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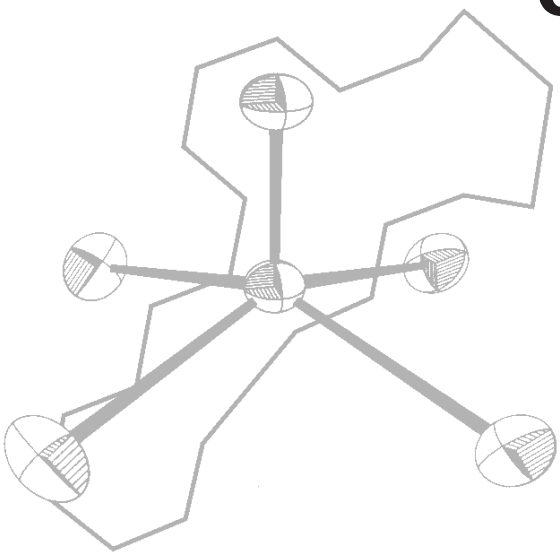

Volume 50, 1997

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Aust. J. Chem., 1997, **50**, 149–152

Synthesis of Diastereoisomeric 1,2,3-Triphenylindans

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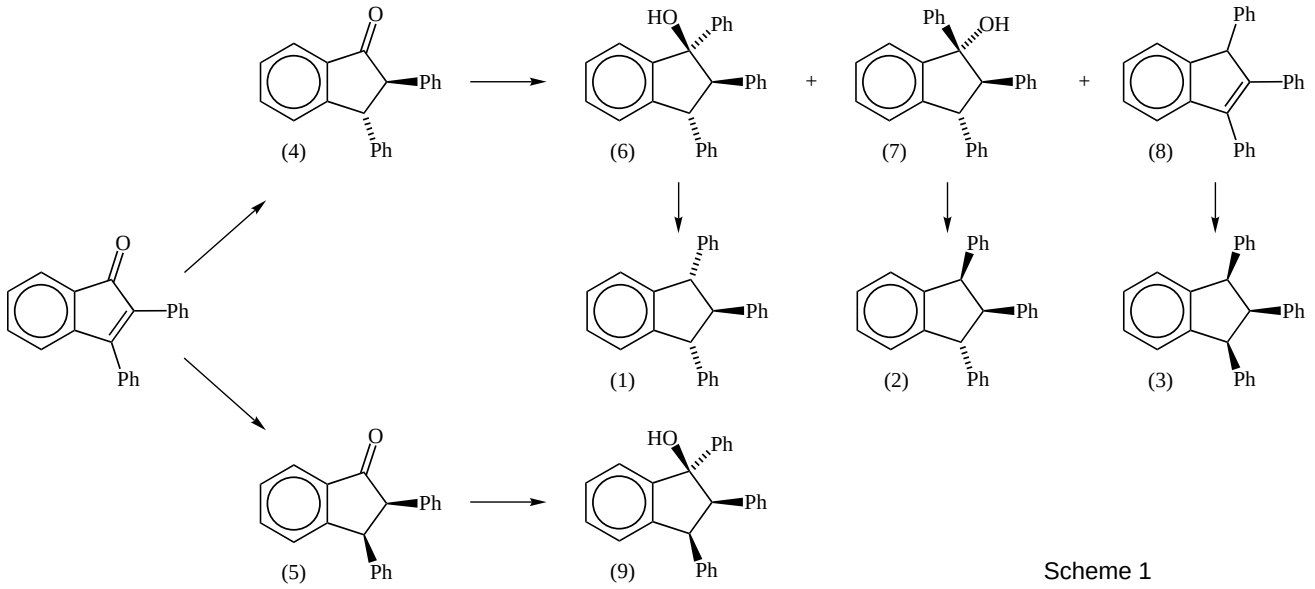
The stereoisomers of 1,2,3-triphenylindans were synthesized via 1,2,3-triphenylindan-1-ols. The configurational assignments of all the compounds were made by chemical and spectroscopic methods. An unexpected compound was isolated as a by-product of the Grignard reactions and was identified as *r*-2-hydroxy-2,*t*-3-diphenylindan-1-one.

Introduction

There is little information in the literature[1] on the stereochemical effects exerted by substituents and manifested by the chemical shift of carbon atoms belonging to the indan five-membered ring in ^{13}C n.m.r. spectroscopy. In our view, a suitable system to initiate such studies is provided by the three diastereoisomers of 1,2,3-triphenylindan (Scheme 1).

In 1932, Kohler and Mydans[2] reported that treatment of $Ph_2C{=}CPhCOPh$ with hydriodic acid and red phosphorus rendered one of the three possible stereoisomers of 1,2,3-triphenylindan, with a melting point of 154°. Years later, on studying sigmatropic rearrangements in 1,2,3-triphenylindene, Miller and Boyer[3] obtained another of the stereoisomers, with a melting point of 146°. They tentatively assigned the *trans*,*trans* configuration to this compound on the basis of ^{1}H n.m.r. data, which indicated its symmetry, and on comparison of the chemical shifts of the hydrogen atoms of the five-membered ring to those observed for *cis*- and *trans*-1,2-diphenylindan.[3] Lastly, Marcuzzi and Melloni[4] described the preparation of all three diastereoisomeric indans, whose melting points were 154, 143 and 125°. Configurational assignments of the isomeric indans were made by ^{1}H n.m.r. spectroscopy, bearing in mind not only the protective effect exerted by a phenyl group on β-hydrogen atoms, but also the value of the vicinal coupling constants ($J_{1,2}$ or $J_{2,3}$). Thus, the compound with a melting point of 154° was assigned the *trans*,*cis* configuration ($J_{1,2}$ 10·1, $J_{2,3}$ 8·2 Hz), the one with a melting point of 143° was assigned as *cis*,*cis* ($J_{1,2} = J_{2,3} = 8{\cdot}2$ Hz) and the one with a melting point of 125° was assigned as *trans*,*trans*



Scheme 1

Manuscript received 5 December 1995 10.1071/CH95266 0004-9425/97/020149$05.00

($J_{1,2} = J_{2,3} = 10 \cdot 2$ Hz). On assigning these configurations, the above authors disagreed with Miller and Boyers' report[3] with regards to the configuration of the stereoisomer with the melting point of 146[3] or 143°.[4]

The present work affords a new synthesis for the three stereoisomeric indans (Scheme 1) and records their respective ^{13}C n.m.r. data. However, it should be pointed out that although the ^{1}H n.m.r. spectra recorded for the synthesized products and their configurational assignments agree substantially with previously reported data,[4] melting point values were found to be interchanged.

Synthesis

Catalytic hydrogenation of 2,3-diphenylinden-1-one performed under various conditions rendered *trans*-2,3-diphenylindan-1-one (4) and *cis*-2,3-diphenylindan-1-one (5), whose configurations were assigned by comparison with data from the literature.[5,6]

Treatment of *trans*-2,3-diphenylindan-1-one (4) with PhMgBr in tetrahydrofuran led to a mixture of the indanols (6) and (7), together with the indene (8). These compounds were separated by preparative layer chromatography (p.l.c.). The configurational assignment of C 2 and C 3 in the indanols (6) and (7) was made by considering the configuration of the initial indanone and the coupling constant of the hydrogen atoms on C 2 and C 3 ($J_{2,3}$ 10 Hz for both indanols). In turn, the C 1/C 2 configuration was established by the symmetry presented by the hydrogenolysis products which formed with configuration retention [Raney nickel (W-2)].[7] The indanol (6) produced the *trans*, *trans* stereoisomer (m.p. 125°) and the indanol (7) produced the *trans*,*cis* stereoisomer (m.p. 147°).

Lastly, the *cis*,*cis* hydrocarbon (m.p. 154°) was prepared by catalytic hydrogenation of the indene (8) by employing 10% Pd/C. It was found that when 5% Pd/C as catalyst was used, the indan (2) (*trans*,*cis*) was also obtained.

Treatment of *cis*-2,3-diphenylindan-1-one (5) with PhMgBr rendered the indanol (9), whose configuration was assigned as for the indanols (6) and (7). Hydrogenolysis with Raney nickel (W-2) produced the indan (2) (*trans*,*cis*).

Besides the indanols (6), (7) and (9), together with the indene (8), the reaction of PhMgBr with the indanones (4) and (5) led to the unexpected compound (10). This last compound was likewise obtained when other Grignard reagents such as CH_3MgI were allowed to react with the indanone (4) in tetrahydrofuran. Spectroscopic data, including i.r., mass spectrometry, and ^{1}H and ^{13}C n.m.r., suggested a hydroxy phenylindanone structure for compound (10) (Fig. 1). Its melting point and chemical shifts in the ^{13}C n.m.r. spectrum were identical to those of the compound described by Kirrstetter and Vagt[6] as 2-hydroxy-2,3-diphenylindan-1-one and by Monahan *et al.*[8] as 3-hydroxy-2,3-diphenylindan-1-one. In order to assign the definitive structure of (10), COLOC n.m.r. experiments, setting the J_{CH} value at 10 and 5 Hz, were conducted. Both sets of spectroscopic data failed to locate the position of the aliphatic hydrogen. No correlations $^{3}J_{CH}$ were found, either between the aromatic H 4 and the aliphatic carbon signals, or between the aliphatic hydrogens and C 4.

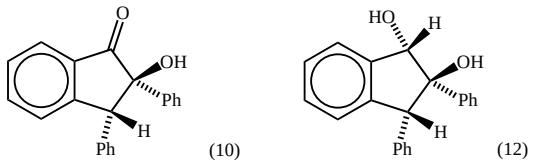
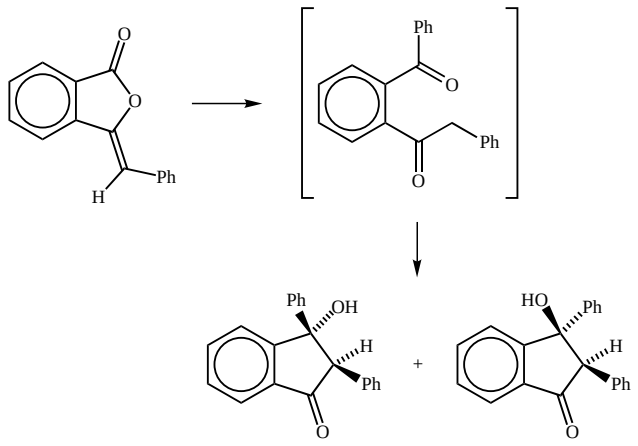


Fig. 1. Reduction product (12) obtained by treatment of (10) with $NaBH_4$.

An unequivocal synthesis of 3-hydroxy-2,3-diphenylindan-1-one was carried out starting from benzalphthalide and PhMgBr[9] (Scheme 2). Thus, the two possible stereoisomers [(11a) and (11b)] of 3-hydroxy-2,3-diphenylindan-1-one were obtained. Configuration assignment was made bearing in mind that (11b) spontaneously dehydrates to 2,3-diphenylinden-1-one. The physical and spectroscopic data for the stereoisomers (11) failed to agree with those of compound (10).



Scheme 2 (11a) (11b)

Furthermore, when compound (10) was reduced with $NaBH_4$ in methanol the diol (12) (Fig. 1) was obtained. The ^{1}H n.m.r. spectrum exhibits two singlets which correspond to the uncoupled protons of the five-membered ring, so that the 2-hydroxy-2,3-diphenylindan-1-one structure[6] is proposed for (10). The difficulty to dehydrate compound (10) allowed it to be assigned the *r*-2-hydroxy-2,*t*-3-diphenylindan-1-one configuration (Fig. 1).

On the other hand, the configuration of the methine protons in compound (12) was determined by nuclear Overhauser effect (n.O.e.) experiments. Irradiation of H 1 produced an enhancement in the intensity of H 3 and vice versa, a result which suggests that these two protons are aligned on the same side of the five-membered ring in the indan system. The configuration

at C 2 was determined to be the same as that of (10) on the bases of the close similarities of their ^{1}H n.m.r. spectra coupled with the fact that compound (12) resisted the dehydration reaction.

Nuclear Magnetic Resonance

Table 1 shows the chemical shifts of the carbon atoms belonging to the five-membered ring in compounds (6), (7) and (9), as well as those in the indans (1), (2) and (3).

Table 1. Selected ^{13}C n.m.r. chemical shifts (ppm) of the aliphatic carbons of some indanols and indans

Full spectra are given in the Experimental section

Cpd	C 1	C 2	C 3	Cpd	C 1	C 2	C 3
(1)	58·4	67·6	58·4	(6)	84·8	69·9	52·8
(2)	54·1	62·1	56·1	(7)	87·2	71·1	51·9
(3)	56·2	62·8	56·2	(9)	85·8	67·1	53·7

In isomers (1) (*trans*,*trans*) and (3) (*cis*,*cis*), the ^{13}C n.m.r. signals for each pair of diastereotopic atoms disclose a significant difference in shielding [C 1 and C 3 at 56·2 ppm and C 2 at 62·8 ppm for the indan (3) versus C 1 and C 3 at 58·4 ppm, and C 2 at 67·6 ppm for the indan (1)], which had already been observed for *cis*- and *trans*-1,2-disubstituted indans.[1] The spectrum for compound (2) presents three distinct signals (54·1, 56·1 and 62·1 ppm). Recalling previous data,[1] the 54·1 ppm chemical shift was assigned to the dibenzylic carbon located in the *cis* position with regards to the C 2 substituent, that of 56·1 ppm to the carbon in the *trans* position with regards to the C 2 substituent and that of 62·1 ppm to C 2 itself. However, values for C 1 and C 3 are lower than those corresponding to compounds (1) and (3). These shifts to higher fields may be explained by taking into account the extreme conformations for each indan (Fig. 2). In compounds (1) and (3) there seems to be a preferential conformation (eq, eq, eq and eq, ax, eq respectively), whereas in compound (2) the two conformations (ax, ax, eq and eq, eq, ax) are expected to have similar weight since they only differ in the spatial location of the phenyl substituent at C 2, which is axial in conformation (2b) and equatorial in conformation (2a), with the former conformer lacking any 1,3-diaxial interactions. A phenyl substituent at one of the dibenzylic carbon atoms would therefore be invariably found in a pseudo-axial position, thus exerting a shielding γ-*gauche* effect on the other dibenzylic carbon atom.

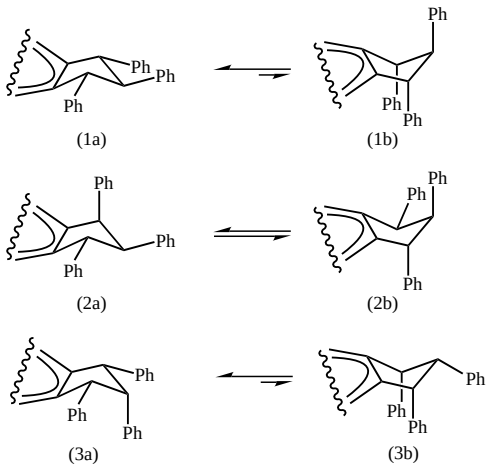


Fig. 2. Extreme conformations for indans (1)–(3).

Experimental

The ^{1}H and ^{13}C n.m.r. spectra were recorded with a Bruker AC-200 spectrometer by employing Me_4Si (δ 0·00) as an internal standard. Two-dimensional spectra were recorded on a Bruker A-300 Fourier-transform instrument by using standard Bruker software. Mass spectra were obtained by direct injection of the samples as chloroform solutions into a Shimadzu GCQP 1·000 mass spectrometer operating at an ionizing electron energy of 20 eV. Elemental analyses were carried out in our laboratories with a Coleman Analyzer. Melting points (uncorrected) were obtained with a Thomas Hoover apparatus. Preparative thin-layer chromatography (p.l.c.) was performed on 20 by 20 cm glass plates coated with silica gel 60 F-254 (0·50 mm).

trans-*2,3-Diphenylindan-1-one (4)*

This ketone was obtained by hydrogenation of 2,3-diphenylinden-1-one (3·0 g) with PtO_2 (100 mg) in KOH solution (1%) in ethyl acetate/ethanol (1 : 2, 200 ml) at 40 psi (1 psi = 6·9 kPa) during 1·5 h. Yield 70%, m.p. 98–99° (ethanol) (lit.[5] 98–100°).

cis-*2,3-Diphenylindan-1-one (5)*

This ketone was obtained from 2,3-diphenylinden-1-one (2·0 g) by hydrogenation with PtO_2 (200 mg) in ethyl acetate (200 ml) at 40 psi during 40 min. Yield 62%, m.p. 138–140° (methanol) (lit.[5] 138°).

Reaction of trans-*2,3-Diphenylindan-1-one (4) with PhMgBr*

The indanone (4) (2·0 g, 7·04 mmol) in anhydrous tetrahydrofuran (9 ml) was added dropwise to an excess of phenylmagnesium bromide (35 mmol). After the addition was complete, the mixture was stirred for 8 h at room temperature. The reaction mixture was poured into NH_4Cl/H_2O and extracted with chloroform; the organic layer was dried with $MgSO_4$ (anhydrous) and evaporated in vacuum. The residue was purified by p.l.c. (chloroform). Compound (7) (640 mg) was isolated from the upper band, compound (6) (540 mg) from the medial band and compound (10) (430 mg) from the lower band.

*1,*c-*2,*t-*3-Triphenylindan-*r-*1-ol (6).* Yield 21%, m.p. 120–122° (ethanol) (Found: C, 89·7; H, 6·2. $C_{27}H_{22}O$ requires C, 89·6; H, 6·1%). ^{1}H n.m.r. δ ($CDCl_3$) 2·10, br s, 1H, OH; 4·00, d, $J_{2,3}$ 9·0 Hz, 1H, H 2; 4·15, d, $J_{2,3}$ 9·0 Hz, 1H, H 3; 7·15–7·60, m, 19H, Ar. ^{13}C n.m.r. δ 52·8, 69·9, 84·8, 124·7, 125·1, 126·4, 126·6, 126·8, 127·1, 127·6, 127·8, 128·0, 128·3, 128·7, 129·1, 129·4, 129·5, 135·2, 141·9, 144·5, 146·9.

*1,*t-*2,*c-*3-Triphenylindan-*r-*1-ol (7).* Yield 26%, m.p. 146–148° (ethanol) (Found: C, 89·6; H, 6·0. $C_{27}H_{22}O$ requires C, 89·6; H, 6·1%). ^{1}H n.m.r. δ ($CDCl_3$) 3·05, br s, 1H, OH; 4·25, d, $J_{2,3}$ 9·0 Hz, 1H, H 2; 4·85, d, $J_{2,3}$ 9·0 Hz, 1H, H 3; 6·95–7·15, m, 19H, Ar. ^{13}C n.m.r. δ 51·9, 71·1, 87·2, 123·7, 124·8, 126·3, 126·9, 127·3, 127·7, 128·0, 128·3, 128·6, 129·1, 136·8, 141·5, 142·4, 145·2, 147·0.

r-*2-Hydroxy-2,*t-*3-diphenylindan-1-one (10).* Yield 21%, m.p. 126–128°. I.r. 3425 (OH), 1700 cm^{-1} (CO). ^{1}H n.m.r. δ ($CDCl_3$) 3·53, s, 1H, OH; 4·85, s, 1H, H 3; 6·78–7·05, m, 10H, Ar; 7·31, d, J_{ortho} 7·6 Hz, 1H, H 4; 7·51, t, J_{ortho} 7·6 Hz, 1H,

H 6; 7·65, t, J_{ortho} 7·6 Hz, 1H, H 5; 7·95, d, J_{ortho} 7·6 Hz, 1H, H 7. ^{13}C n.m.r. δ 59·2, 86·6, 123·9, 126·2, 126·8, 127·1, 127·4, 129·1, 129·4, 129·6, 135·5, 135·7, 137·5, 140·4, 146·8, 153·4, 207·0. Mass spectrum (20 eV) m/z 300 (100%), 282 (9·2), 195 (92·8), 105 (22·6), 94 (5·6).

When the reaction mixture was poured into acetic acid/water solution the major products, purified by p.l.c. (chloroform), were compound (8) (1·3 g), yield 51% (upper band), and compound (10) (220 mg), yield 11% (lower band).

1,2,3-Triphenylindene (8). M.p. 125–127° (ethanol) [lit.[2] 135° (methanol)]. ^{1}H n.m.r. δ ($CDCl_3$) 5·30, s, 1H, H 3; 7·25–7·75, m, 19H, Ar.

Reaction of cis-2,3-Diphenylindan-1-one (5) with PhMgBr

The ketone (5) was obtained by a procedure similar to that used for the indanone (4). The reaction mixture when purified by p.l.c. (chloroform) gave the indanol (9) (1 g, yield 57%) (upper band) and the hydroxy ketone (10) (340 mg, yield 21%) (lower band).

*1,*c*-2,*c*-3-Triphenylindan-*r*-1-ol (9).* M.p. 108–110° (ethanol) (Found: C, 89·5; H, 6·2. $C_{27}H_{22}O$ requires C, 89·6; H, 6·1%). ^{1}H n.m.r. δ ($CDCl_3$) 2·55, s, 1H, OH; 4·20, d, $J_{2,3}$ 7·7 Hz, 1H, H 2; 5·90, d, $J_{2,3}$ 7·7 Hz, 1H, H 3; 6·75–6·95, m, 2H, Ar; 7·00–7·75, m, 17H, Ar. ^{13}C n.m.r. δ 53·7, 67·1, 85·8, 123·9, 125·7, 126·3, 126·6, 127·1, 127·4, 127·8, 128·0, 128·6, 129·3, 129·5, 129·8, 130·5, 139·8, 140·8, 145·0, 145·6, 148·2.

Hydrogenolysis with Raney Nickel (W-2)

General procedure. A mixture of the corresponding indanol (150 mg), Raney nickel (W-2) (6 g) and dry ethanol was shaken under a hydrogen atmosphere at 20 psi during 8 h. The ethanolic solution was filtered and the solvent was removed in vacuum. The mixture was purified by p.l.c. (benzene). The following compounds were obtained by using this procedure.

r-*1,*t-*2,*c-*3-Triphenylindan (1).* The title compound was obtained from (6), m.p. 124–125° (ethanol) (lit.[4] 125°). ^{13}C n.m.r. δ ($CDCl_3$) 58·4, 67·6, 124·7, 126·5, 127·7, 128·0, 128·3, 128·6, 129·2, 129·4, 142·7, 146·8, 148·1.

r-*1,*c-*2,*t-*3-Triphenylindan (2).* The title compound was obtained from (7) or (9), m.p. 147–149° (ethanol) (lit.[4] 154°). ^{13}C n.m.r. δ 54·1, 56·1, 62·1, 125·1, 125·4, 126·1, 126·5, 127·4, 127·5, 127·6, 128·4, 128·5, 128·8, 129·1, 139·4, 140·9, 142·8, 145·2, 147·0.

r-*1,*c-*2,*c-*3-Triphenylindan (3)*

The indene (8) (200 mg) was hydrogenated with Pd/C (10%; 250 mg) in ethanol (80 ml) at 50 psi during 8 h. After workup (3) (120 mg) was obtained. Yield 60%, m.p. 153–154° (ethanol) (lit.[4] 143–144°). ^{13}C n.m.r. δ 56·2, 62·8, 124·9, 125·9, 126·0, 126·7, 127·5, 129·5, 129·9, 137·9, 139·2, 145·2.

3-Hydroxy-2,3-diphenylindan-1-ones (11a) and (11b)

Benzalphthalide (1 g) was treated with phenylmagnesium bromide in tetrahydrofuran by following the procedure of Clark.[9] The mixture was then poured into NH_4Cl/H_2O and the organic product extracted with chloroform. After evaporation of the solvent the residue was purified by p.l.c. (chloroform), affording (11a) (400 mg) (upper band) and a mixture of (11a,b) (200 mg) (2 : 1).

r-*3-Hydroxy-*t-*2,3-diphenylindan-1-one (11a).* (Found: C, 84·0; H, 5·3. $C_{21}H_{16}O_2$ requires C, 84·1; H, 5·4%). ^{1}H n.m.r. δ ($CDCl_3$) 2·30, br s, 1H, OH; 4·33, s, 1H, H 2; 6·75–7·72, m, 13H, Ar; 7·92, d, J_{ortho} 7·9 Hz, 1H, H 7. ^{13}C n.m.r. δ 69·2, 80·1, 123·6, 125·5, 126·1, 127·4, 128·1, 128·4, 128·5, 128·8, 129·7, 130·5, 133·6, 135·9, 144·7, 157·0, 203·6.

Mixture of (11a,b). ^{1}H n.m.r. δ ($CDCl_3$) 1·60, br s, OH; 2·30, br s, OH; 4·33, s, H 2; 4·40, s, H 2; 6·65–8·03, m, Ar. ^{13}C n.m.r. δ 69·2, 70·5, 80·1, 84·0, 123·6, 125·5, 126·1, 126·5, 126·8, 127·2, 127·4, 127·7, 128·1, 128·4, 128·5, 128·8, 129·5, 129·7, 130·1, 130·5, 131·4, 133·2, 134·3, 135·8, 135·9, 142·6, 144·7, 155·7, 157·0, 191·2, 203·6.

*2,*c-*3-Diphenylindan-*r-*1,*t-*2-diol (12)*

Compound (10) was reduced with $NaBH_4$ in methanol by employing the procedure described previously by us.[10] Yield 72%, m.p. 144–145° (ethanol–water) (Found: C, 83·4; H, 6·1. $C_{21}H_{18}O_2$ requires C, 83·5; H, 6·0%). ^{1}H n.m.r. δ ($CDCl_3$) 2·60, br s, OH; 3·15, br s, OH; 4·70, s, H 3; 5·50, s, H 1; 6·75–7·60, m, 14H, Ar. ^{13}C n.m.r. δ 60·5, 83·9, 92·7, 122·2, 125·1, 126·7, 126·8, 127·3, 127·5, 127·6, 127·8, 128·1, 129·6, 136·9, 138·5, 140·1, 143·3.

Acknowledgments

The authors express their gratitude to the Secretaria de Ciencia y Técnica, Universidad de Buenos Aires, and CONICET for support of this study.

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