Alkylation of Allylic Derivatives. 7.[1] Stereochemistry of Alkylation of the Isomeric *trans*-α,γ-Methyl(phenyl)allyl Acetates with Lithium Dialkylcuprates and Alkylcyanocuprates

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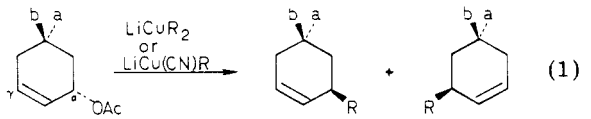
Alkylation of the isomeric *trans*-α,γ-methyl(phenyl)allyl acetates (**2**-OAc and **3**-OAc) with lithium dialkylcuprates or alkylcyanocuprate is stereospecific. The α-alkylation product is formed with excess inversion, and the γ-alkylation product results from excess anti bonding. Stereospecificity ranges from about 85 to 95% in this sterically unbiased system.

In earlier work we investigated the alkylation of 5-methyl-2-cyclohexenyl acetate (**1**) with lithium dimethylcuprate ($LiCuMe_2$).[2] In this cyclic system, α-alkylation proceeds with inversion of configuration, and γ-alkylation involves anti stereochemistry, as shown by eq 1. More recently, similar results have been reported for



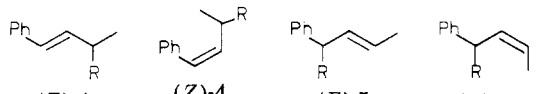
cis-**1**, a = Me; b = H
trans-**1**, a = H; b = Me

α alkylation γ-alkylation

other cyclohexenyl systems.[3,4] In work to be reported elsewhere, we have observed the same stereochemistry for the regiospecific (excess γ-alkylation) alkylation of **1** with lithium cyanomethylcuprate [LiCu(CN)Me],[5] as indicated in eq 1.

We have now extended our studies to an acyclic system. This paper reports an investigation of the stereochemistry of alkylation of the isomeric *trans*-α,γ-methyl(phenyl)allyl acetates (**2**-OAc and **3**-OAc) with lithium dialkylcuprates and alkylcyanocuprates.

2-OAc **3**-OAc

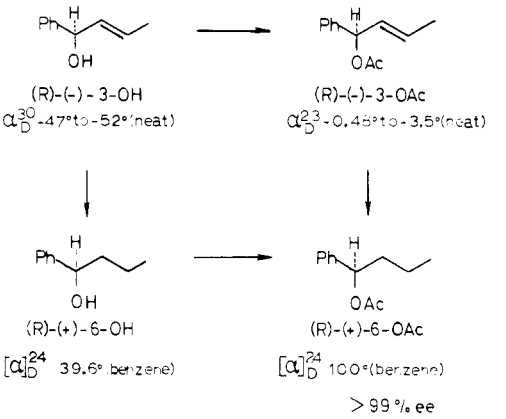


(*E*)-**4** (*Z*)-**4** (*E*)-**5** (*Z*)-**5**

a, R = Me; b, R = Bu

An investigation of the regiochemistry of alkylation of **2**-OAc and **3**-OAc with $LiCuMe_2$ and $LiCu(n\text{-}Bu)_2$ has been reported.[6] Possible alkylation products for this system include two conjugated isomers, (*E*)- and (*Z*)-3-alkyl-1-phenyl-1-butene (**4**), and two unconjugated isomers, (*E*)- and (*Z*)-1-alkyl-1-phenyl-2-butene (**5**). These olefins were characterized earlier.[6] In this work we have related configurations and enantiomeric excesses (ee) for reactants

Scheme I. Correlation of (*R*)-**3**-OH and (*R*)-**3**-OAc with Optically Pure (*R*)-**6**-OAc



and products for alkylation of optically active **2**-OAc and **3**-OAc.

The (*R*)-(+)-**2**-OAc, $[\alpha]^{20}_D$ 150° ($CHCl_3$), used in the present work was shown to have an enantiomeric composition of >99% ee with a chiral shift reagent, $Eu(hfbc)_3$.[7] The minor enantiomer could not be detected in the shifted spectrum. The absolute configuration is known from correlations outlined earlier.[8]

The absolute configuration of active **3**-OH is known from correlation with the saturated analogue, 1-phenyl-1-butanol (**6**-OH), of known absolute configuration.[10] In other work, we prepared (*R*)-(-)-**3**-OH, $[\alpha]^{30}_D$ -50.4° (neat), and reported that this material was 63% optically pure.[11] This was determined by the method of Mislow and Raban,[12] which involves esterification with excess optically pure *O*-methylmandelyl chloride and determination of the ratio of the resulting two diastereomers by NMR analysis. In this work we have reexamined the absolute rotations for **3**-OH and **3**-OAc by diimide reduction of optically active samples to the saturated analogues (**6**) and direct determination of the enantiomeric composition of the resulting active **6**-OAc with a chiral shift reagent, $Eu(hbfc)_3$.[13] Samples of (*R*)-(-)-**3**-OH, derived[11] from the (-)-

(1) Previous paper in this series: Goering, H. L.; Singleton, V. D., Jr. *J. Org. Chem.* **1983**, *48*, 1531.
(2) Goering, H. L.; Singleton, V. D., Jr. *J. Am. Chem. Soc.* **1976**, *98*, 7854.
(3) Gallina, C.; Ciattini, P. G. *J. Am. Chem. Soc.* **1979**, *101*, 1035.
(4) Kreft, A. *Tetrahedron Lett.* **1977**, 1035.
(5) Kantner, S. S., unpublished work in these laboratories.
(6) Goering, H. L.; Seitz, E. P., Jr.; Tseng, C. C. *J. Org. Chem.* **1981**, *46*, 5304.
(7) Goering, H. L.; Eikenberry, J. N.; Koermer, G. S.; Lattimer, C. J. *J. Am. Chem. Soc.* **1974**, *96*, 1493.
(8) Goering, H. L.; Kantner, S. S.; Tseng, C. C. *J. Org. Chem.* **1983**, *48*, 715.
(9) Kenyon, J.; Partridge, S. M.; Phillips, H. *J. Chem. Soc.* **1937**, 207.
(10) MacLeod, R.; Welch, F. J.; Mosher, H. S. *J. Am. Chem. Soc.* **1960**, *82*, 876. Peters, H. M.; Feigl, D. M.; Mosher, H. S. *J. Org. Chem.* **1968**, *33*, 4245.
(11) Goering, H. L.; Koermer, G. S.; Linsay, E. C. *J. Am. Chem. Soc.* **1971**, *93*, 1230.
(12) Raban, M.; Mislow, K. *Top. Stereochem.* **1967**, *2*, 199.
(13) Shift reagents catalyze the allylic rearrangement of **3**-OAc to **2**-OAc. Thus, chiral shift reagents are not applicable for determination of enantiomeric compositions in this reactive allylic system.

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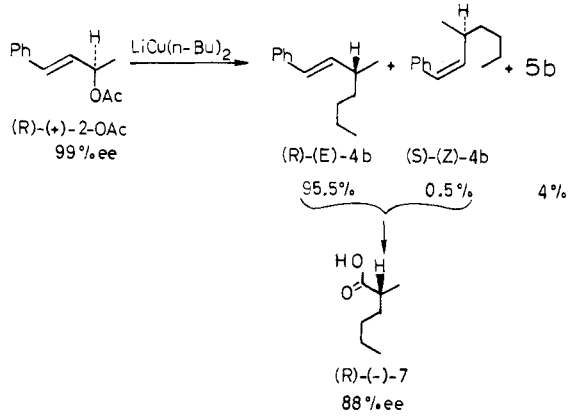
Scheme II. Stereochemistry and Regiochemistry of Alkylation of (*R*)-2-OAc with $LiCu(n\text{-}Bu)_2$



cinchonidine salt of the acid phthalate derivative that had been recrystallized to constant rotation, had rotations that varied over the range shown in Scheme I. Similarly, rotations for different samples of (*R*)-(−)-**3**-OAc varied as indicated. However, all of these samples were converted to (*R*)-(+)-**6**-OAc, $[\alpha]^{24}_D$ 100° (benzene), which was shown to have an ee of >99% with $Eu(hfbc)_3$.

The absolute rotation for **6**-OH in Scheme I is somewhat higher than the rotation reported by Levene and Marker, $[\alpha]^{24}_D$ −35.8° (benzene),[14a] but lower than that reported by Kenyon and Partridge, $[\alpha]_D$ −45.9° (benzene).[14b] The reason for the discrepancy is not clear. The rotation for **6**-OAc is in excellent agreement with that calculated from the highest reported rotation for a neat sample[10] and the ratio of rotations for neat samples and benzene solutions.[14a]

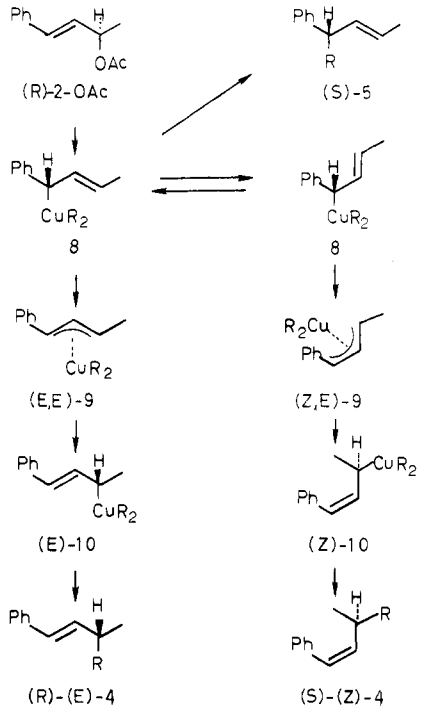
We have no explanation for variations of rotations of evidently optically pure samples of the allylic compounds (**3**-OH and **3**-OAc). Such variations were not observed for the saturated analogues (**6**-OH and **6**-OAc). The present results show that the sample of (−)-**3**-OH, $[\alpha]^{30}_D$ −50.4° (neat), that we had in hand earlier[11] was in fact optically pure instead of 63% optically pure. Presumably, the reason for the earlier erroneous determination is that the *O*-methylmandelyl chloride was partially racemic.

In other work[6] we observed that products for alkylation of **2**-OAc and **3**-OAc with lithium dialkylcuprates are very similar and consist primarily (90–95%) of the conjugated alkylation product, (*E*)-**4**. Thus, **2**-OAc gives primarily the α-alkylation product, and **3**-OAc gives mainly γ-alkylation.

The results for α-alkylation of (*R*)-(+)-**2**-OAc with $LiCu(n\text{-}Bu)_2$ are shown in Scheme II. The composition of the alkylation product was determined by capillary GC. The α-alkylation product (*E*-**4b**) was shown to have the *R* configuration by Lemieux oxidation (sodium periodate–potassium permanganate)[15] to (*R*)-(−)-2-methylhexanoic acid [(*R*)-(−)-**7**]. The absolute configuration of the latter is known from correlation[16] with 2-methylbutyric acid, which in turn has been related to glyceraldehyde.[17]

The absolute rotation for **7** was established as follows. Resolution of **7** to constant rotation as described earlier[18] gave (*S*)-(+)-**7**: $[\alpha]^{25}_D$ 17.7° (neat), $[\alpha]^{22}_D$ 21.2° (ether). Treatment with diazomethane gave (*S*)-(+)-methyl 2-methylhexanoate, $[\alpha]^{20}_D$ 23.0° ($CHCl_3$), which was shown to be 97% optically pure with a chiral shift reagent, $Eu(hfbc)_3$.[7] It has been reported[19] that attempts to apply chiral shift reagents to this system were unsuccessful. However, we find that the enantiopic 2-methyl signals (doublets) are completely separated from each other and from all other signals in the shifted 270-MHz spectrum. The present results indicate that the absolute rotation for **7** is α^{25}_D 18.2° (neat) and $[\alpha]^{22}_D$ 21.9° (ether),[20] and the absolute rotation for methyl 2-methylhexanoate is $[\alpha]^{20}_D$ 23.7° ($CHCl_3$).

Scheme III. Mechanism and Stereochemisty of Alkylation of (*R*)-2-OAc with Dialkylcuprates

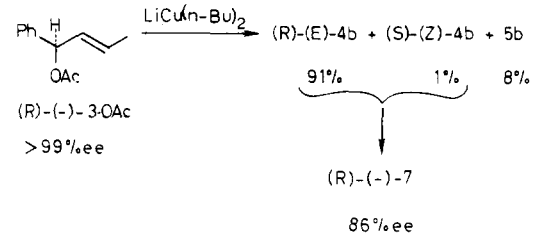


The configuration of (*Z*)-**4b** could not be determined and is of little consequence because it is present in only trace amounts. However, we presume this product has the indicated *S* configuration on the basis of mechanistic considerations outlined in Scheme III. For reasons discussed elsewhere,[21] we believe that oxidative addition involves bonding of the copper to the anti side of the γ-carbon atom to give the S_N2' σ-(allyl)copper(III) complex (**8**). This initial oxidative addition product can undergo (1) reductive elimination with retention of configuration[22] to give the anti γ-alkylation product [(*S*)-**5**], (2) stereospecific allylic rearrangement via the π-allyl complex [(*E*,*E*)-**9**] to give (*E*)-**10**, which leads to (*R*)-(*E*)-**4**, and (3) allylic rearrangement via (*Z*,*E*)-**9** to give (*Z*)-**10**. Reductive elimination of the latter with retention leads to (*S*)-(*Z*)-**4**.

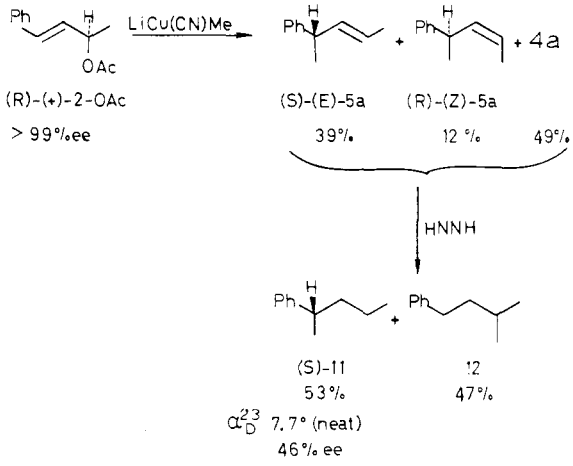
As shown in Scheme II, the (*R*)-**7** derived from the alkylation product has an ee of 88%. Thus, α-alkylation proceeds with about 90% excess inversion. Presumably,

(14) (a) Leven, P. A.; Marker, R. E. *J. Biol. Chem.* **1932**, *97*, 379. (b) Kenyon, J.; Partridge, S. M. *J. Chem. Soc.* **1936**, 128.
(15) (a) Lemieux, R. U.; von Rudloff, E. *Can. J. Chem.* **1955**, *33*, 1701. (b) *Ibid.* **1955**, *33*, 1710. (c) von Rudloff, E. *Ibid.* **1955**, *33*, 1714. (d) Pelletier, S. W.; Iyer, K. N.; Chang, C. W. J. *J. Org. Chem.* **1970**, *35*, 3535.
(16) Levene, P. A.; Marker, R. E. *J. Biol. Chem.* **1933**, *103*, 299.
(17) Crombie, L.; Harper, S. H. *J. Chem. Soc.* **1950**, 2685.
(18) Levene, P. A.; Bass, L. W. *J. Biol. Chem.* **1926**, *70*, 211.
(19) Meyers, A. I.; Knaus, G.; Kamata, K. *J. Am. Chem. Soc.* **1974**, *96*, 268.
(20) The highest reported rotations for **7** are as follows: $[\alpha]^{22}_D$ 19.6° (ether), ref 18; α^{25}_D 18.7° (neat), Leven, P. A.; Marker, R. E. *J. Biol. Chem.* **1932**, *98*, 1. In recent stereochemical studies, these rotations were assumed to be absolute rotations: Reference 19. Larcheveque, M.; Ignatova, E.; Cuvigny, Th. *J. Organomet. Chem.* **1979**, *177*, 5. Terashima, S.; Tseng, C. C.; Koga, K. *Chem. Pharm. Bull.* **1979**, *27*, 747. Evans, D. A.; Takacs, J. M. *Tetrahedron Lett.* **1980**, 4233.
(21) Goering, H. L.; Kantner, S. S. *J. Org. Chem.* **1983**, *48*, 721.
(22) Whitesides, G. M.; Fischer, W. F., Jr.; San Fillipo, J., Jr.; Bashe, R. W.; House, H. O. *J. Am. Chem. Soc.* **1969**, *91*, 4871. Johnson, C. R.; Dutra, G. A. *Ibid.* **1973**, *95*, 7777, 7783.

Scheme IV. Stereochemistry and Regiochemistry of Alkylation of (*R*)-3-OAc with LiCu(*n*-Bu)$_2$



Scheme V. Stereochemistry and Regiochemistry of Alkylation of (*R*)-2-OAc with LiCu(CN)Me

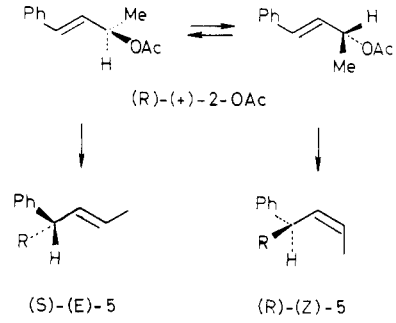


the 10% loss of configuration (5% retention) occurs in the 2-OAc → 8 transformation, which we believe involves two steps, complexation of the cuprate with the double bond to give an olefin–copper(I) π complex, followed by conversion to the S_N2' σ-allyl complex (8).[21,23] Evidently the stereochemistry is determined in the initial complexation step, which presumably occurs on the least hindered side of the double bond.[23] In sterically unbiased systems this is the anti side and this leads to anti γ-alkylation and α-alkylation with inversion. In other work we have found that steric hinderance can alter the stereochemistry of α- and γ-alkylation without any important change in regiochemistry. For example, in the *exo*-bicyclo[3.2.1]oct-3-en-2-yl system, only syn γ-alkylation and α-alkylation with retention are observed for alkylations with dialkyl- and alkylcyanocuprates.[5]

Results for γ-alkylation of (*R*)-(−)-3-OAc with LiCu(*n*-Bu)$_2$ are presented in Scheme IV. The γ-alkylation product, (*E*)-**4b**, containing <1% of the *Z* isomer, was shown to have the *R* configuration by conversion (Lemeux oxidation)[15] to (*R*)-(−)-**7**. As indicated, the latter is 86% optically pure. Because the (*R*)-(*E*)-**4b** is contaminated with about 1% (*S*)-(*Z*)-**4b** [which leads to (*S*)-(+)-**7**], we conclude that the (*R*)-(*E*)-**4b** has an ee of ~88%. Thus, γ-alkylation involves ~94% anti and 6% syn bonding.

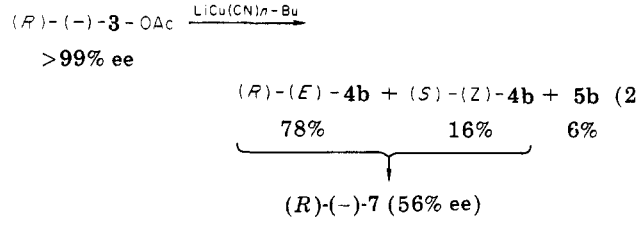
Results for alkylation of (*R*)-2-OAc with LiCu(CN)Me are presented in Scheme V. This reaction is regiospecific[23] and gives substantial γ-alkylation (51%), as would be expected from other work.[25] Diimide reduction gave a binary mixture of (*S*)-(+)-2-phenylpentane (**11**)[8] and 1-phenyl-3-methylbutane (**12**), which after isolation in pure form (preparative GC) consisted of 53% (*S*)-**11** and 47% **12**. The rotation for (+)-**11** shown in the scheme has been corrected for dilution with 47% of achiral **12**. The magnitude and sign of the rotation identify the active material as (*S*)-**11** with an ee of 46%.[26]

Scheme VI. Products Resulting from Anti γ-Alkylation of (*R*)-2-OAc



For reasons outlined in Scheme VI, we conclude that (*E*)- and (*Z*)-**5** (γ-alkylation product) derived from active **2**-OAc have opposite configurations, as indicated in Scheme V, and are of equal optical purity. Anti γ-alkylation of the two reactive conformers of (*R*)-**2**-OAc gives (*S*)-(*E*)-**5** and (*R*)-(*Z*)-**5**. Diimide reduction converts these to enantiomers. Thus, the ee of the reduction product (**11**) will be less than that for (*E*)- and (*Z*)-**5**. The information in Scheme V shows that the composition of the γ-alkylation product is 76% (*E*)-**5a** and 24% (*Z*)-**5a**. Thus, the optical purity of **11** derived from this mixture will be 48% less than that of the (*E*)- and (*Z*)-**5a**. The observed ee for (*S*)-**11** derived from the alkylation product is 46%. Thus, that for (*E*)- and (*Z*)-**5a** is ~95%. This shows that the γ-alkylation in Scheme V involves 95% excess anti bonding or about 5% loss of optical configuration.

Alkylation of (*R*)-**3**-OAc with LiCu(CN)*n*-Bu gives the product distribution shown in eq 2 (see Schemes II and IV for structures). The regiochemistry (94% γ-alkylation) is similar to that observed with LiCu(*n*-Bu)$_2$ (92% γ-alkylation); however, there is a striking difference in the *E*/*Z* ratio for the γ-alkylation product (**4b**). With the dibutylcuprate, (*Z*)-**4b** is formed in only trace amounts (Scheme IV), whereas the γ-alkylation product (**4b**) obtained with the butylcyanocuprate contains 17% of the *Z* isomer.



Lemieux oxidation of the alkylation product led to (*R*)-(−)-**7**, 56% ee, as illustrated by eq 2. For reasons analogous to those outlined in Scheme VI, we conclude that (*E*)- and (*Z*)-**4b** have opposite configurations, as indicated in eq 2, and are of equal optical purity. The optical purity of **7** derived from a mixture of 17% (*S*)-(*Z*)-**4b** and 83% (*R*)-(*E*)-**4b** will be 34% less than that of (*E*)- and (*Z*)-**4b**. The optical purity of **7** (56%) indicates that that of (*E*)- and (*Z*)-**4b** is about 85%. Thus, in this case the anti/syn ratio for γ-alkylation is about 93:7.

The above experiments show that alkylation reactions in this sterically unbiased acyclic system are stereospecific.

(23) Goering, H. L.; Kantner, S. S. *J. Org. Chem.* **1981**, *46*, 2144.
(24) The term regiospecific is used as defined earlier (footnote 3, ref 1).
(25) Levisalles, J.; Rudler-Chauvin, M.; Rudler, H. *J. Organomet. Chem.* **1977**, *136*, 103. Trost, B. M.; Klun, T. P. *J. Org. Chem.* **1980**, *45*, 4256.
(26) The absolute configuration and rotation for 2-phenylpentane (**11**) were established previously (ref 8).

α-Alkylation proceeds with excess inversion (Scheme II), and γ-alkylation involves excess anti bonding (Schemes IV and V and eq 2). It is significant that the stereospecificity is the same (~90%), within experimental error, for α- and γ-alkylation. This is in agreement with our proposed[1,21] mechanistic pathway in which the S_N2' σ-(allyl)copper(III) complex is the initial oxidative addition product [i.e. the (*R*)-**2**-OAc → **8** transformation in Scheme III]. Presumably, the stereospecificity for both α- and γ-alkylation is the same as for the initial oxidative addition reaction.

Experimental Section

General Methods. Spectra of optically active samples were indistinguishable from those for authentic racemic samples.[6] Optical rotations were determined with a Perkin-Elmer Model 141 polarimeter using a water-jacketed 1-dm cell. Ethyl ether was distilled from lithium aluminum hydride. Solutions of methyllithium in ether and *n*-butyllithium in *n*-hexane were standardized[27] prior to use. Cuprous cyanide was purified by a standard method.[28] Dioxane used for the Lemieux oxidation was pretreated with $KMnO_4$[15] and diglyme was dried over molecular sieve 4A. The alkylation products, **4a,b** and **5a,b**, were characterized in earlier work.[6]

Materials. (*R*)-(+)-α-Methyl-γ-phenylallyl alcohol (2-OH)[8] and (*R*)-(−)-α-phenyl-γ-methylallyl alcohol (3-OH)[11] were prepared as described earlier. The absolute rotations of (+)-2-OH and (*R*)-(+)-2-OAc were established in the earlier work.[8] Optical purities and absolute rotations for (*R*)-(−)-3-OH and (*R*)-(−)-3-OAc were established as follows. Three crops of (*R*)-(−)-3-OH, α^{30}_D −46.8, −48.6, and −52.1° (neat), were converted[6] to three samples of (*R*)-(−)-3-OAc, α^{23}_D −0.48, −1.61, and −3.50° (neat). The sample of (*R*)-(−)-3-OAc with α^{23}_D −0.48° was reduced with diimide[6] to **(R)-(+)-1-phenyl-1-butyl acetate (6-OAc)**, $[\alpha]^{24}_D$ 100° (benzene). In a similar way, the sample of (*R*)-(−)-3-OAc with α^{23}_D −1.61° was converted to (*R*)-(+)-6-OAc, $[\alpha]^{24}_D$ 99.4° (benzene). Diimide reduction of the sample of (*R*)-(−)-3-OH with α^{30}_D −46.8° gave **(*R*)-(+)-1-phenyl-1-butanol (6-OH)**, $[\alpha]^{24}_D$ 39.6° (benzene) which was converted to (*R*)-(+)-6-OAc, $[\alpha]^{24}_D$ 100° (benzene). The NMR spectrum of the latter ($CDCl_3$) in the presence of Eu(hfbc)$_3$[7] with an *R*/*S* ratio of 0.25 showed the sample to be optically pure. Under these conditions, $\Delta\Delta\delta$ = 0.065 ppm for the enantiotopic acetoxy methyl signals. In another experiment, a mixture of 140.6 mg of (*R*)-(+)-6-OAc, $[\alpha]^{24}_D$ 100° (benzene), and 138.8 mg of *dl*-6-OAc was prepared. This mixture had $[\alpha]^{24}_D$ 50.6° (benzene). The NMR spectrum in the presence of Eu(hfbc)$_3$ as described above showed the ee for the mixture was 51%. Thus, the absolute rotation for (*R*)-(+)-6-OAc is $[\alpha]^{24}_D$ 100° (benzene) and that for (*R*)-(+)-6-OH is $[\alpha]^{24}_D$ 39.6° (benzene). These correlations show that the three samples of (*R*)-(−)-3-OH, α^{30}_D −46.8 to −52.1°, and the three samples of (*R*)-(−)-3-OAc, α^{23}_D −0.48 to −3.50°, were optically pure The reason for the variation of rotations for different samples of optically pure 3-OH and 3-OAc is not known.

The absolute rotation for **2-methylhexanoic acid (7)** was established as follows. A sample of (*S*)-(+)-**7**, $[\alpha]^{22}_D$ 21.2° (*c* 5.5, ether), was prepared by a reported method.[18] This sample was converted to **(*S*)-(+)-methyl 2-methylhexanoate**, $[\alpha]^{20}_D$ 23.0° (*c* 5.6, $CHCl_3$), by reaction with diazomethane. This was shown to be 97% optically pure with Eu(hfbc)$_3$.[7] Thus, the absolute rotation for **7** is $[\alpha]^{22}_D$ 21.9° (ether). The NMR spectrum ($CDCl_3$) of the methyl ester of **7** in the presence of Eu(hfbc)$_3$, *R*/*S* ratio 0.6, had a $\Delta\Delta\delta$ of 0.179 ppm for the enantiotopic 2-methyl signals (doublet). Thus, the ee can readily be determined by this method.

Reaction of (R)-(+)-2-OAc with Lithium Di-*n*-butylcuprate. The results of a typical experiment are outlined in Scheme II. In this experiment, a 500-mL three-necked flask equipped with a stirrer and septum was charged with 12.3 g of CuI (64.6 mequiv). After the flask was flushed with dry N_2, 80 mL of anhydrous ether was added, and the flask was cooled to −3 °C, after which 49.1 mL of a 2.63 M solution of *n*-BuLi in *n*-hexane (129 mmol) was added. The dark reddish-brown solution was stirred for 1.5 h at −3 °C, after which a solution of 4.6 g of (*R*)-(+)-2-OAc (24.2 mmol), $[\alpha]^{20}_D$ 150° ($CHCl_3$) >99% ee,[8] in 20 mL anhydrous ether was added, and stirring was continued for 7 h at −3 °C. The reaction was quenched with aqueous NH_4Cl, and the resulting precipitate was removed by filtration. The clear solution was extracted with several portions of ethyl acetate, and the precipitate was washed thoroughly with ethyl acetate. The ethyl acetate extracts were combined, washed with brine, dilute $Na_2S_2O_3$, and brine, and dried over $MgSO_4$. The solvent was carefully removed by distillation, and the residue was purified by column chromatography (SiO_2, pentane/ether = 10), followed by vacuum distillation. The composition of the 2.85 g (63%) of colorless oil, bp 98–99 °C (2 mm), was determined by capillary GC as described earlier.[6] This composition is shown in Scheme II.

Determination of Enantiomeric Excess of Alkylation Product 4b. As indicated in Schemes II and IV and eq 2, the ee for this product was established by Lemieux oxidation[15] to 2-methylhexanoic acid (**7**). In a typical experiment, the alkylation product described in the preceeding section (and in Scheme II) was oxidized as follows. A flask equipped with a stirrer and septum was charged with 70 mL of dioxane and 1.38 g (7.3 mmol) of the above olefinic mixture containing 96% **4b**. The flask was placed in an ice bath and a chilled (0 °C) solution of 12.5 g (58.4 mmol) of $NaIO_4$, 0.8 g (5.1 mmol) of $KMnO_4$ and 0.4 g of Na_2CO_3 in 40 mL of water was added to the dioxane solution of olefins. The resulting purple mixture was stirred at room temperature for 48 h, after which 10 mL of 30% H_2O_2 was carefully added to the chilled (0 °C) solution. The brown precipitate was filtered and washed thoroughly with ether. The aqueous filtrate was saturated with NaCl and extracted with ether and $CHCl_3$. The organic extracts were combined and concentrated by distillation. The residue was extracted with three portions of 5% Na_2CO_3. The aqueous basic extracts were combined, washed well with ether, and acidified. The product (**7**) separated as an oil and was isolated by extraction with ether. After the product was dried ($MgSO_4$) and the ether was removed (rotary evaporation), a pale yellow oil was obtained. The crude product was purified by column chromatography (SiO_2, pentane/ether = 1), followed by vacuum distillation. The clear colorless product (**7**) had bp 92–93 °C (4.5 mm) and $[\alpha]^{22}_D$ −19.5° (*c* 5.9, ether) (88% ee). The spectral properties (IR and NMR) were the same as those of an authentic sample of *dl*-**7**.[18]

Reaction of (*R*)-(−)-3-OAc with Lithium Di-*n*-butylcuprate. The results of this experiment are outlined in Scheme IV. The procedures for alkylation, isolation of product, and oxidation of the alkylation product mixture to **7** were the same as described above for alkylation of 2-OAc (Scheme II). In this experiment, oxidation of the alkylation product gave (*R*)-(−)-**7**: bp 76–77 °C (1.8 mm), $[\alpha]^{22}_D$ −18.8° (*c* 6, ether) (87% ee). The spectral properties (NMR and IR) were the same as for an authentic sample of *dl*-**7**.[18]

Reaction of (*R*)-(+)-2-OAc with Lithium Methylcyanocuprate. The results of a typical experiment are outlined in Scheme V. In this experiment a 250-mL three-necked flask equipped with a stirrer and septum was charged with 3.8 g of CuCN (40 mequiv). After the flask was flushed with N_2, 60 mL of anhydrous ether was added, and the flask was cooled to −3 °C. A chilled (−3 °C) solution of 1.6 M CH_3Li in ether (25 mL, 40 mmol) was added, and the cooled mixture was stirred for 1 h. The cooling bath was removed and a solution of 2.8 g of (*R*)-(+)-2-OAc (15 mmol) in 6 mL of anhydrous ether was added. The resulting mixture was stirred for 20 h at room temperature, after which the reaction was quenched with aqueous NH_4Cl. The alkylation product was extracted, isolated, and purified as described above for alkylation of 2-OAc with LiCu(*n*-Bu)$_2$. The purified colorless product, bp 59 °C (3.3 mm), was obtained in 76% yield (1.66 g). The composition of this oil was determined by capillary GC as described earlier.[6] As shown in Scheme V, the ee of the (*E*)- and (*Z*)-**5a** in the product was determined by reduction to 2-phenylpentane (**11**). The procedure for this reduction and determination of the absolute rotation for **11**, α^{23}_D 16.7° (neat), has been reported elsewhere.[8] In this experiment the reduction product was a binary mixture of 53% **11** and 47% **12** and had α^{23}_D 4.10° (neat). After correction for dilution by the achiral **12**, the rotation for **11** is 7.7° (neat). This corresponds to an ee of

(27) Reference 6, footnote 15.
(28) Barber, H. J. *J. Chem. Soc.* **1943**, 79.

46%. Components in the binary mixture of 11 and 12 were identified by comparison of spectral properties and GC retention times with those of authentic samples.[8]

Alkylation of (*R*)-(−)-3-OAc with Lithium *n*-Butylcyanocuprate. The pertinent results are presented in eq 2. The procedure for alkylation was the same as described above for alkylation of 2-OAc with $LiCu(CN)CH_3$, except that 2.6 M *n*-BuLi in *n*-hexane was used instead of ethereal MeLi. The isolated alkylation product had bp 85–86 °C (1.4 mm). The composition shown in eq 2 was determined by capillary GC as described earlier.[6] Oxidation by the procedure described above for determination of the enantiomeric excess of active **4b** gave (*R*)-(−)-**7**, $[\alpha]^{22}_D$ −12.3° (*c* 6, ether). Spectral properties were the same as for an authentic sample of *dl*-**7**.

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Registry No. (*R*)-(+)-**2**-OH, 62413-47-2; (*R*)-(+)-**2**-OAc, 84519-63-1; (*R*)-(−)-**3**-OH, 87246-95-5; (*R*)-(−)-**3**-OAc, 87246-94-4; (*R*)-(+)-**6**-OH, 22144-60-1; (*R*)-(+)-**6**-OAc, 84194-64-9; (*R*)-(−)-**7**, 51703-97-0; $LiCu(n\text{-}Bu)_2$, 24406-16-4; LiCu(CN)Me, 41753-78-0.

Further Examples of Enhanced Lengthening of Strained Carbon-Carbon Bonds by Orbital Interactions[1]

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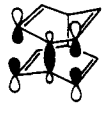
Three examples are given to supplement our previous observation of effective orbital interactions between π orbitals through a strained σ bond to give extraordinarily long C–C bonds. They are 3,5-disubstituted 2,6-diphenylpentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-4,8,11-trione (**3b,c**), pentacyclo[8.6.0.0^{1,5}.0^{2,9}.0^{6,11}]hexadeca-3,7,13,15-tetraene (**4a**), and *anti*-5,6-di-*n*-butyl-5,6-diphenyldecane (**5a**). One of the cyclobutane bonds in **3b,c** and **4a**, as well as the central bond of **5a**, well exceeds 1.6 Å. The operation of the through-bond coupling between phenyl or vinyl groups in these molecules has been inferred from combined molecular mechanics and semiempirical MNDO molecular orbital calculations. Effects of para substituents in 1,4-diphenylbicyclo[2.2.0]hexane (**7c**) have been studied computationally by using the MNDO method, and π donor groups such as O^- and CO_2^- are found to further elongate the central bond up to 0.02 Å. Direct substitution of π donor groups at C_1 and C_4 of the bicyclo[2.2.0]hexane skeleton is predicted to be more effective in giving longer lengths for the C_1–C_4 bond. Strong steric interactions among alkyl side chains in **5** are analyzed.

Recently, Mislow and his collaborators[3] proposed that when a C–C σ bond is surrounded by parallel π systems as in the central bond of 1,1′,4,4′-biphenylene (**1**), the bond



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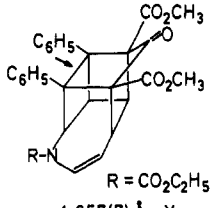

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is elongated as the result of "through-bond" orbital interactions.[4] Among a number of orbital interaction modes, two of them, $\pi_- \rightarrow \sigma^*$ and $\sigma \rightarrow \pi_+^*$, contribute to the bond elongation, the former by increasing antibonding character in the occupied orbital and the latter by donating bonding electrons to the unoccupied orbital (Figure 1). Quantitative perturbational molecular orbital treatment of orbital interactions in **1** indicates that the former type, $\pi_- \rightarrow \sigma^*$, is dominant, because of greater overlap between these orbitals than that between σ and π_+^* orbitals.[3b] The elongated bond often exceeds 1.6 Å.

We have recently realized that a remarkably long C–C bond found in cage molecule **2** provides an interesting extension of Mislow's bond-elongation mechanism: when the intervening σ bond has some prestrain, the bond-lengthening effect is strongly enhanced.[5] This finding

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