weight are given in Table II. The results were simplified by ignoring isotopic variations.

The infrared spectra of the products were very similar, in particular for absorptions in the regions 3.18–3.50 (w, aryl H), 7.36–7.48 and 6.50–6.60 (s, NO_2), 6.20–6.40 (m, aryl ring), and 11.0–14.0 μ (s, Hal).

Registry No.—**1**, 2146-66-9; **3** (Hal = F), 30669-49-9; **3** (Hal = Cl), 30669-50-2; **3** (Hal = Br), 30669-51-3; **3** (Hal = I), 30669-52-4; α,α,α-trichloro-5-fluoro-2-nitrotoluene, 712-17-4.

Stereochemical Considerations of the Reactions of Phenylmagnesium Bromide and Phenyllithium with Isomeric Methylcyclohexanones

JOHN R. LUDERER, JOHN E. WOODALL, AND JAMES L. PYLE*

Hughes Chemical Laboratories, Miami University, Oxford, Ohio 45056

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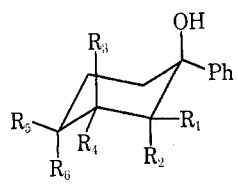
We wish to describe the preparation of isomeric methyl-1-phenylcyclohexanols (**1**–**6**) prepared by the addition of phenylmagnesium bromide or phenyllithium to the corresponding methylcyclohexanones. In each



1, R_1 = CH_3; all others H
2, R_2 = CH_3; all others H
3, R_3 = CH_3; all others H
4, R_4 = CH_3; all others H
5, R_5 = CH_3; all others H
6, R_6 = CH_3; all others H

instance the possibility of formation of two geometric isomeric products exists. The relative propensity of the phenyl to add cis or trans to the methyl as a function of the position and conformation of the methyl, and as PhMgBr or PhLi, is of interest. Also we wish to describe the respective separations of the 2-methyl, 3-methyl, and 4-methyl mixtures and the distinctions which permit structure assignments.

The results of the syntheses of the respective isomers are given in Table I. In each instance the percentages refer to material recovered by elution from a silica gel column. Some olefin formation arising from dehydration of the carbinols during work-up was usually observed, but this was not significant. The analysis of the 2-methyl mixture was also accomplished by gas chromatographic separation on Carbowax 20M and gave the same result as elution from silica gel. The other carbinol mixtures did not separate under the same conditions by gas chromatography.

The establishment of stereochemistry was based on the frequency of the OH stretching absorption in the infrared spectra, on the relative mobility on the silica column, and most importantly on the nmr spectrum. In the case of the 4-methyl system the compounds had previously been reported and their structures rationalized by a similar approach.[1]

It is known that the coupling of a methyl group with an adjacent methine proton in a cyclohexane ring will be dependent upon the conformational status of the coupling moieties.[2] If the methyl is equatorial, signal broadening due to virtual coupling reduces the apparent coupling constant. If one can assign a preferred conformation to the molecule on the basis of the steric requirements of CH_3, OH, and C_6H_5, then the nmr spectra may distinguish the stereoisomers.

Upon consideration of conformational preferences and relative stabilities of the two chair conformations, it is clear that the phenyl-equatorial, hydroxyl-axial arrangement is energetically preferred in all isomers except that of **3**, where there is a serious 1,3-cis diaxial interaction in that conformation between the methyl and hydroxyl groups.[3] The pyridine solvent shift for **3** also questions this latter conformation. A methyl–hydroxyl cis diaxial arrangement would be expected to lead to a deshielding of the methyl signal in pyridine of about 0.20–0.40 ppm compared with the chemical shift in $CDCl_3$.[4] No such deshielding is observed.

The nmr spectra of the 4-methyl compounds **5** and **6** are in agreement with these configurational and conformational assignments, with the predicted J values observed (Table I). Moreover, the expected assignment conforms with the observed elution order from silica–**5** is eluted first—and a slight difference in the infrared spectrum showing more extensive H bonding in **6** where the OH is less hindered. The 3-methyl compounds **3** and **4** show similar correlation of coupling constants with elution order. The more hindered **3** is eluted first. No definitive difference is observed in the infrared spectra.

The coupling constant for **2** is consistent with prediction, but that for **1** is larger than expected for the equatorial methyl–axial proton coupling. Moreover, methyl signals in both compounds are significantly shielded compared to the other isomers. The effect of the phenyl group is expected to cause the shielding observed for the 2-methyl, and its effect on the axial 2-methine proton can explain the large J observed for **1**. The shielding of this proton by the phenyl results in a larger value for $\Delta\nu/J$ than observed in the other instances. Hence, virtual coupling of the methyl signal disappears. The significant diminution in H bonding in **1** and the elution order both support these structure assignments. It is also noteworthy that the less polar **1** is the only isomer of the six compounds reported here which is a liquid at ambient conditions.

Reported results of additions of Grignard reagents or organolithium reagents to cycloalkanones vary markedly depending upon reagents and conditions. One tendency noted, however, is that 2-substituted alkylcycloalkanones result in preference for the product in which the adding group is trans to the alkyl group in the

(1) E. W. Garbisch, Jr., and D. B. Patterson, *J. Amer. Chem. Soc.*, **85**, 3228 (1963).

(2) L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance in Organic Chemistry," 2nd ed, Pergamon Press, London, 1969, p 298, and references cited therein.

(3) E. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill, New York, N. Y., 1962, p 236; J. A. Hirsch, *Top. Stereochem.*, **1**, 199 (1967).

(4) P. V. DeMarco, E. Farkas, D. Doddrell, B. L. Mylari, and E. Wenkert, *J. Amer. Chem. Soc.*, **90**, 5480 (1968); B. V. Paranjape and J. L. Pyle, *J. Org. Chem.*, **36**, 1009 (1971).

TABLE I
STEREOCHEMICAL DISTRIBUTION AND CH_3 PMR DATA OF CARBINOL PRODUCTS FORMED BY REACTION OF THE CORRESPONDING METHYLCYCLOHEXANONE WITH PhMgBr OR PhLi

Compd	PhMgBr, %	PhLi, %	J, Hz	δ, ppm
1-Phenyl-*c*-2-methyl-*r*-cyclohexanol[a] (1)	87	88	6	0.60
1-Phenyl-*t*-2-methyl-*r*-cyclohexanol (2)	13	12	6	0.62
1-Phenyl-*c*-3-methyl-*r*-cyclohexanol (3)	59	56	6	0.95
1-Phenyl-*t*-3-methyl-*r*-cyclohexanol (4)	41	44	3	0.93
1-Phenyl-*c*-4-methyl-*r*-cyclohexanol (5)	54	47	0	0.99
1-Phenyl-*t*-4-methyl-*r*-cyclohexanol (6)	46	53	7	0.92

[a] Nomenclature usage is in conformity with IUPAC Tentative Rules for the Nomenclature of Organic Chemistry, Section E. Fundamental Stereochemistry. See *J. Org. Chem.*, **35**, 2849 (1970).

ketone.[5] In cyclohexanones with substituents at more remote positions, the usual result is that there is no such preference for one addition mode to the other.[6] The results reported herein appear consistent with these trends.

Experimental Section[7]

Preparation of 1-Phenylmethylcyclohexanols. A. From Phenylmagnesium Bromide.—The Grignard reagent was prepared from Mg (10 g, 417 mg-atoms) and bromobenzene (67.5 g, 430 mmol) in ether. The appropriate methylcyclohexanone (39.0 g, 350 mmol) was added drop by drop in ether solution. The product was hydrolyzed with 10% NH_4Cl and ice, the ether layer was separated, and the standard work-up involved ether extraction, washing with $NaHCO_3$, drying overnight (Drierite), removal of the ether, and vacuum distillation of the carbinol product. The yields of carbinol mixtures recovered from the distillation were 2-methyl-1-phenylcyclohexanols (58%), 3-methyl-1-phenylcyclohexanols (54%), and 4-methyl-1-phenylcyclohexanols (53%).

B. From Phenyllithium.—The typical preparation involved preparation of phenyllithium from bromobenzene (31.0 g, 198 mmol) and lithium (1.8 g, 260 mg-atoms) in ether solution. The appropriate methylcyclohexanone was added drop by drop, and the product was isolated as described in procedure A. The yields were for 2-methyl-1-phenylcyclohexanols, 75%; 3-methyl-1-phenylcyclohexanols, 68%; and 4-methyl-1-phenylcyclohexanols, 74%.

Separation of Stereoisomers.—The crude carbinol product (1.00 g) was chromatographed on a 2.5 × 30 cm silica gel column slurry packed in hexane. The column was eluted with hexane in 125-ml fractions and then by hexane solutions of gradually increasing ether concentration. The 4-methyl isomer **5** eluted at 2% ether–hexane and **6** at 15% ether–hexane. The 2-methyl isomer **1** eluted at 5% ether–hexane and **2** at 7.5% ether–hexane. The 3-methyl isomer **3** eluted at 7.5% ether–hexane and **4** at 10% ether–hexane.

These compounds and their properties are as follows.

1 gave $n^{22}D$ 1.5331; ir (neat) 3509 cm^{-1} (OH); methyl nmr ($CDCl_3$) δ 0.60 (d, J_{Me-H} = 6 Hz); mass spectrum (70 eV) *m/e* (rel intensity) 190 (0.041), 172 (0.592), 157 (0.265), 147 (0.163), 143 (0.265), 134 (0.122), 133 (1.00), 130 (0.816), 129 (0.796), 115 (0.490), 105 (0.510).

Carbinol **2** gave mp 56.5–57.5°; ir (KBr) 3413 cm^{-1} (OH); methyl nmr ($CDCl_3$) δ 0.62 (d, J_{Me-H} = 6 Hz); mass spectrum (70 eV) *m/e* (rel intensity) 172 (M^+ − 18) (0.619), 157 (0.323), 143 (0.355), 130 (0.897), 129 (1.00), 115 (0.581), 104 (0.155), 91 (0.665).

Carbinol **3** gave mp 61–63°; ir (KBr) 3356 cm^{-1} (OH); methyl nmr ($CDCl_3$) δ 0.95 (d, J_{Me-H} = 6 Hz); mass spectrum (70 ev) *m/e* (rel intensity) 172 (M^+ − 18) (0.773), 157 (0.665), 143 (0.324), 130 (0.481), 129 (1.00), 115 (0.481), 91 (0.702).

Carbinol **4** gave mp 118–119°; ir (KBr) 3340 cm^{-1} (OH); methyl nmr ($CDCl_3$) δ 0.93 (d, J_{Me-H} = 3 Hz); mass spectrum (70 eV) *m/e* (rel intensity) 172 (M^+ − 18) (0.734), 157 (0.605), 143 (0.323), 130 (0.532), 129 (1.00), 115 (0.500), 104 (0.153), 91 (0.965).

Carbinol **5** gave mp 62–64° (lit.[1] 63.5°); ir (KBr) 3413 cm^{-1} (OH); methyl nmr ($CDCl_3$) δ 0.99 (m); mass spectrum (70 eV) *m/e* (rel intensity) 172 (M^+ − 18) (0.553), 157 (0.288), 143 (0.258), 130 (0.902), 129 (1.00), 115 (0.785), 104 (0.492), 91 (0.394).

Carbinol **6** gave mp 66–67° (lit.[1] 68–69.5°); ir (KBr) 3268 cm^{-1} (OH); methyl nmr ($CDCl_3$) δ 0.92 (d, J_{Me-H} = 7 Hz); mass spectrum (70 eV) *m/e* (rel intensity) 172 (0.507), 157 (0.239) 143 (0.224), 130 (0.791), 129 (0.776), 115 (0.522), 104 (0.433), 91 (0.313), 28 (1.00).

Anal. Calcd for $C_{13}H_{18}O$ (1–6): C, 82.06; H, 9.53. Found for **1**: C, 81.88; H, 9.62. Found for **2**: C, 82.10; H, 9.43. Found for **3**: C, 81.84; H, 9.38. Found for **4**: C, 82.13; H, 9.75. Found for **5**: C, 82.03; H, 9.73. Found for **6**: C, 81.84; H, 9.78.

Registry No.—**1**, 30689-79-3; **2**, 30689-80-6; **3**, 30689-81-7; **4**, 30689-82-8; **5**, 30689-83-9; **6**, 30689-84-0; phenylmagnesium bromide, 100-58-3; phenyllithium, 591-51-5.

(5) J. Ficini and A. Maujean, *C. R. Acad. Sci., Ser. C*, **266**, 227 (1968); G. D. Maio, M. T. Pellegrini, and P. A. Tardello, *Ric. Sci.*, 240 (1968).

(6) F. Rocquet, J. P. Battioni, M. L. Capman, and W. Chodkiewicz, *C. R. Acad. Sci., Ser. C*, **269**, 1449 (1969); *Bull. Soc. Chim. Fr.*, 976 (1969); H. O. House, Abstracts, Twentieth National Organic Chemistry Symposium, Burlington, Vt., June 1967, p 99.

(7) Spectroscopic information was obtained using a JEOL-C6OH nmr spectrometer, Perkin–Elmer 237B infrared spectrometer, and Hitachi RMU-6B mass spectrometer. All melting points are corrected.

Group III Metal Complexes in the Preparation of Vitamin E

PIUS A. WEHRLI,*[1] R. IAN FRYER, AND WERNER METLESICS

Chemical Research Department, Hoffmann-La Roche Inc., Nutley, New Jersey 07110

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Karrer, *et al.*,[2] in their numerous syntheses of vitamin E **3** and analogs have alkylated methyl-substituted hydroquinones with phytol or isophytol **2** in boiling formic acid. This method, as well as an alternative one employing phytyl bromide, $ZnBr_2$, and trimethylhydroquinone (TMHQ) **1** at 80–100°,[3] suggests a carbonium ion mechanism as outlined in Scheme I. Later modifications[4] of the same reaction employ strong Brønsted acids (HCl, *p*-toluenesulfonic acid) in combination with a Lewis acid catalyst such as those used in typical Friedel–Crafts reactions (BF_3, $ZnCl_2$, $FeCl_2$, etc.). In the cases described, the water formed in the reaction is removed azeotropically.

With the advent of more sophisticated methods of analysis, it became evident that *dl*-α-tocopherol pro-

(1) To whom correspondence should be addressed.

(2) P. Karrer and H. Fritzsche, *Helv. Chim. Acta*, **21**, 1234 (1938).

(3) P. Karrer, H. Fritzsche, B. H. Ringier, and H. Saloman, *ibid.*, **21**, 520 (1938); P. Karrer and A. Kugler, *ibid.*, **28**, 436 (1945).

(4) See patent literature, compiled by W. F. Kujawski in "Annotated Bibliography of Vitamin E," Distillation Products Industries, Rochester, N. Y. 14603.