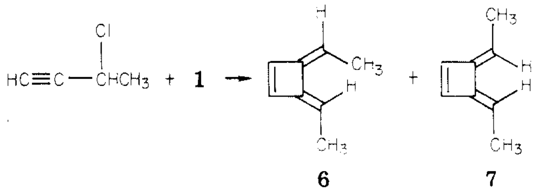

7 on the basis of their NMR spectra.[13]

The following is a typical procedure for the reductive cyclodimerization reaction. Bis(triphenylphosphine)nickel(II) dibromide (5 mmol) and triphenylphosphine (10 mmol) are dissolved in 50 mL of tetrahydrofuran at 25 °C under an argon atmosphere. Powdered zinc (50) mmol) is added and the reaction mixture is stirred at 25 °C for 30 min. The deep-red solution is cooled to 0 °C and 25 mmol of the propargyl chloride is added. (It is to be noted that the reaction is catalytic in 3 in the presence of excess zinc, although the reaction decreases in reactivity with further extent of the reaction.) After 10 min, 400 mL of pentane is added. The organic layer is decanted and is washed with ice water and is then dried ($MgSO_4$). The pentane is removed by distillation and the product is purified by trap-to-trap distillation on a vacuum line, giving 65–75% yields of product. All manipulations must be carried out under an argon atmosphere in order to avoid polymerization of the product.[8]

The mechanism of this very interesting reductive cyclodimerization is currently being investigated in our laboratories.

Acknowledgement is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for the support of this research (PRF No. 11713-AC1,3).

Registry No. 3, 15133-82-1; **4a**, 1111-97-3; **4b**, 999-79-1; **5a**, 3642-14-6; **5b**, 80865-52-7; **6**, 80865-53-8; **7**, 80865-54-9; 3-chloro-1-butyne, 21020-24-6; *cis*-1,2-diisopropylcyclobutane, 80865-55-0.

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(12) **5a**: ^{1}H NMR (C_6D_6) δ 1.76 (s, 6 H), 1.93 (s, 6 H), 6.84 (s, 2 H); ^{13}C NMR (C_6D_6, proton decoupled) δ 18.6, 19.6, 111.3, 136.0; ^{13}C NMR (C_6D_6, proton nondecoupled) δ 18.6 (q of q, J = 125, 4.5 Hz, inner CH_3's, 19.6 (q of q, J = 125, 4.5 Hz, outer CH_3's), 111.3 (s, isopropylidene C), 136.0 (s, C_3 and C_4 of ring), 136.0 (d, J = 173 Hz, C_1 and C_2 of ring); mass spectrum, parent ion calcd for $C_{10}H_{14}$ m/e 134.110, observed m/e 134.111. **5b**: ^{1}H NMR (C_6D_6) δ 1.85 (s, 6 H), 1.91 (s, 6 H), 1.96 (s, 6 H); GC/MS parent ion m/e 162.

(13) NMR spectrum of the volatile fraction. **6**: (C_6D_6) δ 1.61 (d), 1.77 (d), 5.01 (q), 5.32 (q), 6.56 (s), 6.72 (s); **7**: δ 1.79 (d), 5.02 (q), 6.74 (s).

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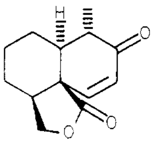
tert-Butyllithium Additions to Enones. Preferential Axial Attack

Summary: The conjugate addition of *tert*-butyllithium to cyclic enones has been shown to occur preferentially in an axial fashion.

Sir: Six-membered rings bearing *axial tert*-butyl groups are rare. In most cases compounds which have a *tert*-butyl substituent adopt a conformation in which the bulky group is equatorial. This tendency for the *tert*-butyl group to anchor a particular chair conformation has been exploited often in studies of cyclohexane chemistry.[1]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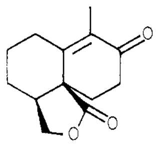
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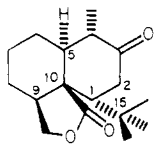

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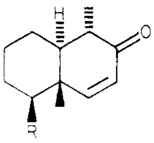
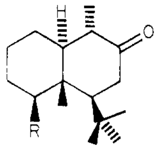
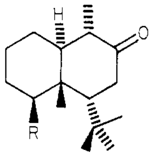

4, R = OMe
5, R = H


6, R = OMe
8, R = H


7, R = OMe
9, R = H

Recently, however, a number of axial *tert*-butyl-substituted compounds have been reported.[2-6] For most of these substances the axial disposition of the bulky group results from the interplay and balance of various conformational interactions in which a particular conformer having an axial *tert*-butyl group either dominates or substantially contributes to the conformational equilbrium in solution.[2,3] For some examples an axial *tert*-butyl conformer has been shown to exist in the solid state but not necessarily in solution.[4-6] In only one case, that of 8β-*tert*-butyl-*trans*-decahydroquinoline,[7] is the *tert*-butyl group constrained to be axial regardless of the conformation of the ring system. In this report we present the preparation of three new carbocyclic compounds containing *configurationally fixed axial tert-butyl groups*. Each of the compounds is produced, moreover, as the *major product of a kinetically controlled conjugate addition reaction.*

Enone lactone 1,[8] prepared from the previously described 2[9] was treated in THF solution with 1 equiv of *tert*-butyllithium at ambient temperature. A single product,[10] the saturated keto lactone 3, mp 124–125 °C, was obtained in 60% yield. The stereochemistry assigned

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(1) Eliel, E. L. "Stereochemistry of Carbon Compounds"; McGraw-Hill: New York, 1962; Chapter 8.

(2) (a) Eliel, E. L.; Knoeber, M. C. *J. Am. Chem. Soc.* **1966**, *88*, 6347. (b) *Ibid.* **1968**, *90*, 3444.

(3) (a) Van de Graaf, B.; van Bekkum, H.; van Koningsveld, H.; Sinnema, A.; van Veen, A.; Wepster, B. M.; van Wijk, A. M. *Recl. Trav. Chim. Pays-Bas.* **1974**, *93*, 135. (b) Van de Graaf, B.; Baas, J. M. A.; Wepster, B. M. *Ibid.* **1978**, *97*, 268.

(4) van Koningsveld, H. *Acta Crystallogr., Sect. B* **1973**, *29*, 1214.

(5) Johnson, F.; Zito, S. W.; Sarma, R.; McKeever, B. M. *Tetrahedron Lett.* **1978**, 753.

(6) Geneste, P.; Kamenka, J-M.; Roques, R.; DeClercq, J. P.; Germain, G. *Tetrahedron Lett.* **1981**, 949.

(7) (a) Hargrave, K. D.; Eliel, E. L. *Tetrahedron Lett.* **1979**, 1987. (b) 1-*tert*-Butyladamantane must also necessarily have an axial *tert*-butyl group as well as an equatorial one: Woodworth, C. W.; Buss, V.; Schleyer, P. v. R. *J. Chem. Soc., Chem. Commun.* **1968**, 569.

(8) For **1**: ^{1}H NMR ($CDCl_3$) δ 6.90 (d, J = 10 Hz, 1 H), 6.20 (d, J = 10 Hz, 1 H), 4.70 (dd, J = 9, 4 Hz, 1 H), 4.05 (d, J = 9 Hz, 1 H), 1.35–2.50 (m, 8 H), 1.15 (d, J = 7 Hz, 3 H); IR ($CHCl_3$) 1770, 1685 cm^{-1}; mp 120–121 °C. For **3**: ^{1}H NMR ($CDCl_3$) δ 3.89 (dd, J = 9.5, 4.1 Hz, 1 H), 3.79 (d, J = 9.5, 1 H), 3.17 (qd, J = 13, 6.6 Hz, 1 H), 2.86 (m, 1 H), 2.71 (ddd, J = 15.1, 6.8, 1.1 Hz, 1 H), 2.53 (dd, J = 15.1, 2.4 Hz, 1 H), 2.05 (dd, J = 6.8, 2.4 Hz, 1 H), 1.98 (m, 1 H), 1.86–1.04 (m, 6 H), 1.02 (s, 9 H), 1.00 (d, J = 6.6 Hz, 3 H).

(9) (a) Goldsmith, D. J.; John, T. K.; vanMiddlesworth, F. *Synth. Commun.* **1980**, *10*, 551. (b) Enone lactone **1** was converted into **2** in 73% overall yield by the following sequence: (1) H_2, Pd, HOAc, $HClO_4$, (2) LDA, PhSeBr, (3) O_3, CH_2Cl_2 (4) Δ, Et_2NH.

(10) Satisfactory elemental analyses or precise mass measurements were obtained for all new compounds reported herein.

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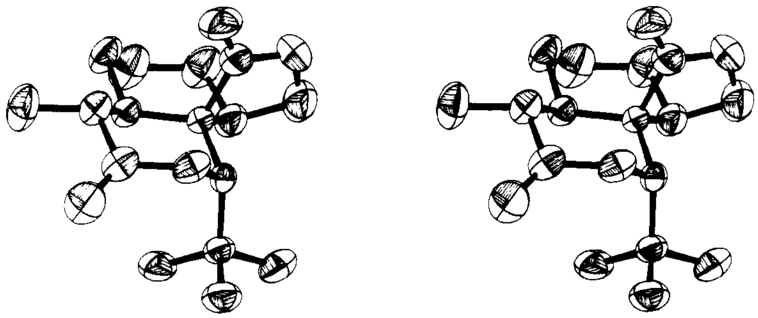

Figure 1. Stereoscopic view of compound **3**.

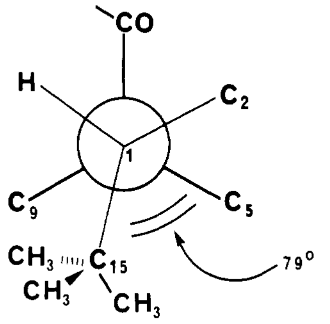

Figure 2. Dihedral angle distortion in compound **3**.

to **3** was based on the observed C-1–C-2 coupling constants in the ^{1}H NMR spectrum measured at 300 MHz.[11] J values of 6.8 and 2.4 Hz are found for the coupling of the C-2 methylene protons with the single proton at C-1. For the methylene protons themselves, J_{AB} = 15 Hz. These values are compatible with an equatorial assignment for the C-1 proton, and thus an axial placement of the *tert*-butyl group. An X-ray structure determination provided conclusive proof for this stereochemistry (Figure 1)[12].

In accord with the results of Hargrave and Eliel,[7] only minor distortions of the ring system seem to be necessary to accomodate the bulky *tert*-butyl substituent. Thus, for example, the experimentally found dihedral angle for C-15, C-1, C-10, C-5 (Figure 2) is 79°, a distortion which serves to bend the *tert*-butyl group away from the axial protons at C-5 and C-9.

In contrast to the unique production of the axial compound from enone **1**, treatment of enones **4** and **5** with *tert*-butyllithium gave mixtures of 1,2- and 1,4-addition products. In each case, however, the conjugate addition product constituted the major fraction of the material. Thus from **4** we obtained the equatorial and axial 1,4-addition products **6** and **7**[13] in 65% yield. The ratio of **6** to **7** was 1:4.6, and the two isomers were readily identified from their ^{1}H NMR spectra. For the crystalline isomer **7**, mp 129–131 °C, the C-2 methylene protons exhibit an overlapping d,d,d pattern at δ 2.54. Since the coupling constants for these protons with the C-1 proton, 3.7 and 6.1 Hz, are comparable with those found in the spectrum of **3**, isomer **7** must be the axial-substituted one. In contrast, the spectrum of **6** shows J values for the C-2–C-1 couplings of 12.1 and 5.5 Hz, indicative of an axial proton and an equatorial *tert*-butyl group at C-1.

Similar NMR data[14] support the structural and stereochemical assignments for **8** and **9**, the conjugate addtion products formed from enone **5**[15] and *tert*-butyllithium. Adducts **8** and **9** were obtained in 65% yield and in a ratio 1:1.9.

Tertiary alkyllithium reagents are known to add preferentially to enones in conjugate fashion,[16] and evidence has been adduced to show that the mechanism of the reaction is a kinetically controlled electron-transfer process.[17] We have now shown that *axial* addition is the preferred stereochemical mode of these reactions. From our results with enone **5**, it is clear that this preference is small when little or no difference in hindrance from either the axial or equatorial direction of approach is present. For **4**, a substrate bearing a group larger than hydrogen in the equatorial plane, the preference for axial attack increases by a factor of approximately 2. In the case of enone **1**, however, hindrance of the approach of the reagent from the equatorial direction does not appear to be the major factor in the exclusive formation of the axial isomer. Enone lactone **1** has a particularly low reduction potential, $E_{1/2}$ = −1.81 V (vs. SCE in DMF). For enones **4** and **5**, the $E_{1/2}$ values are −2.11 and −2.12 V. Thus, it is likely that addition of a single electron to **1** involves both carbonyl groups and that electron transfer from *tert*-butyllithium to **1** produces radical-anion **10** as an intermediate.[18]

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[11] We thank Dr. Robert C. Long, Jr., of this department, for obtaining the 300-MHz spectra.

[12] The crystallographic structure determination for **3** has been reported by Rubin, B.; Danoff, T.; Brooks, L. *Acta Crystallogr.* **1981**, in press. Crystallographic data: $C_{17}H_{26}O_3$, orthorhombic, $P2_12_12_1$, a = 11.598 (2) Å, b = 9.382 (3) Å, c = 13.985 (3) Å, Z = 4, D_{calcd} = 1.214, D_{meas} = 1.23 (3) mg m^{-3}, λ = 1.5418, F(000) = 608, fw 278. In Pasteurian fashion compound **3** spontaneously resolves when crystallized.

[13] For **6**: ^{1}H NMR (CHCl$_3$) δ 3.20 (s, 3 H), 3.07 (dd, J = 10.3, 4.4 Hz, 1 H), 2.57 (dd, J = 17.6, 5.5 Hz, 1 H), 2.32 (ddd, J = 17.6, 12.1, 1.5 Hz, 1 H), 2.06 (m, 1 H), 1.71 (m, 1 H), 1.57 (dd, J = 12.1, 5.5 Hz, 1 H), 1.54 (m, 2 H), 1.0–1.3 (m, 4 H), 1.04 (d, J = 7 Hz, 3 H), 0.94 (s, 9 H), 0.91 (s, 3 H). For **7**: ^{1}H NMR (CDCl$_3$) δ 3.5 (dd, J = 4.8, 10.7 Hz, 1 H), 3.18 (s, 3 H), 2.54 (ddd, J = 16.5, 6.1, 3.7 Hz, 2 H), 2.11 (m, 1 H), 2.04 (dd, J = 6.1, 3.7 Hz, 1 H), 1.99 (m, 1 H), 1.76 (m, 2 H), 1.6–1.1 (m, 4 H), 1.00 (d, J = 7 Hz, 3 H), 0.97 (s, 12 Hz, 3 H).

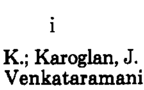
[14] For **8**: ^{1}H NMR (CDCl$_3$) δ 2.50 (dd, J = 14.5, 5.1 Hz, 1 H), 2.40 (ddd, J = 14.5, 13.1, 1.3 Hz, 1 H), 2.15 (m, 2 H), 1.85–1.12 (m, 9 H), 1.05 (s, 3 H), 1.00 (s, 9 H), 0.96 (d, J = 7 Hz, 3 H). For **9**: ^{1}H NMR (CDCl$_3$) δ 2.56 (dd, J = 15.4, 5.9 Hz, 1 H), 2.53 (ddd, J = 15.4, 6.4, 0.9 Hz, 1 H), 2.0 (qd, J = 11.4, 7.3 Hz, 1 H), 1.9–1.4 (m, 1 H), 1.13 (s, 3 H), 1.02 (s, 9 H), 1.02 (d, J = 7.3 Hz, 3 H).

[15] (a) Piers, E.; Phillips-Johnson, W. M.; Berger, C. *Can. J. Chem.* **1975**, *53*, 1291. (b) Agami, C.; Chauvin, M.; Levisalles, J. *Tetrahedron Lett.* **1979**, 1855.

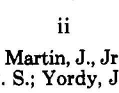
[16] (a) Jallabert, C.; Spassky, A. *C. R. Hebd. Seances Acad. Sci., Ser. C* **1973**, 879. (b) House, H. O., *Acc. Chem. Res.* **1976**, *9*, 59.

[17] Still, W. C.; Mitra, A. *Tetrahedron Lett.* **1978**, 2659.

[18] Enone i has an $E_{1/2}$ value of −1.95 V (vs. SCE/DMF), while its corresponding monoketal derivative (saturated carbonyl) has an $E_{1/2}$ value of −2.11 V. On reduction with lithium in ammonia, i forms the cyclopropyl ketol ii:

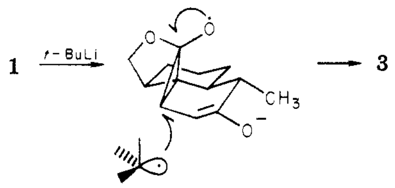


i



ii

Reusch, W.; Grimm, K.; Karoglan, J. E.; Martin, J., Jr.; Subrahammanian, K. P.; Toong, Y-C.; Venkataramani, P. S.; Yordy, J. D.; Zouterdam, P. *J. Am. Chem. Soc.* **1977**, *99*, 1953.



10

Combination of **10** with the *tert*-butyl radical should then occur with inversion to produce the observed axially substituted product **3**.

Acknowledgment. This work was supported by a grant from the National Institutes of Health (ES-01615).

Registry No. **1**, 80865-72-1; **2**, 76140-17-5; **3**, 80865-73-2; **4**, 80865-74-3; **5**, 56763-86-1; **6**, 80865-75-4; **7**, 80865-76-5; **8**, 80865-77-6; **9**, 80924-98-7; *tert*-butyllithium, 594-19-4.

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