

Friedel-Crafts Acylations of Aromatic Hydrocarbons. Part XIII.¹ Syntheses of Methyl-substituted Naphthalenes. Some Anomalous Gattermann Formylation Reactions

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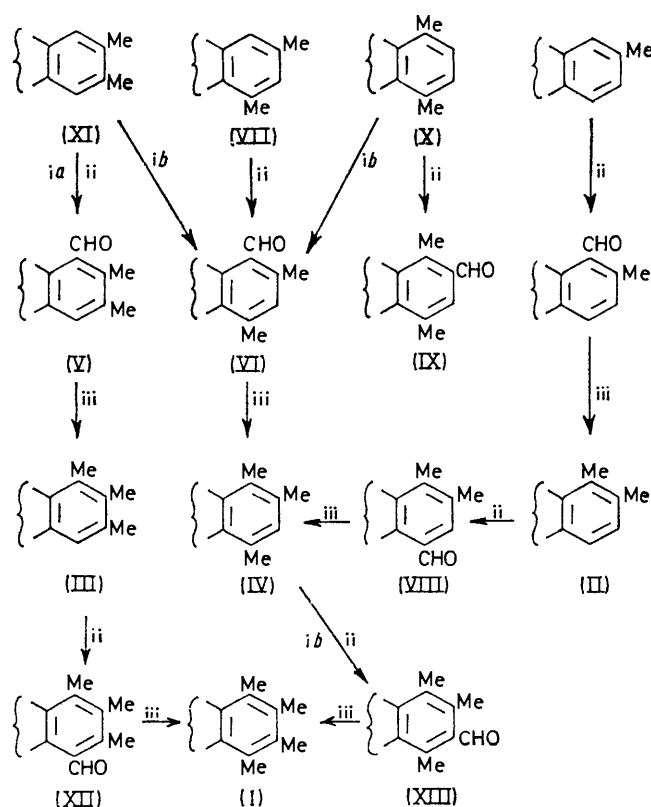
New syntheses of 1,2-dimethyl-, 1,2,3- and 1,2,4-trimethyl-, and 1,2,3,4-tetramethyl-naphthalenes are described. Gattermann formylations can proceed abnormally above 65°, both 2,3- and 1,4-dimethylnaphthalenes affording 2,4-dimethylnaphthalene-1-carbaldehyde.

We wished to prepare 1,2,3,4-tetramethylnaphthalene (I)¹ and found the literature procedure² unreliable. We now report a stepwise introduction of methyl groups into a naphthalene nucleus, which provides the best available methods of preparation of 1,2-dimethylnaphthalene (II), 1,2,3-trimethylnaphthalene (III), 1,2,4-trimethylnaphthalene (IV), and 1,2,3,4-tetramethylnaphthalene (I). Each step involves formylation, generally by use of dichloromethyl methyl ether with titanium(IV) chloride as catalyst,³ followed by Huang-Minlon reduction of the aldehyde. The reactions studied are summarised in the Scheme.

For the preparation of 2,3-dimethylnaphthalene-1-carbaldehyde (V) a Gattermann aldehyde reaction and a working temperature of 70° had been recommended⁴ (*cf.* ref. 5). We have found that aldehyde (V), m.p. 78°, can be obtained reliably only if the temperature does not exceed 55°. Above 65° 2,4-dimethylnaphthalene-1-carbaldehyde (VI), m.p. 86.5°, is obtained instead. Identification of this anomalous product is based on (i) its ¹H n.m.r. spectrum (Table), (ii) an independent synthesis from 1,3-dimethylnaphthalene (VII), and (iii) its reduction to the known 1,2,4-trimethylnaphthalene (IV). 3,4-dimethylnaphthalene-1-carbaldehyde (VIII) and 1,4-dimethylnaphthalene-2-carbaldehyde (IX), either of which could also give rise, on reduction, to hydrocarbon (IV), were obtained by formylation of 1,2-

dimethylnaphthalene (II) and 1,4-dimethylnaphthalene (X), respectively.

It is evident that formation of the aldehyde (VI) from



SCHEME Reagents: i, Gattermann aldehyde synthesis (a) at 50°, (b) at 65°; ii, dichloromethyl methyl ether method; iii, Huang-Minlon reduction.

¹ Part XII, P. H. Gore and J. A. Hoskins, *J. Chem. Soc. (C)*, 1971, 3347.

² C. L. Hewett, *J. Chem. Soc.*, 1940, 293; *cf.* J. C. Smith, *J. Inst. Petroleum*, 1947, **33**, 511.

³ A. Rieche, H. Gross, and E. Höft, *Org. Synth.*, 1967, **47**, 1; *Chem. Ber.*, 1960, **93**, 88.

⁴ R. C. Fuson, E. C. Horning, M. L. Ward, S. P. Rowland, and J. L. Marsh, *J. Amer. Chem. Soc.*, 1942, **64**, 30.

⁵ L. E. Hinkel, E. E. Ayling, and J. H. Beynon, *J. Chem. Soc.*, 1936, 339.

2,3-dimethylnaphthalene (XI) involves the migration of a methyl group. Analogous rearrangements accompanying the Gattermann aldehyde synthesis applied to substituted benzenes have long been known.^{6,7} Thus, *o*- or *p*-xylene have both been reported to give 2,4-dimethylbenzaldehyde in Gattermann formylation reactions carried out at 100°; ^{6,7} methyl migrations were similarly observed in reactions of pseudocumene and mesitylene.⁸ These Gattermann formylations involve the use of solid aluminium chloride (which dissolves substantially only

Only the expected aldehydes are formed when dichloromethyl methyl ether and titanium(IV) chloride³ are used for formylation. These reactions proceed normally, as they are carried out at a relatively low temperature (40°) and with a catalyst which is not present in high local concentrations.

The ¹H n.m.r. spectra of the compounds prepared are summarised in the Table. α - and β -Naphthyl methyl signals are generally readily differentiated.¹¹ The aromatic protons of the unsubstituted ring in some cases

¹H N.m.r. spectra of methylnaphthalene derivatives ^a

Naphthalene	τ Values *											CHO		
	1-CH ₃	2-CH ₃	3-CH ₃	4-CH ₃	1-H	2-H	3-H	4-H	5-H	6-H	7-H		8-H	
2,3-Dimethyl- ^{b,c} (XI)		7.76	7.76		2.54			2.54		2.2—2.8(c)				
1,2,3-Trimethyl- (III)	7.52	7.76	7.67					2.62br		2.0—2.8(c)				
1,2,4-Trimethyl- ^c (IV)	7.50	7.62		7.42			2.91br ^d		2.05(m)	2.58(m)	2.58(m)	2.05(m)		
1,2,3,4-Tetramethyl- ^{c,e} (I)	7.38	7.58	7.58	7.38					1.96(m)	2.59(m)	2.59(m)	1.96(m)		
1-Formyl-2,3-dimethyl- (V)		7.52	7.66							2.2—2.8(c)		1.37(m)	—0.78	
1-Formyl-2,4-dimethyl- (VI)		7.46		7.28			2.41(m)			1.1—1.93(c)		0.93	—1.40	
1-Formyl-3,4-dimethyl- (VIII)			7.45	7.35	1.90(m)					2.1—2.6(c)		0.75	—0.30	
1-Formyl-2,3,4-trimethyl- (XII)		7.48	7.48	7.26					1.9(m)	2.5(m)	2.5(m)	1.9(m)	—0.75	
2-Formyl-1,4-dimethyl- (IX)	7.00			7.31			2.26br		1.98(m)	2.2—2.5(c)		1.75(m)	—0.63	
2-Formyl-1,3,4-trimethyl- (XIII)	7.20		7.43	7.40					1.9(m)	2.4(m)	2.4(m)	1.9(m)	—0.80	
2-Bromo-1,3,4-trimethyl-	7.22		7.42br	7.42br					2.0(m)	2.55(m)	2.55(m)	2.0(m)		
2-Cyano-1,3,4-trimethyl-	7.03		7.34 ^g	7.28 ^g					1.75(m)	2.2(m)	2.2(m)	1.75(m)		

* Signals are singlets, unless otherwise stated; c = complex.

^a In deuteriochloroform, unless otherwise stated. ^b Cf. P. H. Gore, C. K. Thadani, and S. Thorburn, *J. Chem. Soc. (C)*, 1968, 2502. ^c Lit.,¹¹ in CCl₄: signals for (XI) at τ 7.65; for (IV) at τ 7.48 (1-CH₃), 7.62 (2-CH₃), and 7.43 (4-CH₃); for (I) at τ 7.44 (1- and 4-CH₃) and 7.63 (2- and 3-CH₃). ^d $J_{3-H,4-CH_3}$ ca. 1.8 Hz. ^e Ref. 2. ^f Solvent CCl₄. ^g In CCl₄ solution the 3- and 4-CH₃ signals merge (τ 7.42).

towards the end of the reactions), the presence of which can cause alkyl migration.⁹

It has been shown¹⁰ that with catalytic amounts of boron trifluoride and a large excess of hydrogen fluoride at 70° a rapid equilibration takes place between the following three hydrocarbons (equilibrium isomer distribution in parentheses): 2,3-dimethylnaphthalene (XI) (35%), 1,3-dimethylnaphthalene (VII) (64%), and 1,4-dimethylnaphthalene (X) (1%). With 1 mol. equiv. of boron trifluoride at 28°, the equilibrated mixture contains >99% of hydrocarbon (VII).¹⁰ If formylation of hydrocarbon (XI) is slow compared with its rearrangement, in the presence of the catalyst aluminium chloride at elevated temperatures, it may be concluded that both 2,3- (XI) and 1,4-dimethylnaphthalene (X) could act as sources of hydrocarbon (VII). Formylation of the new substrate then affords the 'anomalous' aldehyde (VI). In confirmation of this interpretation, hydrocarbon (X) was shown similarly to give the aldehyde (VI) by a Gattermann formylation carried out at 65°.

⁶ R. Heise and A. Töhl, *Annalen*, 1892, **270**, 155.

⁷ E. L. Niedzielski and F. F. Nord, *J. Org. Chem.*, 1943, **8**, 147.

⁸ W. E. Truce, *Org. Reactions*, 1957, **9**, 48.

gave complex multiplets, in others well separated signals of α - and β -protons. In derivatives of naphthalene-1-carbaldehyde the furthest downfield aromatic signal is that of the *peri*- (8-) proton.

EXPERIMENTAL

2,4-Dinitrophenylhydrazones were purified by chromatography over alumina, followed by crystallisation from ethyl acetate.

Aldehyde Syntheses.—(a) *Normal Gattermann formylations.* 2,3-Dimethylnaphthalene-1-carbaldehyde (V). A stream of dry hydrogen chloride was passed into a stirred mixture of 2,3-dimethylnaphthalene (14.6 g), zinc cyanide (17 g), and tetrachloroethane (120 ml) for ca. 4 h. To the mixture, cooled in ice, anhydrous aluminium chloride (25 g) was added with stirring. Hydrogen chloride was then passed again for 6 h through the stirred mixture kept at 50 (\pm 2)°. The mixture was poured with stirring into ice-hydrochloric acid; the product was set aside for 12 h, and then heated with occasional stirring on a water-bath. The organic

⁹ D. A. McCauley, in 'Friedel-Crafts and Related Reactions,' ed. G. A. Olah, Interscience, New York, 1964, vol. II, p. 1049.

¹⁰ G. Suld and A. P. Stuart, *J. Org. Chem.*, 1964, **29**, 2939.
¹¹ Foch Fu-Hsieh Yew, R. J. Kurland, and B. J. Mair, *Analyt. Chem.*, 1964, **36**, 843.

layer was separated, combined with chloroform extracts of the aqueous layer, and then washed with water. The solvent was then removed (*in vacuo*, or by steam distillation), and the crude product was taken up in benzene, and dried (MgSO_4). The solution was passed through a short column of alumina (Spence type H) and the product was crystallised (ethanol). The pure aldehyde (V) (15.1 g, 89%) had m.p. 76–77° (lit.,⁴ 77.5–78.5°) (Found: C, 84.7; H, 6.7. Calc. for $\text{C}_{13}\text{H}_{12}\text{O}$: C, 84.75; H, 6.6%), ν_{max} 1665 cm^{-1} (C=O); 2,4-dinitrophenylhydrazone, m.p. 222–223° (Found: C, 62.4; H, 4.6; N, 15.8. $\text{C}_{19}\text{H}_{16}\text{N}_4\text{O}_4$ requires C, 62.6; H, 4.4; N, 15.4%).

1,3,4-Trimethylnaphthalene-2-carbaldehyde (XIII). An analogous reaction with 1,2,4-trimethylnaphthalene at 65° gave the aldehyde (XIII) (0.4%), m.p. 121° (from ethanol) (Found: C, 84.1; H, 7.2. $\text{C}_{14}\text{H}_{14}\text{O}$ requires C, 84.8; H, 7.1%), ν_{max} 1682 cm^{-1} (C=O); 2,4-dinitrophenylhydrazone, m.p. 244–245° (Found: C, 63.4; H, 4.7; N, 15.0. $\text{C}_{20}\text{H}_{18}\text{N}_4\text{O}_4$ requires C, 63.45; H, 4.8; N, 14.8%).

(b) *Abnormal Gattermann formylations.* 2,4-Dimethylnaphthalene-1-carbaldehyde (VI). (i) *From 2,3-dimethylnaphthalene.* The reaction was carried out as for the normal Gattermann formylation except that hydrogen chloride was passed through the mixture, after addition of aluminium chloride, for 6 h at 69°. The aldehyde (VI) (71%) formed yellow crystals (from ethanol), m.p. 86–86.5° (Found: C, 84.5; H, 6.9. $\text{C}_{13}\text{H}_{12}\text{O}$ requires C, 84.75; H, 6.6%), ν_{max} 1670 cm^{-1} (C=O); 2,4-dinitrophenylhydrazone, m.p. 241° (Found: C, 62.6; H, 4.2; N, 15.1. $\text{C}_{19}\text{H}_{16}\text{N}_4\text{O}_4$ requires C, 62.6; H, 4.4; N, 15.4%).

Analogous reactions carried out at 62 or 65° for 6 h gave yields (crude product) of 54 and 65%, respectively; the products contained small amounts of the 'normal' aldehyde (V).

(ii) *From 1,4-dimethylnaphthalene.* A similar reaction with 1,4-dimethylnaphthalene, carried out for 1.2 h at 65°, afforded the crude aldehyde (VI) (56%), m.p. 80–83°, identical with material from method (i) (mixed m.p.; i.r. spectrum).

(c) *Dichloromethyl methyl ether method.* 2,3-Dimethylnaphthalene-1-carbaldehyde (V). To 2,3-dimethylnaphthalene (4 g) in dry dichloromethane (35 ml) kept at 0°, titanium(IV) chloride (8.5 g) was added. Dichloromethyl methyl ether (3.0 g) in dichloromethane (5 ml) was then added during 0.5 h. The mixture was boiled gently for 2 h, cooled, and poured on crushed ice. The aldehyde (V) (69%) was isolated as before, m.p. and mixed m.p. 76–77°.

Other aldehydes obtained analogously were 2-methylnaphthalene-1-carbaldehyde, needles (26%), b.p. 135–140° at 2 mmHg, m.p. 51.5–52° (Found: C, 84.8; H, 5.9. $\text{C}_{12}\text{H}_{10}\text{O}$ requires C, 84.7; H, 5.9%), ν_{max} 1672 cm^{-1} (C=O); 3,4-dimethylnaphthalene-1-carbaldehyde, crystals (95%), m.p. 81–82° [mixed m.p. with aldehydes (V) and (VI) showed depression] (Found: C, 84.6; H, 6.7. $\text{C}_{13}\text{H}_{12}\text{O}$ requires C, 84.75; H, 6.6%), ν_{max} 1675 cm^{-1} (C=O); 2,4-dimethylnaphthalene-1-carbaldehyde (VI) crystals (97%), m.p.

84–85°, identical (mixed m.p. and i.r. spectrum) with that prepared before; 1,4-dimethylnaphthalene-2-carbaldehyde, crystals (95%), m.p. 72–73° (Found: C, 84.6; H, 6.6. $\text{C}_{13}\text{H}_{12}\text{O}$ requires C, 84.75; H, 6.6%), ν_{max} 1675 cm^{-1} (C=O) [mixed m.p. with aldehyde (V) showed depression]; 1,3,4-trimethylnaphthalene-2-carbaldehyde (XIII), crystals (17%), m.p. 118–119°, identical with that prepared before (mixed m.p.; i.r. spectrum); and 2,3,4-trimethylnaphthalene-1-carbaldehyde, yellow crystals (95%), m.p. 129.5–130.5° (Found: C, 84.4; H, 7.3. $\text{C}_{14}\text{H}_{14}\text{O}$ requires C, 84.8; H, 7.1%), ν_{max} 1665 cm^{-1} (C=O).

Huang-Minlon Reductions.—1,2,3-Trimethylnaphthalene was obtained by the general method recommended by Durham *et al.*¹² as plates (78%), m.p. 28–29° (lit.,² m.p. 27–28°). 1,2-Dimethylnaphthalene was obtained as an oil¹³ (67%). 1,2,4-Trimethylnaphthalene was formed by reduction of the aldehyde (VI) as crystals (60%), m.p. 56° (lit.,¹³ 54–55°) (Found: C, 91.8; H, 8.2. Calc. for $\text{C}_{13}\text{H}_{14}$: C, 91.7; H, 8.3%). Reduction of aldehyde (VIII) gave the same hydrocarbon (90%), m.p. 53–55° (mixed m.p.; i.r. spectrum), ν_{max} 1380 cm^{-1} (CH_2). 1,2,3,4-Tetramethylnaphthalene was obtained as crystals (32%), m.p. 107–107.5° (lit.,² 106.5–107.5°) (Found: C, 91.6; H, 8.2. Calc. for $\text{C}_{14}\text{H}_{16}$: C, 91.25; H, 8.75%), from the aldehyde (XIII), and was identical (i.r. spectrum) with that (m.p. 106–107°) obtained (76%) by reduction of the aldehyde (XII).

Miscellaneous Preparations.—2-Bromo-1,3,4-trimethylnaphthalene. Bromine (4.7 ml) was added to a solution of 1,2,4-trimethylnaphthalene (0.5 g) in chloroform (2 ml) during 0.5 h. After a further 15 min the mixture was washed with dilute alkali, then water, and dried (MgSO_4). The residue (0.55 g) obtained on evaporation afforded 2-bromo-1,3,4-trimethylnaphthalene (34%), m.p. 105–106° (from ethanol) (Found: C, 62.7; H, 5.2; Br, 31.9. $\text{C}_{13}\text{H}_{13}\text{Br}$ requires C, 62.7; H, 5.3; Br, 32.1%).

1,3,4-Trimethylnaphthalene-2-carbonitrile.—A mixture of 2-bromo-1,3,4-trimethylnaphthalene (3.2 g), copper(I) cyanide (1.45 g), and dry pyridine (4 ml) was heated (bath at 180°) under reflux for 40 h. The product was extracted with benzene; the extracts were washed with dilute ammonia, dilute hydrochloric acid, water, and dried (MgSO_4). On evaporation a white solid (3.5 g) was obtained, which on chromatography from benzene on alumina and crystallisation (from ethanol) afforded 1,3,4-trimethylnaphthalene-2-carbonitrile (2.0 g, 80%), m.p. 152–153° (Found: C, 86.3; H, 6.7; N, 7.3. $\text{C}_{14}\text{H}_{13}\text{N}$ requires C, 86.1; H, 6.7; N, 7.2%), ν_{max} 1386 (CH_2) and 2220 cm^{-1} (C≡N).

1,4-Dimethylnaphthalene-2-carboxylic Acid.—The aldehyde (IX) was oxidised by alkaline permanganate in low yield to 1,4-dimethylnaphthalene-2-carboxylic acid, m.p. 182–183°, identical (mixed m.p.; i.r. spectrum) with an authentic specimen.¹

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¹² L. J. Durham, D. J. McLeod, and J. Cason, *Org. Synth.*, 1958, **38**, 34.

¹³ M. C. Kloetzel, *J. Amer. Chem. Soc.*, 1940, **62**, 1708; cf. L. Ruzicka and L. Ehmann, *Helv. Chim. Acta*, 1932, **15**, 140.