207. *The Action of Methylsuccinic Anhydride on Certain Xylenols, and Synthesis of Some Trimethylnaphthols.*

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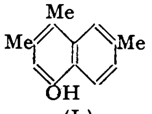
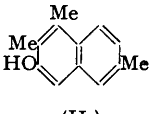
The condensation of methylsuccinic anhydride with *o*-3-, *o*-4-, *m*-4-, and *p*-xylenol has been investigated. 3 : 4 : 6-Trimethyl-1-, 3 : 4 : 7-trimethyl-2-, 2 : 4 : 7-trimethyl-1-, and 1 : 4 : 7-trimethyl-2-naphthols (I to IV, respectively) have been prepared.

The condensation of unsymmetrical succinic anhydrides with aromatic compounds has been extensively studied (cf. Berliner, *Org. Reactions*, 1949, **5**, 242, 275; Bhatt and Nargund, *J. Univ. Bombay*, 1942, II, 131; Cocker *et al.*, *J.*, 1950, 1781; *Chem. and Ind.*, 1949, 641, who review earlier work in this field). It has been shown that, in general, in ionising solvents, α-alkyl(or aryl)-β-aroylpropionic acids are the main products, but in non-ionising solvents the formation of β-alkyl(or aryl)-β-aroylpropionic acids is favoured. We have condensed the methyl ethers of the above xylenols with methylsuccinic anhydride in nitrobenzene, in benzene, and in carbon disulphide. The results of these reactions are expressed in the following table, the relative proportions of products being only approximate.



(I.)



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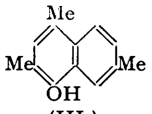

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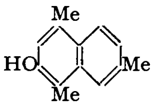


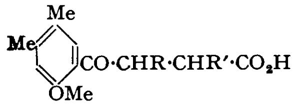
(IV.)

Methyl xylyl ether.	Solvent.	Products : -α- or -β-methylpropionic acid.	α-Isomer, parts.	β-Isomer, parts.
o-4-Xylyl	(*a*) $C_6H_5 \cdot NO_2$	β-(2-Methoxy-4 : 5-dimethylbenzoyl)-	10	1
	(*b*) C_6H_6 (hot)	β-(2-Hydroxy-4 : 5-dimethylbenzoyl)-	3	1
	,, (cold)	β-Benzoyl-	—	None
o-3-Xylyl	(*a*) $C_6H_5 \cdot NO_2$ (cold)	β-(4-Methoxy-2 : 3-dimethylbenzoyl)-	8	1
	(*b*) C_6H_6 (cold)	,, ,, ,,	2	1
m-4-Xylyl	(*a*) $C_6H_5 \cdot NO_2$	β-(5-Methoxy-2 : 4-dimethylbenzoyl)-	—	None
	(*b*) C_6H_6 (cold or hot)	β-Benzoyl-	—	None
	(*c*) CS_2 (cold)	(No reaction)		
p-Xylyl	(*a*) $C_6H_5 \cdot NO_2$	β-(4-Methoxy-2 : 5-dimethylbenzoyl)-	—	None
	(*b*) C_6H_6 (hot)	β-Benzoyl-	—	None
	(*c*) CS_2 (cold)	(No reaction)		
	,, (hot)	α-Isomer		

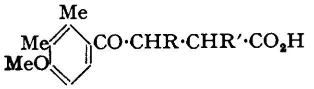
In general, the results conform with previous experience, although it is noteworthy that in the attempted condensation of methylsuccinic anhydride with three of the xylyl ethers in benzene, reaction took place with the solvent in preference to the ether.

Each keto-acid was reduced to the corresponding butyric acid, which was cyclised to the tetralone, from which the required naphthol was obtained by conventional methods. The identity of the keto-acids was determined (*a*) by oxidation with sodium hypochlorite to the known corresponding methoxydimethylbenzoic acid and (*b*) by attempted formation of a semicarbazone of the tetralone obtained, as described above, from the keto-acid. As mentioned by Cocker *et al.* (*J.*, 1950, 1781; cf. Cagniant and Buu-Hoï, *Bull. Soc. chim.*, 1942, **9**, 841), failure of a 1-tetralone to yield a semicarbazone suggests the presence of groups at the 2- and the 8-position. Those semicarbazones which could be formed are described.

The light-absorption characteristics (see Experimental) of the pairs of 1- and 2-naphthols are in agreement with those already described by Cocker *et al.* (*loc. cit.*). Again, the 1- may be clearly distinguished from the 2-naphthols.



(V; R = H, R' = Me.)
(VI; R = Me, R' = H.)



(VII; R = H, R' = Me.)
(VIII; R = Me, R' = H.)

EXPERIMENTAL.

(Analyses are by Drs. Weiler and Strauss, Oxford.)

Absorption spectra were measured with a Beckman Quartz Spectrophotometer, Model D.U., silica cells of thickness 1·000 ± 0·001 cm. being used. Spectra were measured in alcohol, and the initial concentrations were of the order of 20 mg./l., with ten-fold dilution when necessary to bring the high-intensity peaks within the range of the instrument.

A. *Experiments with* o-4-*Xylenol.*

3 : 4 : 6-*Trimethyl*-1-*naphthol* (I).—β-(2-*Methoxy*-4 : 5-*dimethylbenzoyl*)-α- *and* -β-*methylpropionic acids* (V *and* VI). A mixture of methyl *o*-4-xylyl ether (10 g.), methylsuccinic anhydride (10 g.), and dry nitrobenzene (25 c.c.) was slowly treated with a solution of aluminium chloride (25 g.) in nitrobenzene (75 c.c.) at 15—20°, and the mixture was set aside overnight. It was poured into ice and hydrochloric acid, and the solid product (13 g.), consisting largely of (V), m. p. 162—168°, was collected. After being washed with water it was recrystallised from dilute alcohol, yielding needles (10 g.), m. p. 167—168° (Found : C, 67·5; H, 7·3. Calc. for $C_{14}H_{18}O_4$: C, 67·2; H, 7·2%) (Ruzicka *et al.*, *Helv. Chim. Acta*, 1936, **19**, 370, who prepared this ketone by another route, described it as a liquid). Its *semicarbazone* crystallised from dilute alcohol as needles, m. p. 179—180° (Found : C, 58·9; H, 7·1. $C_{15}H_{21}O_4N_3$ requires C, 58·6; H, 6·8%). The nitrobenzene layer from the above condensation was separated, washed successively with hydrochloric acid and water, and extracted several times with 20% ammonia solution. The extract was washed with ether, filtered, and acidified, yielding the *keto-acid* (VI) (1 g.), m. p. 78—88°, which crystallised from benzene–light petroleum (b. p. 40—60°) as needles, m. p. 110° (Found : C, 67·1; H, 7·2. $C_{14}H_{18}O_4$ requires C, 67·2; H, 7·2%). Its *semicarbazone* crystallised from ethyl acetate as needles, m. p. 168—169° (Found : C, 58·6; H, 7·0. $C_{15}H_{21}O_4N_3$ requires C, 58·6; H, 6·8%).

β-(2-*Hydroxy*-4 : 5-*dimethylbenzoyl*)-α- *and* -β-*methylpropionic acids.* A mixture of methyl *o*-4-xylyl ether (4 g.), methylsuccinic anhydride (4 g.), and dry benzene (70 c.c.) was slowly treated with aluminium chloride (10 g.), then refluxed for 2 hours and set aside overnight. It was poured into ice and hydrochloric acid, and the benzene layer separated. After being washed with water, the benzene was removed under reduced pressure and the solid residue was purified by solution in sodium carbonate and reprecipitation. The mixture of keto-acids (6·2 g.; m. p. 125—140°) on repeated crystallisation, alternately from benzene and dilute alcohol, gave a *keto-acid* (3·4 g.), m. p. 158° (Found : C, 66·1; H, 7·2. $C_{13}H_{16}O_4$ requires C, 66·1; H, 6·8%), identical with the product of demethylation of β-(2-methoxy-4 : 5-dimethylbenzoyl)-α-methylpropionic acid (V) with hydriodic acid. From the mother-liquors of the above crystallisations a second keto-acid (1·3 g.), m. p. 142°, identical with the product of demethylation of β-(2-methoxy-4 : 5-dimethylbenzoyl)-β-methylpropionic acid (VI) was obtained.

γ-(2-*Methoxy*-4 : 5-*dimethylphenyl*)-α-*methylbutyric acid.* The keto-acid (V) (9 g.) was refluxed for 48 hours with amalgamated zinc (100 g.), concentrated hydrochloric acid (120 c.c.), and water (90 c.c.) and yielded the required acid (7 g.), b. p. 212°/17 mm. (cf. Ruzicka *et al.*, *loc. cit.*).

5 : 6 : 7 : 8-*Tetrahydro*-5-*keto*-3 : 4 : 6-*trimethyl*-1-*naphthol*, obtained when the butyric acid (3·5 g.) was heated on the water-bath for 2 hours with 80% sulphuric acid, crystallised from dilute alcohol as needles (0·7 g.), m. p. 108—109° (Found : C, 76·2; H, 7·9. $C_{13}H_{16}O_2$ requires C, 76·5; H, 7·8%). Its methyl ether was obtained when the butyric acid (1 g.) was heated on the water-bath for 10 minutes with 98% sulphuric acid (5 g.). It crystallised from dilute alcohol as needles (0·7 g.), m. p. 56° (cf. Ruzicka *et al.*, *loc. cit.*, who describe this as a liquid) (Found : C, 77·0; H, 7·9. Calc. for $C_{14}H_{18}O_2$: C, 77·1; H, 8·3%).

5 : 6 : 7 : 8-*Tetrahydro*-3 : 4 : 6-*trimethyl*-1-*naphthol.* The above hydroxy-ketone (1·1 g.) was reduced during 24 hours with a mixture of concentrated hydrochloric acid (70 c.c.), water (50 c.c.), amalgamated zinc (30 g.), and benzene (20 c.c.). From the benzene layer the *hydroxy-tetralin* (0·7 g.) was obtained as small needles (from dilute alcohol), m. p. 120° (Found : C, 82·1; H, 9·2. $C_{13}H_{18}O$ requires C, 82·1; H, 9·5%). Its *methyl ether* was obtained in a similar manner from the methoxy-tetralone (0·6 g.) as colourless plates (0·5 g.) m. p. 50° (Found : C, 82·6; H, 9·7. $C_{14}H_{20}O$ requires C, 82·4; H, 9·8%).

3 : 4 : 6-*Trimethyl*-1-*naphthol* (I). The hydroxy-tetralin (0·7 g.) was heated with selenium (2·1 g.) for 2·5 hours at 335—340°, and the product extracted with methanol (charcoal) and distilled in steam. The distillate yielded the *naphthol* (0·1 g.), which crystallised from light petroleum (b. p. 40—60°) as needles, m. p. 99—100° (Found : C, 83·7; H, 7·5. $C_{13}H_{14}O$ requires C, 83·9; H, 7·5%). Light absorption : Maxima, 2420, 3070 (3200), and 3300 A.; log ε = 4·65, 3·70 (3·65), and 3·57, respectively. Its *picrate* separated from benzene as scarlet needles, m. p. 159—160° (Found : C, 54·8; H, 4·4. $C_{19}H_{17}O_8N_3$ requires C, 54·9; H, 4·1%). Its methyl ether formed needles (from alcohol), m. p. 88° (cf. Ruzicka *et al., loc. cit.*) (Found : C, 85·0; H, 8·3. Calc. for $C_{14}H_{16}O$: C, 84·0; H, 8·0%).

B. *Experiments with* o-3-*Xylenol.*

3 : 4 : 7-*Trimethyl*-2-*naphthol* (II).—*β*-(4-*Methoxy*-2 : 3-*dimethylbenzoyl*)-*α*-*methyl*- *and* -*β*-*methylpropionic acids* (VII *and* VIII). Methyl *o*-3-xylyl ether (8 g.), methylsuccinic anhydride (8 g.), and aluminium chloride (21 g.) in nitrobenzene (50 c.c.) were allowed to react. The mixture was decomposed with ice and hydrochloric acid, and the solid *acid* (VII) (10 g.) was collected, and crystallised from benzene–light petroleum as plates (8·5 g.), m. p. 137° (Found : C, 67·3; H, 7·2. $C_{14}H_{18}O_4$ requires C, 67·2; H, 7·2%). Its *semicarbazone* crystallised from dilute alcohol as needles, m. p. 196° (Found : C, 59·2; H, 7·0. $C_{15}H_{21}O_4N_3$ requires C, 58·6; H, 6·8%). The residual nitrobenzene from the above was extracted with aqueous ammonia, and the extract shaken with ether and acidified with hydrochloric acid, giving impure *β*-(4-*methoxy*-2 : 3-*dimethylbenzoyl*)-*β*-*methylpropionic acid* (VIII) (3·5 g.), m. p. 111—115°, which crystallised from benzene as plates (1·2 g.), m. p. 112—113° (Found : C, 67·5; H, 7·4. $C_{14}H_{18}O_4$ requires C, 67·2; H, 7·2%).

γ-(4-Methoxy-2 : 3-dimethylphenyl)-α-methylbutyric acid, prepared by reduction of the keto-acid (VII) (8·5 g.), crystallised from benzene–light petroleum as needles (6·5 g.), m. p. 98—99°.

5 : 6 : 7 : 8-*Tetrahydro*-8-*keto*-3 : 4 : 7-*trimethyl*-2-*naphthol* was obtained when the preceding acid (3·5 g.) was heated for 2 hours on the water-bath with 80% sulphuric acid. It crystallised from benzene as needles (1 g.), m. p. 204° (Found : C, 76·3; H, 7·8. $C_{13}H_{16}O_2$ requires C, 76·5; H, 7·8%). Its *methyl ether* crystallised from dilute alcohol as plates, m. p. 76—77° (Found : C, 77·8; H, 7·8. $C_{14}H_{18}O_2$ requires C, 77·1; H, 8·3%). The *semicarbazone* of the methyl ether crystallised from dilute alcohol as plates, m. p. 217—218° (Found : C, 65·6; H, 7·7. $C_{15}H_{21}O_2N_3$ requires C, 65·5; H, 7·6%). 5 : 6 : 7 : 8-*Tetrahydro*-3 : 4 : 7-*trimethyl*-2-*naphthol* was obtained when the hydroxy-tetralone (0·5 g.) was reduced in benzene under Clemmensen conditions. It separated from light petroleum (b. p. 40—60°) as long needles (0·2 g.), m. p. 104—105° (Found : C, 81·4; H, 9·3. $C_{13}H_{18}O$ requires C, 82·1; H, 9·5%).

3 : 4 : 7-*Trimethyl*-2-*naphthol* (II). The preceding compound (0·6 g.) was dehydrogenated with selenium (1·8 g.) at 340—360° for 3 hours. The *naphthol* (0·2 g.) separated from light petroleum (b. p. 60—80°) as long shining needles, m. p. 141° (Found : C, 83·5; H, 7·9. $C_{13}H_{14}O$ requires C, 83·9; H, 7·5%). Light absorption : Maxima, 2340 (2770), 2860 (2970), 3180, and 3320 A.; log ε = 4·9 (3·66), 3·73 (3·60), 3·29, and 3·40, respectively. Its *picrate* crystallised from benzene as scarlet needles, m. p. 152—153° (Found : C, 55·7; H, 3·9. $C_{19}H_{17}O_8N_3$ requires C, 54·9; H, 4·1%). Its *trinitrobenzene* adduct crystallised from benzene as orange needles, m. p. 164° (Found : C, 57·0; H, 4·3. $C_{19}H_{17}O_7N_3$ requires C, 57·1; H, 4·3%).

γ-(4-Methoxy-2 : 3-dimethylphenyl)-β-methylbutyric acid, prepared from the keto-acid (VIII) (1·3 g.) by reduction with amalgamated zinc, separated (1·2 g.) from light petroleum (b. p. 60—80°) as needles, m. p. 115° (Ruzicka *et al., loc. cit.*, who prepared this acid by another route, give m. p. 107—108°) (Found : C, 70·9; H, 8·1. Calc. for $C_{14}H_{20}O_3$: C, 71·2; H, 8·4%). 5 : 6 : 7 : 8-*Tetrahydro*-8-*keto*-3 : 4 : 6-*trimethyl*-2-*naphthol* was obtained from the preceding butyric acid (1·1 g.) on cyclisation with 80% sulphuric acid. It separated from alcohol as needles (0·4 g.), m. p. 128—129° (Found : C, 77·0; H, 8·2. $C_{13}H_{16}O_2$ requires C, 76·5; H, 7·8%). 5 : 6 : 7 : 8-*Tetrahydro*-3 : 4 : 6-*trimethyl*-2-*naphthol*, obtained from this tetralone (0·3 g.) in the usual manner, separated from alcohol as needles (0·1 g.), m. p. 61—62° (Found : C, 81·9; H, 10·1. $C_{13}H_{18}O$ requires C, 82·1; H, 9·5%).

C. *Experiments with* m-4-*Xylenol.*

2 : 4 : 7-*Trimethyl*-1-*naphthol* (III).—*β*-(5-*Methoxy*-2 : 4-*dimethylbenzoyl*)-*α*-*methylpropionic acid* was obtained in the usual way from methyl *m*-4-xylyl ether (12 g.) in nitrobenzene. The crude product (17 g.) was recrystallised from dilute alcohol, from which the required acid separated as plates, m. p. 110° (Found : C, 67·3; H, 7·3. $C_{14}H_{18}O_4$ requires C, 67·2; H, 7·2%). Its *semicarbazone* crystallised from dilute alcohol as needles, m. p. 169° (Found : C, 58·2; H, 6·9. $C_{15}H_{21}O_4N_3$ requires C, 58·6; H, 6·8%). γ-(5-Methoxy-2 : 4-dimethylphenyl)-α-methylbutyric acid, prepared from the acid (7 g.), distilled at 180°/20 mm. (6·5 g.).

5 : 6 : 7 : 8-*Tetrahydro*-8-*keto*-2 : 4 : 7-*trimethyl*-1-*naphthol*. The above compound (6 g.) was heated with 80% sulphuric acid (24 g.) for 2 hours. The *keto-naphthol* separated from dilute alcohol as pale yellow prisms (3 g.), m. p. 56—57° (Found : C, 76·0; H, 7·6. $C_{13}H_{16}O_2$ requires C, 76·5; H, 7·8%).

5 : 6 : 7 : 8-*Tetrahydro*-2 : 4 : 7-*trimethyl*-1-*naphthol* crystallised from light petroleum (b. p. 40—60°) as needles, m. p. 71—72° (Found : C, 81·6; H, 9·3. $C_{13}H_{18}O$ requires C, 82·1; H, 9·5%).

2 : 4 : 7-*Trimethyl*-1-*naphthol* (III). The preceding compound (0·7 g.) was heated with selenium (3·1 g.) at 340—360° for 3 hours. The product was sublimed and then crystallised from light petroleum (b. p. 40—60°), from which the required *naphthol* separated as long needles, m. p. 105—106° (Found : C, 83·7; H, 7·6. $C_{13}H_{14}O$ requires C, 83·9; H, 7·5%). Light absorption : Maxima, 2420, 3030 (3160), and 3300 A.; log ε = 4·63, 3·69 (3·62), and 3·47, respectively. Its *picrate* crystallised from benzene as scarlet needles, m. p. 138—139° (Found : C, 54·6; H, 4·3. $C_{19}H_{17}O_8N_3$ requires C, 54·9; H, 4·1%). Its *carbanilate* crystallised from alcohol as small needles, m. p. 166—167° (Found : C, 78·5; H, 6·2. $C_{20}H_{19}O_2N$ requires C, 78·7; H, 6·2%).

D. *Experiments with* p-*Xylenol.*

1 : 4 : 7-*Trimethyl-2-naphthol* (IV).—β-(4-*Methoxy*-2 : 5-*dimethylbenzoyl*)-α-*methylpropionic acid.* Methyl *p*-xylyl ether (8·5 g.) was condensed with methylsuccinic anhydride (8·5 g.) by use of aluminium chloride (22 g.) in nitrobenzene (70 c.c.). The crude product (5 g.), m. p. 136—139°, when crystallised from dilute alcohol yielded the required *acid* as plates, m. p. 140° (Found : C, 67·0; H, 7·2. $C_{14}H_{18}O_4$ requires C, 67·2; H, 7·2%). Its *semicarbazone* separated from dilute alcohol as needles, m. p. 166° (Found : C, 58·6; H, 7·0. $C_{15}H_{21}O_4N_3$ requires C, 58·6; H, 6·8%).

γ-(4-*Methoxy*-2 : 5-*dimethylphenyl*)-α-*methylbutyric acid.* The keto-acid (4 g.) was reduced by amalgamated zinc (50 g.) to the required *butyric acid*, which separated from light petroleum (b. p. 40—60°) as large prisms (3·2 g.), m. p. 89—90° (Found : C, 70·9; H, 7·7. $C_{14}H_{20}O_3$ requires C, 71·2; H, 8·4%).

5 : 6 : 7 : 8-*Tetrahydro*-8-*keto*-1 : 4 : 7-*trimethyl-2-naphthol.* The above acid (2·5 g.) was heated with 80% sulphuric acid (10 g.) on the water-bath for 2 hours and yielded the required *tetralone*, which crystallised from light petroleum (b. p. 40—60°) as prisms, m. p. 75° (Found : C, 76·5; H, 7·7. $C_{13}H_{16}O_2$ requires C, 76·5; H, 7·8%).

5 : 6 : 7 : 8-*Tetrahydro*-1 : 4 : 7-*trimethyl-2-naphthol.* The foregoing ketone (1·1 g.) was reduced with amalgamated zinc and hydrochloric acid. The required *hydroxy-tetralin* separated from light petroleum (b. p. 40—60°) as needles, m. p. 32° (Found : C, 81·7; H, 9·5. $C_{13}H_{18}O$ requires C, 82·1; H, 9·5%).

1 : 4 : 7-*Trimethyl-2-naphthol* (IV). The hydroxy-tetralin (0·2 g.) was heated with selenium (0·6 g.) at 340—350° for 2 hours and yielded the required *naphthol*, which was extracted from the mixture with methyl alcohol and crystallised from dilute alcohol, from which it separated as long needles, m. p. 48—49° (Found : C, 83·9; H, 7·7. $C_{13}H_{14}O$ requires C, 83·9; H, 7·5%). Light absorption : Maxima, 2370, 2880 (3020), 3250, and 3370 A.; log ε = 4·59, 3·56 (3·46), 3·09, and 3·13, respectively. Its picrate crystallised from benzene as scarlet needles, m. p. 115°, but there was insufficient (2·3 mg.) for analysis.

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