

Synthesis and Proton Magnetic Resonance Studies of 2,2,3-Trimethyl-5,7-dineopentyl-1-indanone and the Corresponding Indanol and Indan

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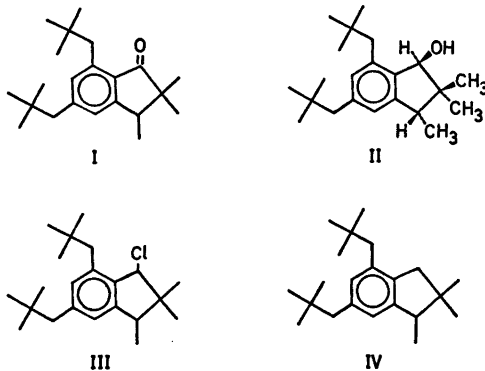
2,2,3-Trimethyl-5,7-dineopentyl-1-indanone was formed by a ring-closure reaction when 1,3,5-trineopentylbenzene was treated with 2,2-dimethylpropanoyl chloride or carbon monoxide under Friedel-Crafts conditions. Its structure was determined by means of several spectroscopic methods including the europium-shift NMR technique. 60 MHz NMR studies showed that the 7-methylene group formed an AB spectrum due to the inherent assymetry in the five-membered ring. Stepwise reduction of 2,2,3-trimethyl-5,7-dineopentyl-1-indanone to the corresponding indanol and indan gave further evidence for the structure. NMR studies of the indanol showed that the configuration of the hydroxyl group at carbon 1 and the methyl group at carbon 3 was *trans*.

In an earlier publication¹ an unsuccessful attempt to prepare 2-(2,2-dimethylpropanoyl)-1,3,5-trineopentylbenzene is described. The main product was isolated from the complex reaction mixture and has now been identified as 2,2,3-trimethyl-5,7-dineopentyl-1-indanone (I). The present paper deals with the preparation and identification of this particular compound and some of its derivatives.

The compound (I) has been prepared in two ways. The first one is by treatment of 1,3,5-trineopentylbenzene with 2,2-dimethylpropanoyl chloride and aluminum chloride in dichloromethane. The second one consists of a reaction between 1,3,5-trineopentylbenzene and carbon monoxide in dichloromethane with aluminum chloride as catalyst.

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The assigned structure of I is based on the following observations. High-resolution mass spectrometry gave the mass 314.261 ± 0.002 u, which gives the molecular formula $C_{22}H_{34}O$. The presence of two *tert*-butyl groups was indicated by the mass spectrum. The IR spectrum had an absorption at the same wave-number (1710 cm^{-1}) as the carbonyl stretching of indanone.² From the NMR spectrum, it could be concluded that the molecule contains two *meta*-coupled ($J = 1\text{ Hz}$) aromatic protons (δ 6.83 and 7.02), two *tert*-butyl groups with different chemical shift values (δ 0.91 and 0.95), two isolated methyl groups with different chemical shift values (δ 1.01 and 1.17), a methyl-methine grouping (δ 1.26 and 3.03, $J = 8\text{ Hz}$), a methylene group with magnetically equivalent protons (δ 2.58), and a methylene group in which the protons are nonequivalent (δ 3.09, $J = 12\text{ Hz}$).



The 2,2,3-trimethyl-1-indanone structure could be assigned to I, in preference to the 2,3,3-trimethyl-1-indanone structure, on the basis of the chemical shifts. The methine and methyl resonances of 2,2,3-trimethyl-1-indanone have been reported to be δ 3.05 (quartet), 1.03 (singlet), 1.20 (singlet), and 1.28 (doublet), respectively, in deuteriochloroform.³ A comparison can also be made with the methyl (δ 1.05) and methine (δ 2.64) resonances of the isopropyl group in 2-(2-methylpropanoyl)-1,3,5-trieneopentylbenzene,¹ whereas in 1,3,5-triisopropylbenzene the methine protons absorb at δ 2.84.

To get further information on the pattern of substitution in the alicyclic ring, I was reduced by lithium tetrahydridoaluminate to the indanol (II). This resulted in changes in the NMR resonance frequencies, but induced no additional splitting of the methine resonance. This indicates that the methyl groups are in the 2,2,3-positions.

The indanol (II) was converted to the corresponding indan (IV) by treatment with sulfinyl chloride to form the chloro-substituted compound III, followed by treatment with lithium in liquid ammonia. The NMR spectrum of (IV) showed *tert*-butyl, 3-methylene and aromatic resonance at δ 0.91, 2.60, and 6.60, respectively. These values are in close agreement with those in 2,2-dimethyl-4,6-dineopentylindan (δ 0.90 and 0.92, 2.65, 6.60 and 6.69).⁴

The chemical shifts of the aromatic hydrogens and the neopentyl groups in the NMR spectrum of I lead us to suggest that the neopentyl groups are in positions 5 and 7 rather than 4 and 6. The hydrogen in the peri-position in 9-fluorenone

absorbs at δ 7.58⁵ and the *ortho* hydrogens in acetophenone absorb at δ 7.95.⁶ The aromatic hydrogens of I absorb at δ 6.83 and 7.02, which is taken as evidence that they are in the 4 and 6 positions. In addition, the large down-field shift of the magnetically nonequivalent methylene hydrogens in one of the neopentyl groups of I indicates that this group is in the 7 position, deshielded by the carbonyl group.

In an attempt to further confirm the structural assignments above, the effect of $\text{Eu}(\text{fod})_3 \cdot d_{27}$,⁷ on the NMR spectrum of I was studied. The paramagnetic pseudocontact shift, ΔE_{Eu} ,⁸ for the different hydrogens was estimated from the NMR data and is tabulated in Table 1. From these data it can be found that all the signals shifted in the manner that could be expected for the suggested structure. A plot of the ΔE_{Eu} -values *vs.* $(3 \cos^2 \theta - 1)/r^3$ according to the McConnell-Robertson equation⁹ gave a good linear correlation (see Fig. 1) if the Eu-ion was placed at a distance of 3.0 Å from the carbonyl oxygen on a straight line connecting the carbon and oxygen atoms of the carbonyl group. The distances r and the angles θ were estimated from a Dreiding molecular model in which the aromatic and five-membered ring and the carbonyl group were coplanar. The suggested non-coplanarity of I (see below) is probably of no importance for these estimations. Much poorer correlation was found with the alternative structure discussed above (see Fig. 2).

Table 1. ΔE_{Eu} -values for compound (I). For the designation of the hydrogens see Fig. 1.

Protons	ΔE_{Eu} (ppm)
a	0.9
b	1.1
c	1.7
d	1.7
e	1.9
f	2.1
g	4.0
h	5.1
i	5.3
j	5.3

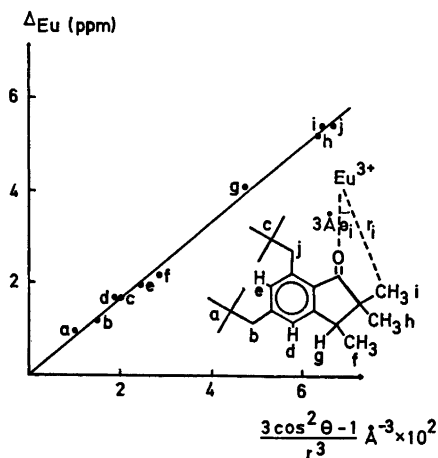


Fig. 1. Plot of ΔE_{Eu} -values *vs.* $(3 \cos^2 \theta - 1)/r^3$ for compound (I).

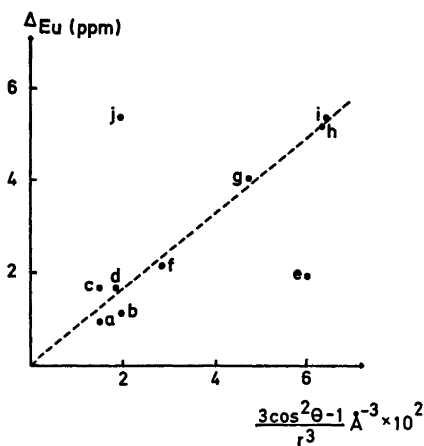


Fig. 2. Plot of ΔE_u -values vs. $(3 \cos^2 \theta - 1)/r^3$ for the hypothetical alternative structure 2,2,3-trimethyl-4,6-dineopentyl-1-indanone. The 5- and 7-aromatic hydrogens are designated d and e, respectively. The hydrogens of the methylene groups of the 4- and 6-neopentyl groups are designated b and j, respectively, and the hydrogens of the *tert*-butyl groups of the 4- and 6-neopentyl groups are designated a and c, respectively. For the designation of the other hydrogens see Fig. 1.

The methylene protons of the neopentyl group at carbon 7 of the indanone (I) are magnetically nonequivalent, but those of the neopentyl group at carbon 5 are magnetically equivalent. Heating I to 200 °C in deuteriobromofrom caused only a slight decrease of the relative chemical shifts between the two methylene protons of the 7-neopentyl group. If the nonequivalence were due to restricted rotation in the molecule, the barrier to internal rotation, ΔG^\ddagger , should have to be at least as high as 23 kcal/mol ($\Delta G^\ddagger(200^\circ\text{C}) = 23.7$ kcal/mol), which is considered less probable.

In order to rationalize this nonequivalence, we suggest that the carbonyl group is noncoplanar with the benzene ring in the predominant conformation of I, due to the unsymmetrical pattern of substitution in the five-membered ring. The nonequivalence of the methylene protons of the 7-neopentyl group would thus mainly be induced by the large magnetic field from the carbonyl group.

The distance between the carbonyl group and the methylene protons of the 5-neopentyl group is too large for the asymmetric field from the

carbonyl group to be of importance, and thus these protons appear as a singlet.

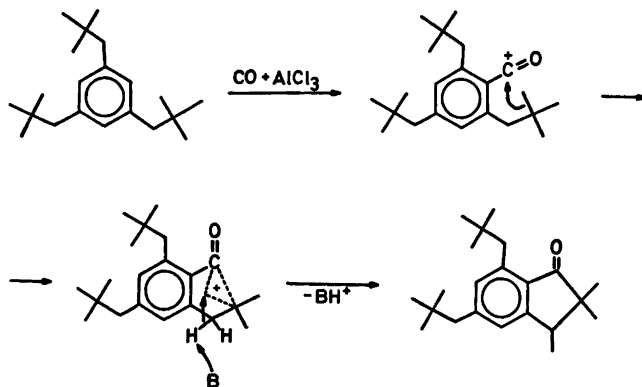
It is interesting to note that 1,2,2-trimethyl-4,6-dineopentylindan (IV) does not show magnetic nonequivalence in the methylene groups. This is explained by the absence of the field from the carbonyl group.

2,2,3-Trimethyl-5,7-dineopentyl-1-indanol (II) has two centers of chirality. Of the two possible (diastereomeric) pairs of enantiomers, only one seems to have been formed in the reduction of I with lithium tetrahydridoaluminate. The close similarity of the shifts of the geminal 2-methyl groups (δ 1.00 and 1.03) indicates that the 1-hydroxyl group and the 3-methyl group are situated on different sides of the plane of the five-membered ring. In contrast it has been reported³ that the product of sodium tetrahydridoborate-reduction of 2,2,3-trimethyl-1-indanone showed NMR resonances at 0.68 and 1.18 ppm for the geminal 2-methyl groups and a structure with the 1-hydroxyl and the 3-methyl group on the same side of the ring plane was there assigned.

The stereoisomeric difference between II and 2,2,3-trimethyl-1-indanol³ may be explained by the difference in the reducing agents¹⁰ and/or in steric hindrance.

The suggested mechanism of formation of I with carbon monoxide is outlined in Scheme 1. It is suggested that the same mechanism is valid for the alternative synthesis, including 2,2-dimethylpropanoyl chloride, since this acyl chloride is known to decarbonylate easily under Friedel-Crafts conditions.¹¹ 1,3,5-Trineopentylbenzene is carbonylated to form an acylium cation, which undergoes an intramolecular reaction between the electron-deficient carbon and a carbon-carbon bond of one of the neighboring *tert*-butyl groups. The methyl group at the two-electron, three-center bond then effects an electrophilic substitution of one of the hydrogens of the methylene group to form the final product. An interesting feature of this mechanism would be that the formation of the three-center bond occurs between the electron-deficient carbon and a carbon-carbon bond and not a carbon-hydrogen bond of a methyl group. The latter mechanism has been suggested for a formation of 1,1-dimethyl-4,6-di-*tert*-butylindan from 2,4,6-tri-*tert*-butylbenzyl alcohol.¹²

We have rejected, as less possible, a mecha-



Scheme 1. Tentative mechanism of formation of 2,2,3-trimethyl-5,7-dineopentyl-1-indanone (I).

nism involving benzylic hydride ion abstraction from 1,3,5-trineopentylbenzene, followed by a 1,2-methyl shift and a carbonylation of the cation thus formed with concomitant ring closure, *cf.* Ref. 13. In a separate study¹ it was shown that commercial aluminum chloride had no effect on 1,3,5-trineopentylbenzene. This is in accordance with the known resistance to oxidation of an aromatic neopentyl group.¹⁴

EXPERIMENTAL

Measurements. Gas chromatographic (GLC) analyses were carried out on a Perkin-Elmer 900 gas chromatograph fitted with a flame ionization detector. The inner diameter of the columns used was 2 mm and the length 2 m. The stationary phase was 3 % of SE-30 silicon gum rubber on Gaschrom Q 100–200 mesh. The areas of the peaks on the gas chromatograms were measured by triangulation.

The IR spectra were recorded on a Beckman IR 9 spectrophotometer using potassium bromide pellets or a potassium bromide cell. The absorption maxima are reported in cm^{-1} and the intensities are characterized as weak (w), medium (m), strong (s), or very strong (vs).

The NMR spectra were recorded on a Varian A 60 spectrometer. About 10 % by weight solutions in carbon tetrachloride were used. The probe temperature was 35 °C. The chemical shifts are reported in ppm downfield from tetramethylsilane as internal standard. The multiplicities of the peaks are reported as singlet (s), doublet (d), and quartet (q). The spectrum of 2,2,3-trimethyl-5,7-dineopentyl-1-indanone (I) was also determined in deuteriochloroform with successive additions of tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl- d_5 -4,6-octanedione- d_8)europium(III), $[\text{Eu}(\text{fod})_3 \cdot d_{27}]$. The chemical shift values found for each protons or group of

protons for each addition of europium(III) were plotted as functions of the molar ratios $X = [\text{Eu}(\text{fod})_3]/[\text{Compound (I)}]$ and linear correlations were made. The ΔE_{Eu} -values were then defined for each proton or group of protons as the difference in the extrapolated chemical shifts for $X=1$ and the actual chemical shifts for $X=0$.

The mass spectra (MS) were determined (at the Department of Medical Biochemistry, University of Göteborg) on an AEI 902 mass spectrometer under the following conditions: electron energy 70 eV, accelerating voltage 8 kV and emission 100 μA , or (at the Department of Medical Chemistry, University of Göteborg) on an LKB 9000 mass spectrometer with an electron energy of 70 eV. The latter mass spectrometer was connected to a gas chromatograph with a column containing 3 % of OV-1. The intensities of the peaks are reported in parenthesis as percentages of the base peak. Only the most abundant peaks are reported, together with the parent peaks and the isotope peaks corresponding to the latter.

Materials. Aluminum chloride: Kistner (*puriss*). Dichloromethane: Fisher (*p.a.*). Lithium tetrahydridoaluminate: Metallgesellschaft AG, Frankfurt a. M. Hexane: Fisher (*p.a.*). Sulfinyl chloride: Kistner (*puriss*). 1,3,5-Trineopentylbenzene was prepared as described by Martinson and Márton.¹⁵

2,2,3-Trimethyl-5,7-dineopentyl-1-indanone (I). a. A stirred suspension of aluminum chloride (7.0 g, 52.2 mmol) in 20 ml of dichloromethane was cooled to -35°C and 2,2-dimethylpropanoyl chloride (6.7 ml, 52.2 mmol) was added. After 15 min, 1,3,5-trineopentylbenzene (5.0 g, 17.4 mmol) dissolved in 10 ml of dichloromethane, was added dropwise. The temperature of the flask was then slowly raised to room temperature and products started to form. Gases evolved during the reaction, and after 10 h the excess of aluminum chloride and 2,2-dimethylpropanoyl chloride was destroyed with

water. The aqueous layer was then extracted several times with hexane, and the combined dichloromethane and hexane layers were washed with 10 % aqueous sodium hydroxide solution, then with water, then with dilute hydrochloric acid and finally again with water. The organic layer was dried over magnesium sulfate, and the solvent was evaporated. The resulting oil was shown, by GLC, to consist of about 40 % of a main product and about 60 % of a complex mixture of about 30 compounds. Partial separation was performed on a column of silica gel. Unreacted 1,3,5-trineopentylbenzene and about 10 products were eluted with hexane. The main product was eluted with benzene and collected together with some other products. The column chromatography (silica gel, benzene) was repeated several times to give 2,2,3-trimethyl-5,7-dineopentyl-1-indanone of 97 % purity (GLC). The yield was 1.5 g (27 %) of an oil. *IR*: 2960vs, 2910m, 2865s, 1710vs, 1607vs, 1587s, 1480vs, 1427w, 1394m, 1367vs, 1304s, 1237s, 1202s, 1192s, 1160w, 1133m, 1095w, 992m, 974s, 918m, 890s, 873s, 746m. *MS*: 29(18), 41(27), 43(8), 57(7), 173(8), 187(18), 188(8), 202(100), 203(16), 243(13), 258(32), 299(14), 314(15.6), 315(3.9), 316(0.5). The mass of the molecule was determined by high-resolution mass spectrometry, and the value 314.261 ± 0.002 u was found. The value 18 for $C_{22}H_{34}O$ is 314.261 u. *NMR*: δ 0.91 (s, 9 H, *tert*-butyl), 0.95 (s, 9 H, *tert*-butyl), 1.01 (s, 3 H, methyl), 1.17 (s, 3 H, methyl), 1.26 (d, 3 H, methyl, $J = 8$ Hz), 2.58 (s, 2 H, methylene), 3.03 (q, 1 H, methine, $J = 8$ Hz), 3.09 (q, 2 H, methylene, $J = 12$ Hz, $\Delta\nu_{AB} = 11$ Hz), 6.83 (d, 1 H, aromatic, $J = 1$ Hz), 7.02 (d, 1 H, aromatic, $J = 1$ Hz).

b. To a suspension of 210 mg (1.58 mmol) of aluminum chloride in 5 ml of dichloromethane, a solution of 150 mg (0.52 mmol) of 1,3,5-trineopentylbenzene in 5 ml of dichloromethane was added, and a slow stream of carbon monoxide was bubbled into the mixture. A GLC analysis of the mixture after 24 h showed that a main product had been formed in about 60 % yield together with about 15 minor products. The work-up procedure described in *a* was then applied, and the total yield was 163 mg of an oil. The oil was investigated with an LKB 9000 mass spectrometer connected to a gas chromatograph. The MS of the main product was identical with that reported in *a* for 2,2,3-trimethyl-5,7-dineopentyl-1-indanone.

2,2,3-Trimethyl-5,7-dineopentyl-1-indanol (II). 2,2,3-Trimethyl-5,7-dineopentyl-1-indanone (0.2 g, 0.64 mmol) in 5 ml of diethyl ether was added to a suspension of 0.24 g (6.4 mmol) of lithium tetrahydridoaluminate in 20 ml of diethyl ether. The mixture was refluxed overnight, and the reaction was then found to be complete (GLC). The flask was cooled and the excess of lithium tetrahydridoaluminate was destroyed with water. The mixture was filtered and the precipitate was washed several times with diethyl ether. The organic and aqueous layers were

separated, and the organic layer was dried over magnesium sulfate. After evaporation of the solvent, the product was recrystallized from ethanol-water. The yield was 0.16 g (80 %) of white crystals which, according to GLC, were more than 98 % pure. *IR*: 3390vs, 2950vs, 2902s, 2862s, 1610m, 1591m, 1478s, 1414m, 1392m, 1384w, 1362s, 1235s, 1200m, 1039s, 1025s, 989m, 902w, 875s, 836m, 771m, 749w, 685m. *MS*: 29(26), 41(36), 43(34), 55(9), 57(100), 69(8), 71(23), 132(8), 171(16), 185(30), 186(77), 187(17), 188(17), 189(28), 203(11), 204(36), 227(10), 241(23), 242(94), 243(28), 254(23), 259(13), 260(47), 261(10), 283(11), 298(15), 301(15), 316(55.5), 317(13.6), 318(1.8). The mass of the molecule was determined by high-resolution mass spectrometry, and the value 316.277 ± 0.002 u was found. The value 16 for $C_{22}H_{36}O$ is 316.277 u. *NMR*: δ 0.91 (s, 9 H, *tert*-butyl), 0.94 (s, 9 H, *tert*-butyl), 1.00 (s, 3 H, methyl), 1.03 (s, 3 H, methyl), 1.21 (d, 3 H, methyl, $J = 7$ Hz), 1.35 (d, 1 H, hydroxylic, $J = 7$ Hz), 2.46 (s, 2 H, methylene), 2.65 (q, 1 H, methine, $J = 7$ Hz), 2.72 (q, 2 H, methylene, $J = 13$ Hz, $\Delta\nu_{AB} = 37$ Hz), 4.70 (d, 1 H, methine, $J = 7$ Hz), 6.76 (d, 1 H, aromatic, $J = 1$ Hz), 6.79 (d, 1 H, aromatic, $J = 1$ Hz). After addition of a small amount of water the coupling between the hydroxylic proton (δ 1.35) and the methine proton (δ 4.70) disappeared.

3-Chloro-1,2,2-trimethyl-4,6-dineopentylindan (III). 2,2,3-Trimethyl-5,7-dineopentyl-1-indanol (120 mg, 0.38 mmol) was dissolved in 5 ml of hexane, and 0.1 ml (1.3 mmol) of freshly distilled sulfinyl chloride was added. The mixture was stirred overnight at room temperature, and the reaction was then found to be complete according to GLC. The solvent and the excess of sulfinyl chloride were evaporated. The yield was 127 mg (100 %) of a crystalline product which was used directly in the next step.

1,2,2-Trimethyl-4,6-dineopentylindan (IV). 3-Chloro-1,2,2-trimethyl-4,6-dineopentylidane (127 mg, non-purified product from the above reaction) was dissolved in 3 ml of hexane and added to a solution of 26.6 mg (3.8 mmol) of lithium in 15 ml of liquid ammonia. The mixture was stirred for 2 h. The excess of lithium was then destroyed with water, and the mixture was neutralized with 6 M hydrochloric acid. The aqueous layer was extracted several times with hexane, and the combined hexane extracts were dried over magnesium sulfate. After evaporation of the solvent, the product was decolorized by adsorption chromatography (silica gel, hexane). The yield was 110 mg (96 %, computed on the indanol) of an oil which, according to GLC, was more than 98 % pure. *IR*: 2950vs, 2900w, 2860m, 2840w, 2710w, 1614w, 1588m, 1478s, 1465m, 1391m, 1285w, 1236s, 1200m, 1169w, 1115w, 1044w, 875s, 750m, 645w, 420m. *MS*: 29(10), 41(21), 43(16), 57(31), 71(9), 143(7), 157(9), 173(21), 187(29), 188(73), 189(11), 143(100), 244(53), 285(10), 300(20.1), 301(4.9), 302(0.6). *NMR*: δ 0.82 (s, 3 H, methyl), 0.91

(s, 18 H, *tert*-butyl), 1.12 (d, 3 H, methyl, $J = 7$ Hz), 1.16 (s, 3 H, methyl), 2.41 (s, 4 H, methylene), 2.60 (s, 2 H, methylene), 2.74 (q, 1 H, methine, $J = 7$ Hz), 6.60 (s, 2 H, aromatic).

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