d, benzylic), 3.2 (1 H, d, benzylic), 3.7 (3 H, s, OCH_3), 5.7 (1 H, s, vinylic), 7.2 (4 H, bs, ArH) (Found: C, 71.45; H, 6.8; $C_{13}H_{14}O_3$ requires: C, 71.54 and H, 6.5%).

6-*Methoxy-2-methyl-1,2,3,4-tetrahydro-2-naphthoic acid* **24**, m.p. 117–119°; ν_{max} 1700, 1600 and 1480 cm^{-1}; 1.1 (3 H, s, CH_3), 1.6–3.2 (6 H, m, methylenes), 3.7 (3 H, s, OMe), 6.6–7.2 (3 H, m, ArH) (Found: C, 70.7; H, 7.3; $C_{13}H_{16}O_3$ requires: C, 70.9 and H, 7.3%).

6-*Methoxy-2-methyl-1,2-dihydro-2-naphthoic acid* **25**, m.p. 147–49°; ν_{max} 1710, 1600 and 1570 cm^{-1}; 1.2 (3 H, s, CH_3), 2.8 (1 H, d, benzylic), 3.2 (1 H, d, benzylic), 3.8 (3 H, s, OMe), 6.1 (1 H, d, vinylic), 6.2 (1 H, d, vinylic), 6.6–7.2 (3 H, m, ArH) (Found: C, 71.44; H, 6.1; $C_{13}H_{14}O_3$ requires: C, 71.54 and H, 6.5%).

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