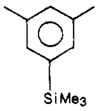
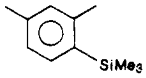
Table II. Selectivity of the Gas-Phase Trimethylsilylation and *tert*-Butylation of Methylbenzenes[a]

substrate	k_S/k_B[b]	k_S/k_T[b]	orientation[c] (%)	
toluene[d]	3.8 (55)	1.00	meta: 14 (6)	para: 86 (94)
o-xylene[e]		3.3 (2.0)		
m-xylene[e]		1.5 (1.6)	 30 (13)	 70 (87)
p-xylene[e]		0.6 (unreactive)		
mesitylene[f]		unreactive (unreactive)		

[a] Values in parentheses refer to *tert*-butylation. [b] Standard deviation ca. 10%. k_S/k_B and k_S/k_T denote the reactivity of the substrate toward the electrophiles, $SiMe_3^+$ and CMe_3^+, relative respectively to that of benzene and of toluene. Such ratios have been calculated from the relative yields of products measured in competition experiments, taking into account the concentrations of the competing substrates. [c] Standard deviation ca. 3%. [d] Data for *tert*-butylation from ref 4. [e] Data for *tert*-butylation from ref 16. [f] Data for *tert*-butylation from ref 17.

amine effectively intercepts the $C_nH_5^+$ and $SiMe_3^+$ ionic precursors, thus depressing the yields. This accounts for the peculiar dependence of the yields on the partial pressure of NEt_3 illustrated in Figure 1. The initial increase, as the amine gradually swamps the adventitious oxygenated nucleophiles, is followed by gradual decline as the higher concentrations allow the amine to intercept most of the charged precursors. The kinetic, rather than thermodynamic character of the factors controlling the k_2/k_3 branching ratio emerges from the effect of the simultaneous addition of NEt_3 and c-$C_6H_{10}O$, and especially of $Me_2NCH_2CH_2OH$, whose PA is as high as of NEt_3,[15] but containing an oxygenated nucleophilic center. The high reactivity of the latter toward $SiMe_3^+$ favors process (eq 2) over deprotonation (eq 3) and hence prevents formation of neutral silylated products.

In conclusion, formation of trimethylphenylsilanes is traced to a reaction sequence initiated by the electrophilic attack (eq 1), followed by deprotonation (eq 3), whose competition with desilylation (eq 2) is affected by the nature of the base.

Table II compares the selectivity of gaseous $SiMe_3^+$[18] and *t*-Bu$^+$ ions. Despite the extremely high k_T/k_B ratio in *tert*-butylation,[19] the substrate and positional selectivity of the cations are similar. This reflects the operation of steric factors which determines, in both cases, the reactivity order of the xylenes. The lack of reactivity of mesitylene has been traced, in the case of *tert*-butylation, to steric hindrance to deprotonation.[17] As a whole, $SiMe_3^+$ appears noticeably *less* selective, as shown, inter alia, by the para:meta ratio in toluene, ca. 12, considerably lower than observed in *tert*-butylation, ca. 32.

Experimental Section

The gases, with a stated purity in excess of 99.99 mol %, were purchased from Matheson Gas Products Inc.; tetramethylsilane, obtained from Fluka A. G., had a purity of 99.5 mol %. The chemicals used as substrates or reference standards in the analyses were obtained from commercial sources, or prepared according to unexceptional procedures, except (trimethylsilyl)arenes which were prepared from the reaction of the corresponding aryl Grignard derivative with trimethylsilyl triflate. The gaseous samples, prepared in a greaseless line by standard vacuum procedures and introduced into 135-mL Pyrex ampules, were irradiated in a 220 Gammacell (Nuclear Canada Ltd.) to a total dose of ca. 10^4 Gy, at a dose rate of ca. 10^4 Gy h^{-1}. The analysis of the irradiated mixture was carried out by GLC and GLC/MS, with the following columns: (i) a 50 m long, 0.2 mm i.d. silica column, coated with methylsilicone SP 2100 fluid, deactivated with Carbowax 20M; (ii) a 3.5 m long, 3 mm i.d. stainless steel column, packed with SP-2100, 20% w/w on 100–200 mesh Supelcoport, deactivated with 1% Carbowax 1500; (iii) a 12-m long, 0.2-mm i.d. silica column, coated with a 0.33-μm film of cross-linked methylsilicone polymer.

The identity of the products was established by comparison of their capacity factors with those of authentic samples, as well as from their mass spectra recorded with a Hewlett-Packard 5970B mass selective detector. The amounts of products formed were determined from the areas of the corresponding elution peaks, by using the internal standard calibration method.

The ICR measurements were carried out at typical pressures of 5×10^{-7} Torr with a Nicolet FT-MS 1000 spectrometer.

Acknowledgment. The work was supported by the Italian National Research Council (C.N.R.) and by the Ministry of Pubblica Istruzione. I am grateful to F. Cacace for useful discussions and to M. E. Crestoni for experimental help.

Registry No. PhH, 71-43-2; PhMe, 108-88-3; $SiMe_3^+$, 28927-31-3; *o*-xylene, 95-47-6; *m*-xylene, 108-38-3.

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(15) The PA of $Me_2NCH_2CH_2OH$ was estimated to be ca. 232 kcal mol^{-1} by applying a group-additivity method to the data from ref 13.

(16) Giacomello, P.; Cacace, F. *J. Am. Chem. Soc.* 1976, *98*, 1823.

(17) Aliprandi, B.; Cacace, F.; Cipollini, R. *Radiochimica Acta* 1982, *31*, 107.

(18) The evidence from chemical ionization mass spectrometry, cf. ref 3, 9–11, suggests that at the relatively high $SiMe_4$ pressures and low temperatures prevailing in the radiolytic experiments, $SiMe_3^+$ is reversibly associated with one or more $SiMe_4$ molecules. The effects on the energetics of eq 1 are probably limited, since there are reasons to believe that the $SiMe_3^+$–$SiMe_4$ binding energy is low.

(19) Sen Sharma, D. K.; Ikuta, S.; Kebarle, P. *Can. J. Chem.* 1982, *60*, 2325.

Achiral Hexaisopropylbenzene Isotopomers: Analogues of the Achiral Trihydroxyglutaric Acid Diastereomers

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Certain derivatives of hexaisopropylbenzene (hib) may exist as achiral diastereomers which are distinguished by the sense of directionality of the isopropyl C–H methine vectors and which, though devoid of conventional stereocenters, are conceptually related to the achiral 2,3,4-trihydroxyglutaric acid diastereomers.[1] We now report the first synthesis of such stereoisomers.

Synthesis and ^{1}H NMR Spectra of Hexaisopropylbenzene-d_{18}. Addition of (3-methyl-1-butyn-1-yl)magnesium bromide to acetone-d_6 afforded 2,5-dimethylhex-3-yn-2-ol-d_6. Reduction of the alcohol functionality yielded diisopropylacetylene-d_6 in which one isopropyl group was perdeuteriated at the methyl positions. Cyclotrimerization of the labeled acetylene yielded hib-d_{18}. In the absence of significant isotope effects, three isomers of hib-d_{18} should be formed in a statistical ratio **1**:**2**:**3** = 2:3:3 (Figure 1), where **2** and **3** are conformational dia-

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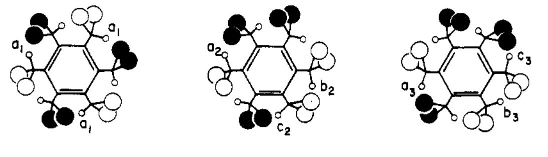

1 2 3

Figure 1. Three isotopomers of hexaiisopropylbenzene-d_{18}. Methyl groups and methine hydrogens are represented by large and small circles, respectively, and protium and deuterium atoms by open and filled circles, respectively. Methine proton environments of unlabeled isopropyl groups are designated by subscripted letters.

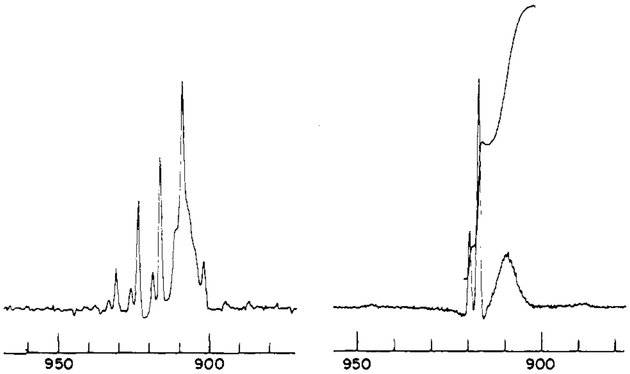

Figure 2. ^{1}H NMR (250 MHz) spectrum (methine region) of a hexaisopropylbenzene-d_{18} isotopomer mixture (Figure 1) in $CDCl_3$ at room temperature. Scale in Hz. Left: convolution difference, resolution-enhanced signals. Right: convolution difference, resolution-enhanced methyl-decoupled methine signals. The two downfield signals are separated by 2.4 Hz while the broad signal (due to $CH(CD_3)_2$ groups) is separated from the upfield signal by 8 Hz. Integration of signals shows an intensity ratio of 1:3:4.

stereomers of the type described above. The ^{1}H NMR spectrum of the mixture is in accord with this conclusion. Both the three unlabeled and the three labeled isopropyl groups are equivalent in 1 and nonequivalent in 2 and 3. The methyl groups, the methine protons of the labeled isopropyl groups, and the methine protons of the unlabeled isopropyl groups should therefore display seven signals each in the NMR spectrum of the mixture. Since all the methyl groups are in spatial proximity to the methine hydrogens, all the methyl protons should be isochronous under the assumption that intrinsic steric isotope effects[2,3] are the sole cause of anisochronies of the NMR signals in the three different groups of protons. Indeed, all methyl protons appear as one doublet at δ 1.22 (J = 7.3 Hz). Two signals are expected for the methine protons of the unlabeled groups: one for the protons pointing toward labeled methyl groups ($3a_1 + a_2 + a_3 + c_2 + c_3$) and the second for the protons pointing to unlabeled methyl groups ($b_2 + b_3$). By a similar analysis, two signals are expected for the methine protons of the labeled isopropyl groups, these signals being shifted upfield (relative to the methine signals on unlabeled isopropyl groups) and broadened due to unresolved H–D coupling. Given the relative statistical weights of the isotopomers, the intensity ratio of the two methine signals of the unlabeled isopropyl groups should therefore be 3 to 1, with the stronger signal due to H/D interactions. Since the more severe H/H interactions are known in similar cases to lead to a downfield shift of the observed proton,[2] the stronger signal should appear at the higher field. This is precisely what was observed for the methine protons on unlabeled isopropyl groups (Figure 2), whereas the corresponding signals at labeled groups appeared unresolved. The presence of a mixture of conformationally stable[3] diastereomers 2 and 3 is thus established beyond any reasonable doubt.

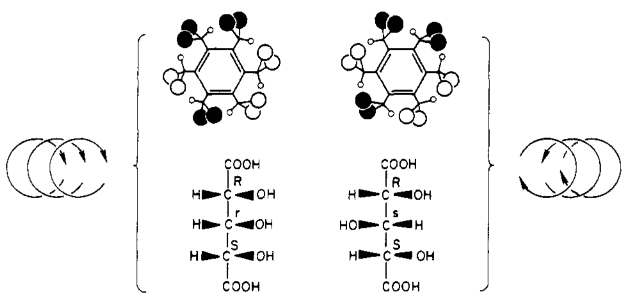

Figure 3. Triplets of arrows symbolize three-tiered directionality in the pair of conformational diastereomers (top) corresponding to 2 and 3 in Figure 1, and in the diastereomers of achiral 2,3,4-trihydroxyglutaric acid (bottom). The sense of directionality is depicted in a view along a normal to the molecular symmetry plane and from outside the molecular model. Because directionality conventions are arbitrary, no one-to-one relationship exists between the individual structures at the top and those at the bottom. For example, 2 may be taken to correspond either to (2*R*,3*r*,4*S*)- or to (2*R*,3*s*,4*S*)-2,3,4-trihydroxyglutaric acid.

Three-Tiered Cyclic Directionality. The relationship between the pair 2/3 and the diastereomeric pair of achiral 2,3,4-trihydroxyglutaric acids is depicted in Figure 3. The model of each of these molecules may be factored into stereochemically significant components, each of which is characterized by a directed cycle that is represented by a curved arrow.[4] In the case of the trihydroxyglutaric acids, the outer components are associated with the enantiotopic CHOH groups centered at C(2) and C(4), whereas in the case of 2/3 they are associated with the enantiotopic substituent patterns above and below the symmetry plane. The inner cycle lies in the molecular symmetry plane and is associated with the CHOH group centered at C(3) in the trihydroxyglutaric acids[6] and with the C–H methine vectors in 2/3. The sense of cyclic directionality, symbolized by the sense, clockwise or anticlockwise, of the curved arrow, is defined by an arbitrary convention,[1] in the case of 2/3 by giving priority to the orientation of the methine vectors (inner cycle) and by associating a sense of directionality with the two labeling patterns of the methyl hydrogens (two outer cycles), i.e., $CD_3 \rightarrow CD_3 \rightarrow CH_3 \rightarrow CH_3 \rightarrow CD_3 \rightarrow CH_3$, and in the case of the trihydroxyglutaric acids by the sequence $H \rightarrow C \rightarrow O$ for each of the three stereocenters. The two diastereomers of each pair can be interconverted by reversal of the sense of directionality of the inner cycle, in the case of the trihydroxyglutaric acids by transposition of the OH and H groups at C(3) and in the case of 2/3 formally by detachment of the methine hydrogens from their carbon atoms and reattachment on the other side.[1,5] The same result is obtained by reversing the sense of directionality of the two outer cycles.[7] The commonality of the cyclic

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(1) Mislow, K. *Chimia* 1986, *40*, 395.

(2) Anet, F. A. L.; Dekmezian, A. H. *J. Am. Chem. Soc.* 1979, *101*, 5449.

(3) Siegel, J.; Gutiérrez, A.; Schweizer, W. B.; Ermer, O.; Mislow, K. *J. Am. Chem. Soc.* 1986, *108*, 1569.

(4) A cycle is defined by three or more noncollinear points in the molecular model. A cycle is undirected if it is bisected by a molecular C_{2n} axis in, or by a molecular σ plane perpendicular to, the mean plane of the cycle. Otherwise it is directed. This definition of cyclic directionality is based on the symmetry of the molecular model and applies to all cyclic arrays, whether they are rings in the chemical sense (i.e., made up of bonded atoms) or not.[1,5]

(5) Singh, M. D.,; Siegel, J.; Biali, S. E.; Mislow, K. *J. Am. Chem. Soc.* 1987, *109*, 3397.

(6) This carbon has been described as "pseudoasymmetric" in the older literature. For a critique of this term, see: Mislow, K.; Siegel, J. *J. Am. Chem. Soc.* 1984, *106*, 3319.

directionality patterns, including the consequences of reversal of sense of directionality, thus reveals the existence of a stereochemical relationship between sets of molecules with utterly disparate structures[8,9] and suggests the possibility that other unsuspected stereochemical similarities may be uncovered by the same type of analysis.

Experimental Section

NMR spectra were measured on a Bruker WM-250 and mass spectra on a Kratos MS 50 RFA spectrometer.

2,5-Dimethylhex-3-yn-2-ol-d_6 was prepared in 67% yield from (3-methyl-1-butyn-1-yl)magnesium bromide and acetone-d_6 (99 atom % D) according to the procedure described for the unlabeled compound.[10] The compound was found by MS to contain 97+ atom % deuterium at the labeled positions.

Diisopropylacetylene-d_6. 2,5-Dimethylhex-3-yn-2-ol-d_6 (10.5 g, 80 mmol) was reacted with dicobalt octacarbonyl (Strem) followed by treatment with $NaBH_4/CF_3COOH$ according to the procedure previously described for the unlabeled compound.[3] The title compound, obtained in 24% yield, was found by MS to contain 93+ atom % of deuterium at the labeled positions. ^1H NMR ($CDCl_3$) δ 1.10 (d, 6 H, $J = 6.7$ Hz, $CH(CH_3)_2$), 2.46 (1 H, $CH(CD_3)_2$, br), 2.49 (d of septets, 1 H, $^3J = 6.7$ Hz, $^5J = 1.8$ Hz, $CH(CH_3)_2$).

Hexaisopropylbenzene-d_{18} was prepared by $Hg[Co(CO)_4]_2$ catalyzed trimerization of diisopropylacetylene-d_6 according to the procedure described for the unlabeled compound.[3] The product was found by MS and the combustion falling-drop method[11] to contain 93+ atom % deuterium at the labeled positions.

Acknowledgment. We thank the National Science Foundation (CHE-8510067) for support of this work.

Registry No. **1**, 112504-73-1; **2**, 112504-74-2; (3-methyl-1-butyn-1-yl)magnesium bromide, 112482-54-9; acetone-d_6, 666-52-4; 2-(methyl-d_3)-5-methylhex-3-yn-2-ol-*1,1,1*-d_3, 112482-52-7; (isopropyl-*1,1,1,3,3,3*-d_6)isopropylacetylene, 112482-53-8.

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(7) Brewster, J. H. *J. Org. Chem.* **1986**, *51*, 4751.

(8) The analogy described above is restricted to achiral molecules in which the two external directed cycles are enantiotopic and in which the reversal of the sense of the central cycle (or, equivalently, of the two outer cycles) leads to an achiral isomer.

(9) A similar correspondence exists between the enantiomeric trihydroxyglutaric acids and, for example, the cycloenantiomeric cyclohexaalanyls.[1]

(10) Burawoy, A.; Spinner, E. *J. Chem. Soc.* **1954**, 3752.

(11) Analysis performed by J. Nemeth, Urbana, IL.

Barrier to Internal Rotation in 1,2-Bis(bromochloromethyl)-3,4,5,6-tetraisopropylbenzene

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The tightly gear meshed arrangement of isopropyl and dichloromethyl groups in hexaisopropyl- and hexakis(dichloromethyl)benzene, respectively, imparts a high barrier to internal rotation. For hexaisopropylbenzene,[1] a lower limit of 22 kcal mol^{-1} was estimated for the topomerization barrier from NMR measurements on a d_{28} isotopomer and a barrier of ca. 35 kcal mol^{-1} was calculated by use of the empirical force field (EFF) method. For hexakis(dichloromethyl)benzene,[2] the calculated (EFF) topomerization barrier was 33.9 kcal mol^{-1}. Consistent with these findings is the lower limit of 24 kcal mol^{-1} estimated (NMR) for the enantiomerization barrier in (1′*RS*,2′*SR*)-1,2-bis(1-bromoethyl)-3,4,5,6-tetraisopropylbenzene.[3]

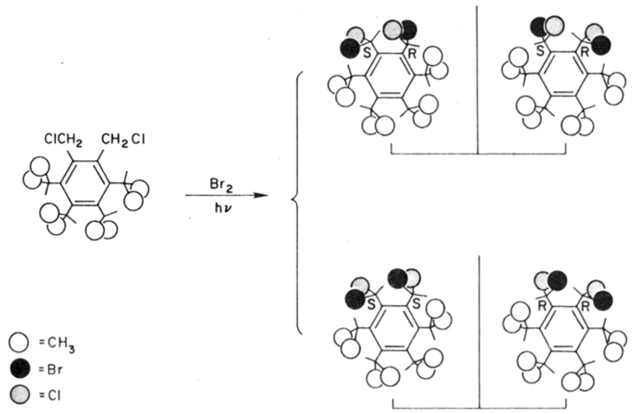

Figure 1. Photobromination of 1,2-bis(chloromethyl)-3,4,5,6-tetraisopropylbenzene to a diastereomeric mixture of 1,2-bis(bromochloromethyl)-3,4,5,6-tetraisopropylbenzene (**1**). Enantiomers are related by vertical mirror lines. Top: 1′*S*,2′*R* and 1′*R*,2′*S* enantiomers. Bottom: 1′*S*,2′*S* and 1′*R*,2′*R* enantiomers.

The title compound **1** was prepared in order to provide an experimental value for this barrier: unlike the diastereomers of 1,2-bis(1-bromoethyl)-3,4,5,6-tetraisopropylbenzene, which suffer dehydrohalogenation at elevated temperature,[3] the diastereomers of **1** are expected to resist decomposition under similar conditions. Cotrimerization of diisopropylacetylene with 1,4-diacetoxy-2-butyne in the presence of $Hg[Co(CO)_4]_2$ gave a mixture of hexaisopropylbenzene, hexakis(acetoxymethyl)benzene, 1,2-bis(acetoxymethyl)-3,4,5,6-tetraisopropylbenzene (**2**), and 1,2-diisopropyl-3,4,5,6-tetrakis(acetoxymethyl)benzene, together with a small quantity of tetraisopropylcyclopentadienone. The mixture was separated, the isolated **2** was hydrolyzed in ethanolic KOH, and the resulting diol was converted to 1,2-bis(chloromethyl)-3,4,5,6-tetraisopropylbenzene (**3**) with thionyl chloride. Photobromination of **3** led to a diastereomeric mixture (Figure 1) that is stereochemically analogous to the mixture depicted in Figure 5 of ref 3.

The two diastereomers are asymmetric on the NMR time scale, and each methyl or methine proton in the mixture should therefore give rise to a distinct NMR signal, barring accidental isochrony. The 250-MHz ^1H NMR spectrum of the mixture in C_6D_6 displays 12 doublets in the methyl region; there is accidental isochrony for four pairs of signals (see Experimental Section). The three doublets at δ 1.58–1.64 appear as an apparent AB quartet, since their coupling (ca. 7.4 Hz) is of the order of their mutual separation. Indeed, when the signal at δ 5.04 was irradiated, the apparent quartet collapsed into three singlets with a 1:2:1 intensity ratio. In the methine region, two overlapping septets were observed at δ 3.65 and 3.70, and the remaining two septets were observed at δ 3.89 and 5.04. The most downfield septet was assigned to the unique isopropyl methine proton in each diastereomer which is tucked into the cleft of a neighboring bromochloromethyl group.[3] In the low-field region, three signals were observed: one at δ 7.61 (integrating for two protons) and the other two (integrating for two protons, and with

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(1) Siegel, J.; Gutiérrez, A.; Schweizer, W. B.; Ermer, O.; Mislow, K. *J. Am. Chem. Soc.* **1986**, *108*, 1569.

(2) Kahr, B.; Biali, S. E.; Schaefer, W.; Buda, A. B.; Mislow, K. *J. Org. Chem.* **1987**, *52*, 3713.

(3) Singh, M. D.; Siegel, J.; Biali, S. E.; Mislow, K. *J. Am. Chem. Soc.* **1987**, *109*, 3397.

0022-3263/88/1953-1318$01.50/0