

1,3,5-Trineopentylbenzene. VIII.* Restricted Rotation of Alkyl and Acyl Substituents

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The barriers to internal rotation of 2-acyl and 2-alkyl substituents in the 1,3,5-trineopentylbenzene system have been determined by means of computer simulation of ¹H NMR exchange-broadened spectra. An increase in barrier height with increasing branching at the C-2 carbon in the acyl or alkyl substituent has been found in both series. A discussion of the possible transition-state conformations for the slowly rotating substituent is presented, as well as the syntheses of the novel compounds utilized in this study.

In a previous investigation¹ of acylation reactions of 1,3,5-trineopentylbenzene under Friedel-Crafts conditions 2-acetyl, 2-propionyl-, 2-(2-methylpropanoyl)- and 2-benzoyl-1,3,5-trineopentylbenzene (Ia–c) and (Ie) were synthesized. The present work deals with the reduction of these compounds to form 2-ethyl-, 2-propyl-, 2-(2-methylpropyl)- and 2-benzyl-1,3,5-trineopentylbenzene (IIa–c) and (IIe), and with the syntheses of 2-(2,2-dimethylpropanoyl)-1,3,5-trineopentylbenzene (Id) and 1,2,3,5-tetraneopentylbenzene (IIId) by lithium-organic reactions. One main purpose of this investigation was the determination of the barriers to internal rotation (ΔG_c^\ddagger , the free energy of activation at the NMR coalescence temperature) for the restricted rotation of the

2-alkyl and 2-acyl groups of the above-mentioned compounds. A discussion of the heights of these barrier and of the conformations of the compounds is presented.

RESULTS AND DISCUSSION

A. Syntheses. In order to carry out a Wolff-Kishner reduction, several attempts were made to convert Ia to a hydrazone. Treatment of Ia with 85 % hydrazine hydrate under reflux in ethanol, butanol, or 1,2-ethanediol did not yield the desired product. The IR spectra of the worked-up products from the syntheses were identical with that of Ia.

A Huang-Minlon synthesis was carried out with Ia according to a method described by Nagata and Itazaki.² This method (designated A in their publication) was reported to be successful for sterically hindered 11-ketosteroids. A method described by Martinson³ for reduction of 1,3,5-tris(2,2-dimethylpropanoyl)benzene under Huang-Minlon conditions was also applied to Ia. Both methods were unsuccessful, and again the IR spectra of the worked-up products from the syntheses were identical with that of Ia.

Several attempts were made to carry out a Clemmensen reduction of Ia according to a method described by Martin,⁴ but the yield of 2-ethyl-1,3,5-trineopentylbenzene was never higher than 5 %. Preparation of amalgamated

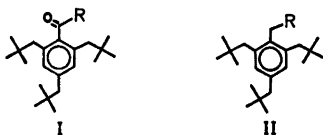


Fig. 1. a: R = methyl, b: R = ethyl, c: R = isopropyl, d: R = *tert*-butyl, e: R = phenyl.

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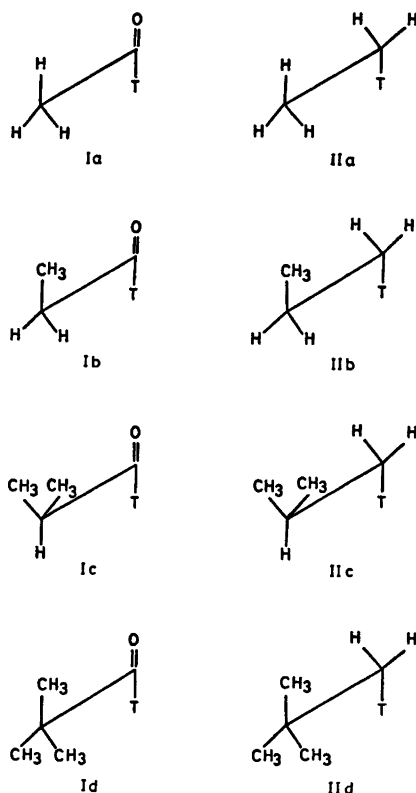


Fig. 2. Suggested transition state conformations of the 2-acyl and 2-alkyl groups of compounds Ia-d and IIa-d. T = 2,4,6-trineopentylphenyl.

zinc dust, as described by Caesar,⁵ prior to the Clemmensen reduction, made no improvement.

The preferred method for synthesis of IIa-c and IIe included reduction with lithium tetrahydridoaluminate in diethyl ether to the corresponding alcohols, conversion to chlorides by sulfinyl chloride in hexane and reduction with lithium in liquid ammonia to yield the alkyl derivatives. The overall yields for the three-step reactions were 76–84% after recrystallization. It was observed that 2-(1-chloroethyl)-1,3,5-trineopentylbenzene was unstable. On standing overnight at room temperature in hexane this compound was converted to 2,4,6-trineopentylstyrene (III). This product was synthesized by treating 2-(1-hydroxyethyl)-1,3,5-trineopentylbenzene with iodine and red phosphorus in cyclohexane. In order to avoid such elimination of hydrogen chloride, the chloroalkyl-1,3,5-trineopentylbenzenes were reduced

with lithium in liquid ammonia immediately after they had been synthesized.

When 2-chloromethyl-1,3,5-trineopentylbenzene was treated with *tert*-butyllithium in pentane, 1,2,3,5-tetraneopentylbenzene (IIId) was formed, in addition to 2-methyl-1,3,5-trineopentylbenzene and 1,2-bis(2,4,6-trineopentylphenyl)ethane. The yields of the three products were 21, 17 and 28%, respectively.

2-(2,2-Dimethylpropanoyl)-1,3,5-trineopentylbenzene (Id) was synthesized by treating 2-iodo-1,3,5-trineopentylbenzene with *tert*-butyllithium in pentane, under a nitrogen atmosphere, to form 2-lithio-1,3,5-trineopentylbenzene, and then adding freshly distilled 2,2-dimethylpropanoyl chloride. In this way Id was formed, in addition to 2-[1-(2,2-dimethylpropanoyloxy)-2,2-dimethylpropyl]-1,3,5-trineopentylbenzene (IV). The yields of Id and IV were 42 and 33%, respectively.

B. ¹H NMR spectra. It is well known that in unhindered aromatic ketones there is resonance energy stabilization due to overlap between the π electrons of the carbonyl group and the π electrons of the aromatic ring. This will lead to a preferred conformation in which the carbonyl group and the aromatic ring are coplanar. In sterically hindered aromatic ketones, deviations from coplanarity has been found.^{6,7}

In 2,2,3-trimethyl-5,7-dineopentyl-1-indanone⁸ the carbonyl group is locked, and the methylene protons of the 7-neopentyl group are in the deshielding zone of the carbonyl group appearing at 3.09 ppm.

In 2-(2,2-dimethylpropanoyl)-1,3,5-trineopentylbenzene (Id), on the other hand, the rotation about the sp^2-sp^3 carbon-carbon bond is sterically restricted at ordinary probe temperature and even at 190 °C. The methylene protons *ortho* to the 2,2-dimethylpropanoyl group appear as an AB pattern centered at 2.31 ppm. The upfield shift of these protons (0.78 ppm with

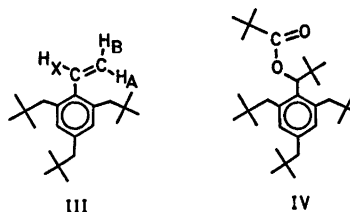


Fig. 3.

respect to the methylene protons of the 7-neopentyl group of 2,2,3-trimethyl-5,7-dineopentyl-1-indanone) shows that they are in the shielding zone of the carbonyl group. The oxygen atom and the *tert*-butyl group of the 2,2-dimethylpropanoyl group are thus situated on different sides of the plane of the aromatic ring.

In 2-(2-methylpropanoyl)-1,3,5-trineopentylbenzene (Ic) and 2-propanoyl-1,3,5-trineopentylbenzene (Ib), no frozen conformation could be detected at ordinary probe temperature, but the methylene protons *ortho* to the acyl groups appear at the same chemical shift (2.30 ppm), which is nearly equal to that found for the *ortho* methylene protons of Id. This indicates that the preferred conformations of these three compounds (Ib–d) must be very similar. The most strain-free conformation of Id is that in which the plane defined by the C-1–C-2 bond of the acyl group and the bond between the acyl group and the aromatic ring is perpendicular to the plane of the latter. This conformation is most probably also the preferred conformation of compounds Ib and Ic, a conclusion based on the chemical shifts mentioned above.

In 2-acetyl-1,3,5-trineopentylbenzene (Ia) the interaction between the acyl group and the *ortho* neopentyl groups is decreased (compared to Ib–d), the *ortho* methylene protons spend more time in the deshielding zone of the carbonyl group, and appear at 2.38 ppm, which is 0.07–0.08 ppm downfield from those of Ib–d. It can be mentioned that in the preferred conformation of 2,4,6-trimethylacetophenone, the dihedral angle between the phenyl and acetyl planes has been reported to be about 45° in the liquid phase.⁶ This value was obtained by matching the experimental and theoretical shielding values. In the same publication it was also reported that 2-methylacetophenone has a preferred conformation in which the acetyl group is coplanar with the phenyl group, with the oxygen atom close to the 2-methyl group. This shows that the "effective size" of the carbonyl oxygen is small compared to that of the methyl group of the acetyl group in their interactions with *ortho* alkyl substituents.

2-Benzoyl-1,3,5-trineopentylbenzene (Ie) shows sterically restricted rotation about the benzoyl-trineopentylphenyl sp^2-sp^2 carbon-

carbon bond at room temperature, and the methylene protons *ortho* to the benzoyl group appear as an AB pattern centered at 2.27 ppm. The small upfield shift of these protons (0.04 ppm compared to those of Id) may be explained by shielding effect of the adjacent phenyl group, and the preferred conformation of this compound is most probably that in which the plane defined by the carbon-oxygen bond and the carbonyl-trineopentylphenyl bond is perpendicular to the plane of the substituted phenyl group, as in Id.

In 1,3,5-trineopentylbenzene,³ the methylene protons appear at 2.43 ppm, which is also found for the *para* methylene protons of Ia–d. It is interesting to note that the *ortho* methylene protons which are situated in the shielding zone of the carbonyl group, as in Id, are shifted 0.12 ppm upfield (compared to 2.43 ppm), while *ortho* methylene protons which are situated in the deshielding zone of the carbonyl group, as in 2,2,3-trimethyl-5,7-dineopentyl-1-indanone, are shifted 0.66 ppm downfield (compared to 2.43 ppm).

In propylbenzene, isobutylbenzene and neopentylbenzene the terminal hydrogens appear at 0.90 ppm (CCl_4).⁹ The effects of the interaction between the 2-alkyl groups and the *ortho* neopentyl groups are unclear, but in the NMR spectra of compounds I Ib–d the terminal hydrogens of the 2-alkyl group appear at 1.03, 0.86 and 0.83 ppm, respectively. The terminal methyl groups thus seem to spend more time in the shielding zone of the aromatic ring with increasing methyl substitution at the β -carbon of the 2-alkyl group.

In the present study, 2-acyl and 2-alkyl derivatives of 1,3,5-trineopentylbenzene were found to give rise to AB patterns for the methylene protons in the 1- and 3-positions at sufficiently low temperatures. At the same temperatures the 5-methylene protons appeared as singlets. The restricted rotation of the acyl or alkyl substituent in the 2-position gives rise to the nonequivalence of the 1- and 3-methylene proton signals. The 1- and 3-methylene groups are enantiotopic due to the symmetry of the molecule, but the methylene protons of the 1- or 3-methylene groups are diastereotopic. These groups would thus appear as only one AB spectrum for each compound, which is consistent with the observed NMR spectral behavior.

Table 1. NMR parameters and ΔG_C^\ddagger values for the restricted rotation of acyl or alkyl groups in 2-substituted 1,3,5-trineopentylbenzenes.

Compound	t_C °C	J_{AB} Hz	$\Delta\nu_{AB}$ Hz	ΔG_C^\ddagger kJ/mol	Solvent
Ia ^a	-47	13.2	28.4	46.5	CHCl ₂ F
Ib ^a	-29	13.2	30.7	51.1	CHCl ₂ F
Ic ^a	-11	12.9	28.0	54.4	CHCl ₂ F
Id ^b	> +190	12.8	17.0	>96	CDBr ₃
Ie ^a	+24	13.4	22.7	63.2	CHCl ₂ F
IIa ^a	-56	13.2	46.9	43.6	CHCl ₂ F
IIb ^a	-53	12.9	44.7	44.0	CHCl ₂ F
IIc ^a	-15	13.3	55.1	52.3	CHCl ₂ F
IId ^b	+82	13.6	42.5	73.3	CDBr ₃
IIe ^a	-54	13.0	41.2	44.8	CHCl ₂ F

^a Determined at low temperature on 100 Hz sweep width (100 MHz). ^b Parameters obtained from 60 MHz spectra.

Complete line-shape investigations are expected to be difficult, especially for compounds Ib and IIb, because the AB spectra were overlapped by the methylene signals of the 5-neopentyl group. Therefore a complete line-shape analysis was only performed on one compound (II d), and for all the other compounds the free energy of activation (ΔG_C^\ddagger) was determined at some temperature near coalescence. The accuracy in such determinations of ΔG_C^\ddagger is estimated to be better than ± 1.3 kJ/mol.

The entropies of activation for the compounds studied are assumed to be close to zero. Support for this assumption is that the ΔS^\ddagger value for the restricted rotation of the 2-neopentyl group in IId was found to be -13.0 ± 8.8 J/(mol K) ($\Delta G^\ddagger_{298} = 73.7 \pm 0.8$ kJ/mol and $\Delta H^\ddagger = 69.9 \pm 2.9$ kJ/mol), and that ΔS^\ddagger values of zero within ± 13 J/(mol K) have been deduced from data for a large series of dihalo and/or methyl substituted 1,3,5-trineopentylbenzenes.¹⁰

In Table 1 we have summarized the ΔG^\ddagger values for the restricted rotation of an ethyl, propyl, 2-methylpropyl, neopentyl and a benzyl group, as well as for an acetyl, propanoyl, 2-methylpropanoyl and a benzoyl group, all as substituents in a nuclear position of 1,3,5-trineopentylbenzene. The rotational barrier of a 2,2-dimethylpropanoyl group could not be determined due to instrumental limitations. The lower limit of this barrier was estimated to be 96 kJ/mol.

In the following discussion of barrier heights, we assume that the initial state is represented by a conformation in which the plane defined by the C-1-C-2 bond of the 2-acyl or 2-alkyl group and the bond attaching the substituent to the trineopentylphenyl residue is perpendicular to the ring plane of the latter moiety, whereas the transition state is assumed to be the conformation in which the C-1-C-2 bond of these groups is in the plane of the aromatic ring.

Although the concept of size of alkyl or acyl groups is poorly defined in their steric interactions with the neopentyl groups, we found that the ΔG^\ddagger values increased in the series ethyl \approx propyl $<$ 2-methylpropyl $<$ 2,2-dimethylpropyl, and, similarly, acetyl $<$ propanoyl $<$ 2-methylpropanoyl \ll 2,2-dimethylpropanoyl (Table 1).

The barriers to internal rotation of the acyl groups were greater than those of the alkyl groups with the same number of carbon atoms. This may be surprising due to an expected resonance energy stabilization of the transition state in the presence of an acyl group, possibly of the order of 33 kJ/mol, as deduced from the magnitude of the rotational barrier in benzaldehyde (¹H NMR studies).¹¹ In addition, the greater bond angle of an acyl group (120°) compared to that of an alkyl group (109.5°) may give rise to smaller non-bonded interactions in the transition state between the alkyl substituent of the 2-acyl group and the 1- or 3-neopentyl group than between the substituent on the benzylic carbon of the 2-alkyl group (which has the same number of carbon atoms as the acyl group) and the 1- or 3-neopentyl group. On the contrary, in the rotational transition state of the acyl derivatives Ia-d, there may also be non-bonded interactions between the carbonyl group and an *ortho* neopentyl group. These interactions are assumed to be greater than those between the benzylic 2-methylene group and an *ortho* neopentyl group in the alkyl derivatives IIa-d.

The increased branching at the C-2 carbon atom in the 2-acyl and 2-alkyl substituents is thus covariant with an increase in the ΔG_C^\ddagger values in both series. Intuitively, the non-bonded interactions between the α -hydrogens of the acyl substituent and an *ortho* neopentyl group will be at a minimum in the transition

state of Ia if one of the α -hydrogens eclipses the carbonyl oxygen, and of Ib if the methyl group eclipses the carbonyl oxygen. Similarly, the interactions in the transition state would be most favorable in IIa and IIb, if the 2-alkyl group of IIa is in one of the staggered conformations, and if this group of IIb is in the staggered conformation in which the methyl group is between the α -methylene hydrogens (see Fig. 2).

Within the estimated limits of error the ΔG_C^\ddagger values for the internal rotation in IIa and IIb are equal, which is most probably explained by the very similar interactions in the transition state (as well as in the ground state). The difference in ΔG_C^\ddagger between Ia and IIa is the same as the difference between Ic and IIc within the limits of error (2.9 and 2.1 kJ/mol, respectively, see Table 1). The difference in ΔG_C^\ddagger between Ib and IIb is greater (7.1 kJ/mol), which may be caused by interactions between the eclipsing methyl group and carbonyl oxygen of the 2-acyl group in the transition state of Ib (see Fig. 2). The higher barrier for the 2-methylpropyl (compound IIc) and the 2-methylpropanoyl group (compound Ic) with respect to the corresponding groups in Ia, Ib, IIa and IIb may be explained in terms of their conformations in the transition state. If the methyl groups and the α -methylene hydrogens of the 2-methylpropyl group of IIc are in the eclipsed conformation, and if the methyl groups and the carbonyl oxygen of the 2-methylpropanoyl group of Ic are in the conformation in which the carbonyl oxygen is between the methyl groups (see Fig. 2) there will be interactions between the methine protons of the 2-alkyl and 2-acyl groups, respectively, and one of the *ortho* neopentyl groups in both the compounds. These interactions will be greater than the corresponding methylene-neopentyl interactions in the most favored conformations of the transition states of Ia, Ib, IIa and IIb. All other conformations of the 2-methylpropyl and 2-methylpropanoyl groups in the transition state will probably be less favorable due to the interactions between the methyl groups and the *ortho* neopentyl groups. Only in the 2,2-dimethylpropyl and 2,2-dimethylpropanoyl compounds (IIId and Id) does a methyl group necessarily have to approach an *ortho* neopentyl group, thus resulting in particularly high ΔG_C^\ddagger values. The difference in ΔG_C^\ddagger (> 22 kJ/mol)

between IIId and Id may be explained in the following way. In the transition state for the rotation of a 2-(2,2-dimethylpropyl) group of IIId, we assume that there are bond angle deformations (in the plane of the benzene ring) at the substituent-carrying aromatic carbon atom as well as at the 2-benzylic carbon atom to minimize the steric interactions between one *ortho* neopentyl group and the passing *tert*-butyl group. In Id a similar deformation would lead to an increased interaction between the carbonyl group and the other neopentyl group, which would raise the barrier of this compound.

The ΔG_C^\ddagger value for the rotation of the benzyl group (*i.e.* compound IIId) is close to that of an ethyl or a propyl group in the alkyl series, while the ΔG_C^\ddagger value of the benzoyl group (*i.e.* compound Ie) falls between that of a 2-methylpropanoyl and a 2,2-dimethylpropanoyl group in the acyl series. The difference in ΔG^\ddagger values between Ie and IIe is 18.4 kJ/mol. This great difference may be explained by the preferred coplanarity within the unsubstituted benzoyl group in the ground state of Ie, causing an increased steric interaction if the coplanarity still exists in the transition state, or an increased energy because of decreased conjugation, if the coplanarity is not retained in the transition state.

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 either a Varian A 60 or a Varian XL-100-15 spectrometer. Solutions, about 10 % by weight in carbon tetrachloride, were used for the purpose of identifying the compounds (Varian A 60), whereas solutions as dilute as possible (< 1 mol %) in the solvents dichlorofluoromethane (compounds Ia–c, Ie, IIa–c and IIe) and deuteriobromofrom (compounds Id and IIId) were used in the variable-temperature studies

(Varian XL-100-15). In the latter studies a small amount of dichloromethane was added as a standard of resolution. The chemical shifts are reported in ppm downfield from tetramethylsilane (probe temperature, 35 °C). The multiplicities of the peaks are reported as singlet (s), doublet (d), triplet (t), quartet (q) and multiplet (m). Temperatures were measured by means of a copper constantan thermocouple which was fixed near the radiofrequency coil. The accuracy in these values is believed to be at least ± 2 °C. The scale expansion and sweep rate for all spectra were 2 Hz/cm and 0.1 Hz/s, respectively.

In the line-shape studies of the 1- and 3-methylene proton signals of II_d, spectra were run at a few temperatures where exchange broadening was of importance, and were visually fitted to theoretical ones made by means of a computer program, described elsewhere.¹² A UNIVAC 1108 computer equipped with a Calcomp plotter was utilized in the calculations. The activation parameters were calculated from the Eyring equation¹³ and the reported errors were obtained by means of a least-squares treatment of the $\ln 1/\tau T$ vs. $1/T$ plot data.

For the other compounds, ΔG_C^\ddagger was calculated by means of the Eyring equation¹³ from iterated rate constants, which were found by visually fitting spectra, obtained near the temperature of coalescence, to theoretical ones made by means of the computer program.¹² The estimated errors in the determined rate constants for the slowly rotating 2-substituent give errors in ΔG_C^\ddagger of ± 0.8 kJ/mol, and the errors in the temperature (± 2 °C) give error in ΔG_C^\ddagger that are less than ± 0.5 kJ/mol. The total error is thus estimated to be less than ± 1.3 kJ/mol.

The mass spectra (MS) were determined (at the Department of Medical Biochemistry, University of Göteborg) on an AEI 902 mass spectrometer with the following conditions: electron energy 70 eV, accelerating voltage 8 kV and emission 100 μ A. The intensities of the peaks are reported in parentheses 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.

The melting points were determined on a Kofler micro hot stage.

Materials. 1,3,5-Trineopentylbenzene was prepared as described by Martinson and Márton.¹⁴ The acyl derivatives of 1,3,5-trineopentylbenzene were prepared as described by Dahlberg, Martinson and Olsson.¹ 2-Chloromethyl-1,3,5-trineopentylbenzene and 2-iodo-1,3,5-trineopentylbenzene were prepared as described by Olsson.¹⁵ All other chemicals were of reagent grade and were used without further purification unless stated otherwise.

2-(1-Hydroxyethyl)-1,3,5-trineopentylbenzene. In a two-necked flask equipped with a magnetic stirring bar, a dropping funnel and a reflux condenser, 6.9 g (182.0 mmol) of lithium tetrahydroaluminate was covered with 50 ml

of diethyl ether. 2-Acetyl-1,3,5-trineopentylbenzene (6.0 g, 18.2 mmol), dissolved in 20 ml of diethyl ether, was added dropwise and the stirred reaction mixture was then refluxed. At regular time intervals small aliquots were withdrawn and analysed by GLC. After 15 h, 2-(1-hydroxyethyl)-1,3,5-trineopentylbenzene had been formed in 99 % yield (GLC). The flask was then cooled with ice water, and 6.9 ml of water, 6.9 ml of 10 % sodium hydroxide solution and 20.7 ml of water were added slowly in that order. 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 diethyl ether, the product was purified by recrystallization from ethanol (water was cautiously added to the hot solution until turbidity appeared). The yield was 5.5 g (91 %) of white crystals. *M.p.* 97–98 °C. *IR:* 3559vs, 2955vs, 2905m, 2865s, 1605m, 1570m, 1478s, 1468w, 1450w, 1425w, 1394s, 1365vs, 1338m, 1280m, 1240s, 1232s, 1200s, 1165w, 1145m, 1129m, 1093s, 1074s, 1016m, 970w, 935w, 916w, 895w, 884s, 874w, 793m, 755w, 723m, 640w, 593m, 488w. *MS:* 29(38), 39(10), 41(54), 43(15), 55(6), 57(100), 73(5), 117(5), 130(6), 131(6), 147(6), 148(7), 149(7), 164(33), 220(15), 317(6), 332(0.016), 333(0.004). *NMR:* 0.92 (s, 9 H, *tert*-butyl), 0.96(s, 18 H, *tert*-butyl), 1.40(d, 3 H, methyl, *J* = 7 Hz), 1.48(s, 1 H, hydroxylic), 2.38(s, 2 H, methylene), 2.76(q, 4 H, methylene, *J* = 13.6 Hz, $\Delta\nu_{AB}$ = 13.0 Hz), 5.35(q, 1 H, methine, *J* = 7 Hz), 6.72(s, 2 H, aromatic).

2-(1-Chloroethyl)-1,3,5-trineopentylbenzene. In a flask equipped with a magnetic stirring bar and a dropping funnel, 3.0 g (9.0 mmol) of 2-(1-hydroxyethyl)-1,3,5-trineopentylbenzene was dissolved in 30 ml of hexane, and 2.0 ml (3.2 g, 27.0 mmol) of freshly distilled sulfinyl chloride was added dropwise. 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 3.2 g (100 %) of an oil which was used immediately in the next step. *NMR:* 0.93(s, 9 H, *tert*-butyl), 1.01(s, 18 H, *tert*-butyl), 1.82(d, 3 H, methyl, *J* = 7 Hz), 2.39(s, 2 H, methylene), 2.77(s, broad, 4 H, methylene), 5.57(q, 1 H, methine, *J* = 7 Hz), 6.80(s, 2 H, aromatic).

2-Ethyl-1,3,5-trineopentylbenzene (IIa). A two-necked flask equipped with a magnetic stirring bar, a dropping funnel and a gas inlet tube was cooled to -50 °C, and 50 ml of ammonia was condensed in the flask. Lithium (0.62 g, 90.0 mmol) was dissolved in the ammonia, and a solution of 3.2 g (9.0 mmol) of 2-(1-chloroethyl)-1,3,5-trineopentylbenzene in 10 ml of hexane was added dropwise. The reaction mixture was stirred at -50 °C, and after 2 h the excess of lithium was destroyed with water and the mixture was neutralised with 6 M hydrochloric acid. The aqueous layer was ex-

tracted 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 (alumina, hexane). Recrystallization from ethanol-water gave 2.6 g (91 %) of white crystals, which according to GLC were more than 99.9 % pure. *M.p.* 39–40 °C. *IR*: 2947vs, 2906m, 2870s, 2742w, 2712w, 1609w, 1575w, 1480vs, 1467w, 1435w, 1394s, 1366vs, 1330w, 1284w, 1235s, 1204m, 1163w, 1082w, 1058s, 1041w, 965w, 935w, 916w, 882vs, 794m, 756w, 733w, 651w, 626m, 560m, 553m, 475w. *MS*: 29(29), 41(25), 43(20), 57(67), 69(20), 71(18), 145(7), 147(20), 148(42), 203(31), 204(57), 205(9), 231(7), 259(100), 260(73), 261(13), 301(30), 302(9), 316(96.2), 317(24.5), 318(3.1). *NMR*: 0.92(s, 27 H, *tert*-butyl), 0.97(t, 3 H, methyl, *J* = 7 Hz), 2.36(s, 2 H, methylene), 2.53(s, 4 H, methylene), 2.74(q, 2 H, methylene, *J* = 7 Hz), 6.65(s, 2 H, aromatic).

2-Propyl-1,3,5-trineopentylbenzene (IIb) was prepared from 2-propanoyl-1,3,5-trineopentylbenzene according to the method used above for the three-step synthesis of 2-ethyl-1,3,5-trineopentylbenzene from 2-acetyl-1,3,5-trineopentylbenzene. 2-Propyl-1,3,5-trineopentylbenzene was separated from unreacted starting materials on a column of silica gel. With hexane only 2-propyl-1,3,5-trineopentylbenzene was eluted. The overall yield was 80 % of an oil. *IR*: 3044w, 2947vs, 2900m, 2962s, 2740w, 2712w, 1609m, 1575w, 1477vs, 1465s, 1425w, 1390s, 1377w, 1361vs, 1328w, 1275w, 1233s, 1200m, 1162w, 1092m, 1040w, 1030w, 973m, 933w, 913w, 881s, 818w, 804w, 748m, 645w, 567w, 551w, 412s. *MS*: 29(17), 41(31), 43(29), 55(10), 57(67), 69(38), 71(33), 120(10), 161(10), 162(27), 176(8), 203(8), 217(29), 218(42), 219(8), 272(65), 273(50), 274(10), 315(23), 330(100), 331(26.2), 332(3.51). *NMR*: 0.91(s, 27 H, *tert*-butyl), 1.03(t, 3 H, methyl, *J* = 7 Hz), 1.0–1.7(m, 2 H, methylene), 2.35(s, 2 H, methylene), 2.53(s, 4 H, methylene), 2.69(t, 2 H, methylene, *J* = 7 Hz), 6.64(s, 2 H, aromatic).

2-(2-Methylpropyl)-1,3,5-trineopentylbenzene (IIc) was prepared from 2-(2-methylpropanoyl)-1,3,5-trineopentylbenzene according to the method used above for the three-step synthesis of 2-ethyl-1,3,5-trineopentylbenzene from 2-acetyl-1,3,5-trineopentylbenzene. 2-(2-Methylpropyl)-1,3,5-trineopentylbenzene was purified as described for 2-propyl-1,3,5-trineopentylbenzene. After recrystallization the overall yield was 76 % of white crystals. *M.p.* 36–37 °C. *IR*: 2964vs, 2908m, 2866s, 2718w, 1609m, 1574w, 1478vs, 1467m, 1426w, 1391s, 1383w, 1364vs, 1332w, 1318w, 1286w, 1280w, 1236s, 1202m, 1163m, 1100m, 1040w, 1030w, 933w, 920w, 913w, 883s, 876s, 854w, 872w, 799m, 749s, 734w, 698w, 648w, 615w, 566w, 551w, 484w, 422w. *MS*: 29(25), 41(43), 43(48), 57(100), 69(50), 71(64), 119(8), 120(9), 133(16), 159(10), 173(11), 175(11), 176(27), 189(18), 231(30), 232(39), 245(43), 246(9), 287(75), 288(50),

289(10), 301(81), 302(20), 329(30), 330(9), 344(84.8), 345(23.6), 346(3.2). *NMR*: 0.86(d, 6 H, methyl, *J* = 7 Hz), 0.92(s, 27 H, *tert*-butyl), 1.1–2.0(m, 1 H, methine), 2.36(s, 2 H, methylene), 2.55 (s, 4 H, methylene), 2.61(d, 2 H, methylene, *J* = 7 Hz), 6.67(s, 2 H, aromatic).

2-Benzyl-1,3,5-trineopentylbenzene (IIe) was prepared from 2-benzoyl-1,3,5-trineopentylbenzene according to the method used for the three-step synthesis of 2-ethyl-1,3,5-trineopentylbenzene from 2-acetyl-1,3,5-trineopentylbenzene. 2-Benzyl-1,3,5-trineopentylbenzene was purified as described for 2-propyl-1,3,5-trineopentylbenzene. After recrystallization the overall yield was 79 % of white crystals. *M.p.* 80–81 °C. *IR*: 3080w, 3063w, 3025w, 2960vs, 2905m, 2865s, 2748w, 2718w, 1942w, 1804w, 1604s, 1575m, 1495s, 1480s, 1463s, 1451s, 1425m, 1391s, 1362vs, 1330m, 1280m, 1235s, 1202m, 1191w, 1166w, 1075m, 1032s, 1002w, 922m, 899w, 873s, 823w, 749w, 724vs, 697s, 653w, 637w, 611m, 548w, 460s. *MS*: 29(16), 41(27), 43(38), 57(68), 71(100), 91(19), 193(9), 209(9), 210(51), 211(9), 266(51), 267(11), 321(14), 322(32), 363(10), 378(54.9), 379(17.0), 380(2.5). *NMR*: 0.93(s, 27 H, *tert*-butyl), 2.41(s, 2 H, methylene), 2.45(s, 4 H, methylene), 4.11(s, 2 H, methylene), 6.73(s, 2 H, aromatic), 6.8–7.3(m, 5 H, aromatic).

1,2,3,5-Tetraneopentylbenzene (IIId). A solution of 60 mmol of *tert*-butyllithium in 30 ml of pentane, under an argon atmosphere, was cooled with ice and 1.0 g (3.0 mmol) of 2-chloromethyl-1,3,5-trineopentylbenzene was added in small portions. The reaction mixture was then stirred at room temperature. A GLC analysis of the mixture after 2 h showed that all 2-chloromethyl-1,3,5-trineopentylbenzene had been consumed and that three products had been formed. The excess of *tert*-butyllithium was destroyed with water. The aqueous layer was neutralized with 6 M hydrochloric acid and extracted several times with pentane. The combined pentane extracts were dried over magnesium sulfate. The products were separated on a column of silica gel with pentane as eluent. The three products were identified as 1,2-bis(2,4,6-trineopentylphenyl)ethane, 2-methyl-1,3,5-trineopentylbenzene and 1,2,3,5-tetraneopentylbenzene. The yields of the compounds were 0.25 g (28 %), 0.15 g (17 %) and 0.22 g (21 %), respectively, of white crystals.

1,2-Bis(2,4,6-trineopentylphenyl)ethane: *M.p.* 213–214 °C. *IR*: 2960vs, 2908m, 2868m, 2748w, 2715w, 1608m, 1572w, 1477vs, 1465w, 1435w, 1392s, 1365vs, 1330w, 1280w, 1236s, 1202m, 1160m, 1125w, 930w, 913w, 881s, 791m, 751w, 682m broad, 633w, 557w, 532w, 445m broad. *MS*: 29(17), 41(7), 43(13), 57(29), 69(8), 71(14), 245(12), 301(100), 302(14), 602(8.6), 603(4.2), 604(1.0). *NMR*: The chemical-shift values were identical with those previously reported.¹⁸ 2-Methyl-1,3,5-trineopentylbenzene: The physical properties were identical with those previously reported.¹⁵

1,2,3,5-Tetraneopentylbenzene: *M.p.* 78–79 °C. *IR*: 2958vs, 2904m, 2862s, 2742w, 2712w, 1606w, 1570w, 1475vs, 1424w, 1392s, 1364vs, 1316w, 1282w, 1234s, 1204m, 1165w, 1153w, 1031w, 935w, 915w, 882w, 876m, 853w, 813m, 751w, 742w, 679s, 643w, 440vs. *MS*: 29(14), 41(22), 43(22), 57(64), 69(17), 71(28), 133(8), 189(11), 190(8), 245(39), 246(17), 301(100), 302(39), 343(9), 358(16.1), 359(4.6), 360(0.6). *NMR*: 0.83(s, 9 H, *tert*-butyl), 0.86(s, 18 H, *tert*-butyl) 0.92(s, 9 H, *tert*-butyl), 2.37(s, 2 H, methylene), 2.64(q, 4 H, methylene, $J=13.6$ Hz, $\Delta\nu_{AB}=42.5$ Hz), 2.78(s, 2 H, methylene), 6.68(s, 2 H, aromatic).

2-(2,2-Dimethylpropanoyl)-1,3,5-trineopentylbenzene (*Id*). To a solution of 2 mmol of *tert*-butyllithium in 10 ml of pentane, under a nitrogen atmosphere, 0.2 g (0.5 mmol) of 2-iodo-1,3,5-trineopentylbenzene was added. The mixture was stirred for 10 min at room temperature and then cooled with ice before 1 ml (0.98 g, 8.1 mmol) of freshly distilled 2,2-dimethylpropanoyl chloride was added dropwise. After 1 h the excess of acyl chloride was destroyed with water. The aqueous layer was extracted several times with hexane, and the combined organic layers were dried over magnesium sulfate. A GLC analysis showed that 1,3,5-trineopentylbenzene and two other products had been formed. The products were separated on a column of silica gel. With hexane 1,3,5-trineopentylbenzene and unreacted 2-iodo-1,3,5-trineopentylbenzene were eluted. The remaining two products were separated by a gradient elution with hexane and benzene. One of the two products was identified as 2-(2,2-dimethylpropanoyl)-1,3,5-trineopentylbenzene and the other as 2-[1-(2,2-dimethylpropanoyloxy)-2,2-dimethylpropyl]-1,3,5-trineopentylbenzene. The yields were 75 mg (42 %) and 73 mg (33 %) respectively, of crystalline products.

2-(2,2-Dimethylpropanoyl)-1,3,5-trineopentylbenzene: *IR*: 2955vs, 2863m, 1695vs, 1608m, 1568w, 1480vs, 1469w, 1445w, 1394m, 1368vs, 1289w, 1237s, 1202m, 1132m, 1095w, 1034w, 955vs, 833m, 870s, 791m, 752w, 643w, 580w. *MS*: 29(19), 41(26), 43(29), 57(67), 71(17), 83(25), 85(17), 202(5), 259(6), 260(10), 315(100), 316(67), 357(25), 358(9), 372(1.1), 373(0.3), 374(0.05). The mass of the molecule was determined by high-resolution mass spectrometry, and the value 372.339 ± 0.002 u was found. The value 17 for $C_{26}H_{44}O$ is 372.339 u. *NMR*: 0.84(s, 18 H, *tert*-butyl), 0.93(s, 9 H, *tert*-butyl), 1.05(s, 9 H, *tert*-butyl), 2.31(q, 4 H, methylene, $J=13$ Hz, $\Delta\nu_{AB}=14$ Hz), 2.43(s, 2 H, methylene), 6.76(s, 2 H, aromatic).

2-[1-(2,2-Dimethylpropanoyloxy)-2,2-dimethylpropyl]-1,3,5-trineopentylbenzene (*IV*): *IR*: 2965vs, 2920w, 2880m, 1727vs, 1607m, 1565w, 1480vs, 1469m, 1397s, 1365s, 1283s, 1240s, 1205m, 1147vs, 1140vs, 1125m, 1045w, 1033s, 980m, 957s, 935w, 918w, 912w, 885m, 831m, 784w, 769w, 755w, 685w, 651w, 575m. *MS*: 29(9), 41(18), 43(18), 57(100), 71(15), 85(45),

299(9), 315(18), 316(5), 317(29), 318(7), 401(45), 458(4.36), 459(1.5), 460(0.3). The mass of the molecule was determined by high-resolution mass spectrometry and the value 458.413 ± 0.002 u. The value 17 for $C_{31}H_{54}O_2$ is 458.412 u. *NMR*: 0.71(s, 9 H, *tert*-butyl), 0.87(s, 9 H, *tert*-butyl), 0.92(s, 18 H, *tert*-butyl), 1.33(s, 9 H, *tert*-butyl), 2.42(s, 2 H, methylene), 2.80(q, 2 H, methylene, $J=13.5$ Hz, $\Delta\nu_{AB}=49.5$ Hz), 2.93(q, 2 H, methylene, $J=13.5$ Hz, $\Delta\nu_{AB}=52.0$ Hz), 6.67(d, 1 H, aromatic, $J=2$ Hz), 6.82(s, 1 H, methine), 6.91(d, 1 H, aromatic, $J=2$ Hz).

Clemmensen reduction of 2-acetyl-1,3,5-trineopentylbenzene. In a three-necked flask equipped with a mechanical stirrer, a reflux condenser and a dropping funnel, 5.5 g (84.1 mmol) of granulated zinc and 0.5 g (1.8 mmol) of mercury(II) chloride were covered with 10 ml of 6 M hydrochloric acid. The mixture was refluxed for 5 min. The aqueous solution was then decanted, and 20 ml of 6 M hydrochloric acid and 2 ml of acetic acid were added. The stirred mixture was then refluxed and a solution of 3.0 g (9.0 mmol) of 2-acetyl-1,3,5-trineopentylbenzene in 10 ml of toluene was added. At the end of each of the first 10 h of the reaction time, 1 ml of conc. hydrochloric acid was added. After 46 h the flask was cooled and the organic and aqueous layers were separated. The aqueous layer was extracted with toluene and the combined organic layers were dried over magnesium sulfate. The solvent was evaporated and 2-ethyl-1,3,5-trineopentylbenzene was separated from unreacted 2-acetyl-1,3,5-trineopentylbenzene on a column of silica gel. With hexane only 2-ethyl-1,3,5-trineopentylbenzene was eluted. Recrystallization of this compound from ethanol-water gave 0.15 g (5 %) of white crystals.

2,4,6-Trineopentylstyrene (*III*). Purified 18 red phosphorus (0.5 g, 4.0 mmol P) was covered with a solution of 0.2 g (0.6 mmol) of 2-(1-hydroxyethyl)-1,3,5-trineopentylbenzene in 50 ml of cyclohexane. The mixture was refluxed, and 0.5 g (2.0 mmol) of iodine dissolved in cyclohexane was added. After the addition of the iodine the reaction mixture was refluxed for 14 h, and the reaction was then found to be complete according to GLC. The flask was cooled, and a solution of 1 g of sodium sulfite in 10 ml of water was added. The organic and aqueous layers were separated and the aqueous layer was extracted with cyclohexane. The combined organic layers were dried over magnesium sulfate. After evaporation of the solvent the product was decolorized by adsorption chromatography (alumina, hexane). The yield was 0.16 g (85 %) of an oily product which was identified as 2,4,6-trineopentylstyrene. *IR*: 3080m, 3050w, 2950vs, 2905m, 2862s, 2740w, 2712w, 1847w, 1631w, 1605m, 1563w, 1477vs, 1465m, 1425w, 1407w, 1392s, 1362vs, 1330w, 1228w, 1234s, 1200m, 1162w, 1035w, 995m, 920s, 879m, 792w, 749w, 733w, 675w, 618w, 541w. *MS*: 26(6), 27(5), 29(19), 39(9), 41(37),

43(27), 55(9), 56(7), 57(100), 71(29), 128(10), 129(13), 131(16), 143(9), 144(7), 145(46), 146(49), 187(25), 201(59), 202(51), 203(9), 257(68), 258(32), 299(19), 314(44.6), 315(11.3), 316(1.4). The mass of the molecule was determined by high-resolution mass spectrometry and the value 314.296 ± 0.003 u was found. The value¹⁷ for $C_{23}H_{38}$ is 314.297 u. *NMR*: 0.88(s, 18 H, *tert*-butyl), 0.93(s, 9 H, *tert*-butyl), 2.42(s, 2 H, methylene), 2.62(s, 4 H, methylene), 5.02(q, H_A , methylene), 5.45(q, H_B , methylene), 6.74(q, H_X , methine), 6.76(s, 2 H, aromatic). $J_{AX} = 18$ Hz, $J_{BX} = 11$ Hz, $J_{AB} = 3$ Hz.

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