Reactions of Pivaloin Derivatives with Lithium Tetramethylpiperidide

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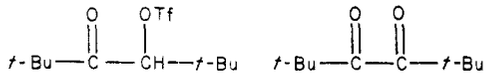
The reaction of lithium tetramethylpiperidide (LiTMP) with a series of derivatives of pivaloin has led to a variety of unusual transformations. The reaction of LiTMP with the triflate derivative of pivaloin (7) gave the reduced ketone 2,2,5,5-tetramethyl-3-hexanone (9), which is suggested to arise via electron transfer from LiTMP. A labeling study confirmed that α-proton abstraction from 7, giving an enolate anion, did not occur. The mesylate derivative of pivaloin (16) on treatment with LiTMP gave both isomers of 2,2,6,6-tetramethylhept-4-en-3-one (17 and 18) in which an additional carbon was incorporated into the carbon skeleton. A mechanism involving deprotonation of the methyl group of the mesyloxy function followed by intramolecular cyclization into the carbonyl function and subsequent reaction is suggested to account for this transformation. The acetate derivative of pivaloin (26) gave a cyclized product derived from proton abstraction from the methyl group of the acetoxy function, while the tosylate derivative of pivaloin (30) gave a product derived from proton abstraction from the ortho position of the aromatic ring. The α-bromo ketone 4-bromo-2,2,5,5-tetramethyl-3-hexanone (38) was reduced to ketone 9 with LiTMP. Reaction of triflate 7 and the triflate derivative of 3-hydroxycamphor (43) with potassium *tert*-butoxide gave the diketones 2,2,5,5-tetramethyl-3,4-hexanedione (8) and camphorquinone (44), respectively, by β elimination of trifluoromethanesulfinic acid.

The high lability of the trifluoromethanesulfonate[2] (triflate) moiety has led to a variety of mechanistic processes unavailable with less reactive groups such as halide or tosylate. Vinyl cations,[3] secondary cyclopropyl cations,[4] and vinyl carbenes[5] have been generated from suitable precursors by using this leaving group. Our interest in the chemistry of triflate derivatives also led us to attempt to generate α-keto carbenes by α elimination of trifluoromethanesulfonic acid from a α-keto triflates.[6] This goal was not realized in reaction of triflate 1 with lithium tetramethylpiperidide (Scheme I). Instead products 2 and 3, which are formal oxidation products, were formed.[6] No products derivable from the α-keto carbene 4 were formed.

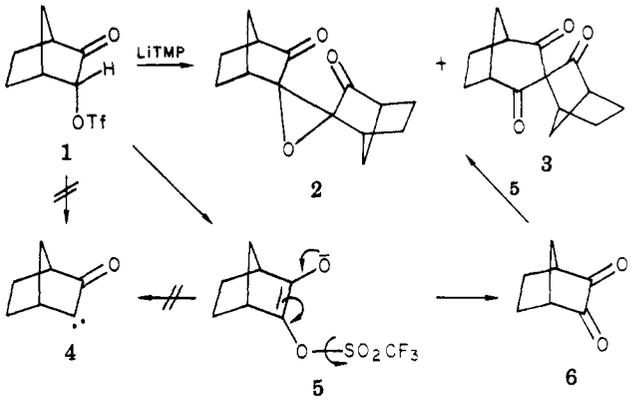
The formation of 2 and 3 was rationalized in terms of a β-elimination (via 5) of trifluoromethanesulfinate leading to norcamphorquinone (6). This is followed by condensation of enolate 5 with the reactive diketone 6 which leads ultimately to the reaction products 2 and 3. No trace of norcamphorquinone (6) could be found. We therefore wanted to obtain further evidence for the intermediacy of this diketone. We also wanted to see if the α elimination of triflic acid (the carbene-forming process) could begin to compete with diketone formation is less rigid systems where the developing vacant orbital of a carbene would not be constrained to an orbital with s character.

It was felt that the triflate derivative of pivaloin (7) was

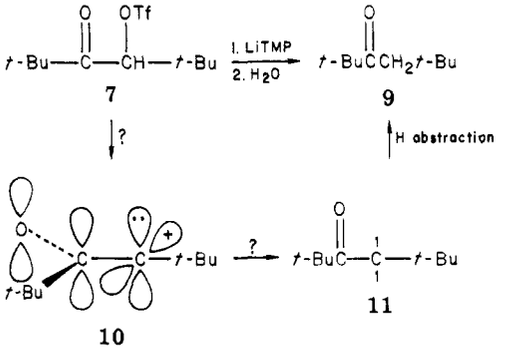


an ideal system for study. The carbene formally derived from 7 would not be constrained in a rigid ring system. Also it was anticipated that diketone 8 should be isolable if the β-elimination process from 7 was important. The expectation is based on the hindered nature of 8 which should render it less susceptible to nucleophilic attack.

Scheme I



Scheme II



Reported here are the results of a study of the reaction of triflate 7 and other derivatives of pivaloin with lithium tetramethylpiperidide.

Results and Discussion

Reaction of Lithium Tetramethylpiperidide (LiTMP) with the Triflate Derivative of Pivaloin. The reaction of lithium diisopropylamide (LDA), a frequently used base for irreversible enolate formation, with triflate 1 has been described.[6] This process results in hydride donation from LDA and concomitant reduction products. The hydride-donating ability of LDA has been investigated in some detail and has been found to be a major competing process in many α-heteroatom-substituted ketones.[8] Consequently this base was not used in

(1) Alfred P. Sloan Fellow, 1977–1980.
(2) Su, T. M.; Sliwinski, W. F.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1969**, *91*, 5386–8.
(3) For leading references, see: Pfeifer, W. D.; Bahn, C. A.; Schleyer, P. v. R.; Bocher, S.; Harding, C. E.; Hummel, K.; Hanack, M.; Stang, P. J. *J. Am. Chem. Soc.* **1971**, *93*, 1513–6.
(4) Creary, X. *J. Org. Chem.* **1975**, *40*, 3326–31.
(5) Stang, P. J. *Acc. Chem. Res.* **1978**, *11*, 107–14.
(6) Creary, X.; Rollin, A. J. *J. Org. Chem.* **1979**, *44*, 1798–1806.

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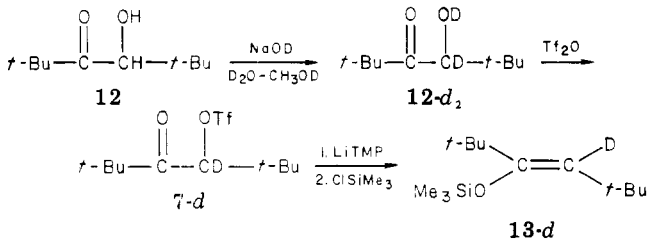
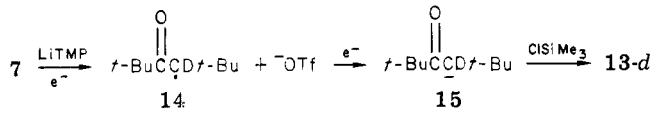
Scheme III



Scheme IV



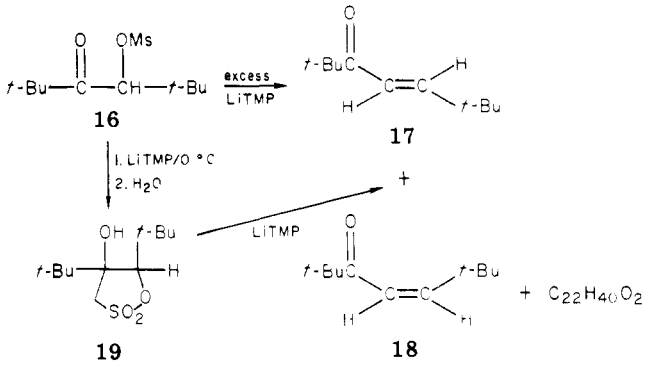
attempts to enolize triflate 7. We have found that LiTMP can be used for irreversible enolate formation in cases where hydride donation from LDA occurs.[8] The previously described[7] triflate 7 was reacted with LiTMP. No reaction occurred at −78 °C, but at room temperature, a smooth reaction ensued giving ketone 9 as the sole product. No trace of diketone 8 could be detected. Ketone 9 is a formal reduction product despite the fact that LiTMP is not capable of β-hydride donation. A potential origin of 9 is shown in Scheme II. If α elimination of triflic acid from 7 occurred forming a linear α-keto carbene 10, then conversion of this singlet to a triplet form (11) might be rapid. Hydrogen-atom abstraction from the solvent, ether, would form the reduction product 9.

The deuterium-labeled triflate 7-*d* was prepared as shown in Scheme III and treated with LiTMP followed by the addition of chlorotrimethylsilane in order to test this mechanistic suggestion. Under these conditions, the unlabeled triflate 7 gave 13, the silyl enol ether derivative of 9. The product of the reaction of labeled 7-*d* was the silyl enol ether 13-*d* in which all of the deuterium was retained. Consequently, the α elimination of triflic acid mechanism (carbene mechanism) of Scheme II has been ruled out.

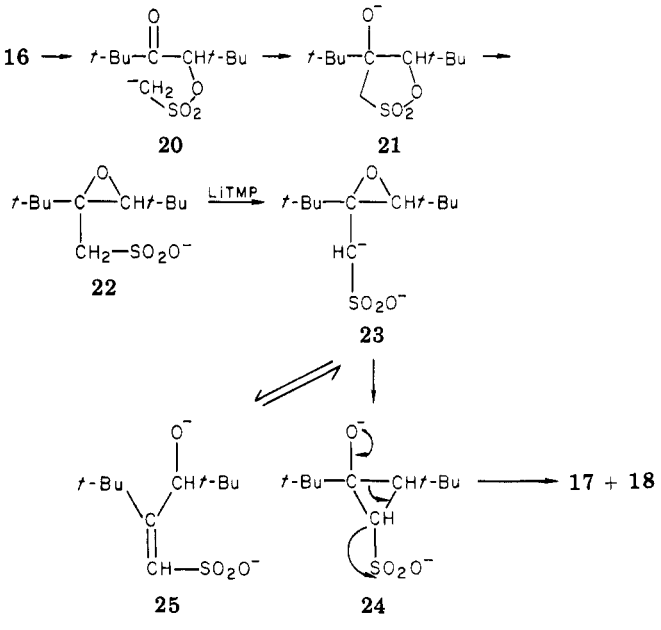
A mechanism which accounts for the observed products is shown in Scheme IV. It is suggested that LiTMP can reduce triflate 7 by an electron-transfer process. Loss of triflate and further reduction of the α-keto radical 14 would give the enolate anion 15 and account for the formation of 9 (or the silyl enol ether derivative 13-*d*).[9] This process would be analogous to dissolving-metal reductions of α-substituted ketones which yield ketone enolate anions.[10] In the present case the electron source is suggested to be LiTMP.

The suggested electron transfer from LiTMP has rare precedence. Scott[11] has obtained evidence that LiTMP can reduce the nonenolizable ketone benzophenone by an electron-transfer process. Ainsworth[12] has also suggested

Scheme V



Scheme VI

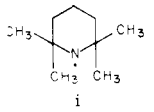


that reduction of a nonenolizable conjugated ynone occurs by electron transfer from LDA.[13] The reduction of 7 is unusual in that the enolizable proton is not abstracted. Additionally, the ketone is not α,β-unsaturated or an aryl ketone, a feature known to lower the reduction potential of ketones.[14] It appears that steric hindrance can reduce the kinetic acidity of the enolizable proton in 7 to the point where the electron-transfer process from LiTMP is faster than enolization.

Reaction of LiTMP with the Mesylate Derivative of Pivaloin. The reaction of LiTMP with triflate 7 is suggested to be initiated by electron transfer. It was therefore felt that any pivaloin derivative with a leaving group α to the carbonyl group should result in a similar electron-transfer reduction to ketone 9 on reaction with LiTMP. Therefore mesylate 16 was prepared and treated with LiTMP at room temperature. However, no ketone 9 was formed. Instead a 4:1 mixture of enones 17 and 18 were produced in 33% yield. A considerable amount of a product which is a formal dimer of 17 (or 18) was also formed (see Scheme V).

An additional carbon atom has been incorporated into the carbon skeleton of 17 and 18. This additional carbon

(7) Creary, X. *J. Org. Chem.* **1979**, *44*, 3938–45.
(8) Kowalski, C.; Creary, X.; Rollin, A. J.; Burke, M. C. *J. Org. Chem.* **1978**, *43*, 2601–8.
(9) As yet we have been unsuccessful in attempts to isolate formal oxidation products which should be derived from i.



i

(10) House, H. O. "Modern Synthetic Reactions", 2nd ed.; W. A. Benjamin: Menlo Park, CA, 1972; pp 156–62.
(11) Scott, L. T.; Carlin, K. J.; Schultz, T. H. *Tetrahedron Lett.* **1978**, 4637–8.
(12) Shen, C. C.; Ainsworth, C. *Tetrahedron Lett.* **1979**, 89–92.
(13) The process seen by Ainsworth could be a simple hydride donation by LDA as well as the suggested electron-transfer, hydrogen-transfer process.
(14) (a) House, H. O. *Acc. Chem. Res.* **1976**, *9*, 59–67. (b) House, H. O.; Prabhu, A. V.; Wilkins, J. M.; Lee, L. F. *J. Org. Chem.* **1976**, *41*, 3067–76, and references therein.

has its origin in the methyl group of the mesyloxy function. When the reaction is carried out at low temperature (−78 to 0 °C) without a large excess of LiTMP, quenching with water gives an 80% yield of the hydroxy sultone **19**. With excess LiTMP at room temperature, **19** is converted to the enone products. A mechanism accounting for these transformations is suggested in Scheme VI. Deprotonation of the methyl group[15] in the mesyloxy function could give **20** and cyclization should afford **21**, accounting for the formation of the hydroxy sultone **19** at low temperature. Epoxide formation via intramolecular displacement of the sulfonate group in **21** should give **22**. Deprotonation of the methylene group in **22** followed by cyclopropane formation could give **24** which should fragment with loss of sulfite ion to give the observed products. While we have no direct evidence for the intermediacy of **22**, **23**, or **24**, this scheme appears reasonable to us. As will be shown, an analogue of **22** can be isolated. The methylene protons of **22** should be acidic enough to be deprotonated by LiTMP.[18] The suggested formation of cyclopropane **24** from **23** might occur in competition with reversible formation of **25**. While this mechanism may be reasonable, we cannot rule out alternative mechanistic possibilities,[16] nor have we attempted to further support the suggested mechanism.

Reaction of LiTMP with the Acetate and Trifluoroacetate Derivatives of Pivaloin. The key to the transformations shown in Scheme VI appears, as before, to be the decreased kinetic acidity of the proton α to the carbonyl group of **16** due to steric factors. Consequently, processes initiated by deprotonation of the mesyloxy group ensue. An analogous process is seen when the acetate derivative of pivaloin (**26**) is treated with LiTMP. Hydroxy lactone **27** is produced quantitatively, presumably by cyclization following deprotonation of **26** at the methyl group of the acetoxy function. This type of process has limited precedent. Lehmann[17] has found that butenolides can be prepared from α-acetoxy ketones, presumably by dehydration of analogues of **27**.

The methyl groups of the mesylate and acetate derivatives of pivaloin are deprotonated by LiTMP more rapidly than electron-transfer processes can occur. It was therefore felt that a leaving group such as trifluoroacetate offered a reasonable chance to observe electron-transfer reduction by LiTMP. However, reaction of trifluoroacetate **28** with LiTMP gave only pivaloin and the trifluoroacetylated amine **29**. Apparently, the carbonyl group of **28** is sufficiently activated by the trifluoromethyl group such that attack by the relatively nonnucleophilic LiTMP occurs faster than electron-transfer or enolization processes.

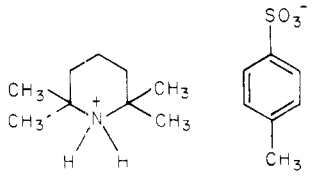
Reaction of LiTMP with the Tosylate Derivative of Pivaloin. As a continuation of our attempt to observe further examples of electron transfer from LiTMP, the tosylate derivative of pivaloin (**30**) was prepared. Since this system does not contain an activated methyl group such as the mesylate **16** or the acetate **26** or a system prone to nucleophilic attack such as trifluoroacetate **28**, it was anticipated that electron-transfer reduction would occur. To our surprise, however, reaction of **30** with LiTMP gave no ketone **9**. Instead a product was produced (quantitative yield) which was assigned structure **31** (an analogue of **22**) on the basis of its elemental analysis and spectral properties. The reaction product **31** has a melting point of greater than 250 °C and contains, by analysis, the elements C, H, O, S, and N, corresponding to a 1:1 adduct between tosylate **30** and tetramethylpiperidine. The infrared spectrum shows no carbonyl group and the ^{1}H NMR spectrum shows three aromatic protons. The ^{13}C NMR spectrum also confirms the presence of a trisubstituted aromatic system. Only three of the aromatic carbons are coupled to adjacent hydrogens. That the product is a tetramethylpiperidinium salt is supported by the similarity of portions of the spectrum of **31** with that of tetramethylpiperidinium *p*-toluenesulfonate (**32**). Both **31** and **32** show equivalent methylene protons at δ 1.62 and equivalent methyl protons at δ 1.49. The ^{13}C NMR spectrum of **32** shows signals at δ 16.4, 21.3, 27.2, 34.5, and 56.8 which correspond to the carbons in the tetra-

(15) The acidity of these protons should be comparable to that of dimethyl sulfone (pK_a = 31.1 in Me_2SO). This is in the range where essentially "irreversible" deprotonation by dialkylamide bases should occur. For a discussion of the acidifying effect of the sulfonyl group, see: Matthews, W. S.; Bares, J. E.; Bartmess, J. E.; Bordwell, F. G.; Cornforth, F. J.; Drucker, G. E.; Margolin, Z.; McCallum, R. J.; McCollum, G. J.; Vanier, N. R. *J. Am. Chem. Soc.* **1975**, *97*, 7006–14.

(16) Other plausible mechanisms include the carbene(oid) processes shown below.

(17) Lehmann, H. G. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 783–4.

(18) The analogous deprotonation of carboxylate salts giving dianions is readily achieved by amide bases. See: (a) Creger, P. L. *J. Am. Chem. Soc.* **1970**, *92*, 1397–8. (b) Creger, P. L. *Ibid.* **1967**, *89*, 2500–1. (c) Adam, W.; Baeza, J.; Liu, J. C. *Ibid.* **1972**, *94*, 2000–6.



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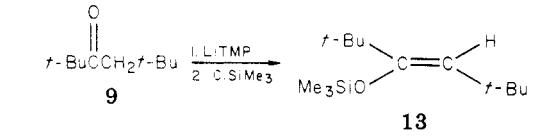
methylpiperidinium ion and the methyl carbon of the sulfonate ion. The corresponding signals in **31** are quite similar in chemical shift. They appear at δ 16.4, 21.2, 27.3, 34.7, and 56.6. The remainder of the ^{13}C NMR spectrum of **31** is entirely consistent with the assigned structure as is the ^{1}H NMR spectrum.

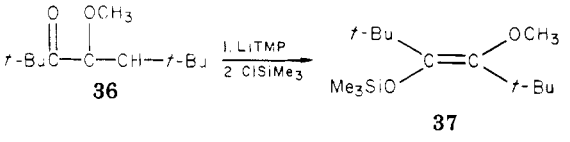
The origin of the epoxy sulfonate salt **31** is suggested in Scheme VII. Deprotonation of the aromatic ring ortho to the sulfonate group would give **33**. Cyclization, in a manner analogous to the formation of **21** and **27**, should produce **34**. Intramolecular sulfonate displacement would form epoxide **35** as the lithium salt. In the workup, the lithium salt **35** is converted to the tetramethylpiperidinium salt **31** during the acid wash to remove tetramethylpiperidine from the organic solvent. The salt **31** remains dissolved in the organic medium.

The fact that even aromatic ring protons are abstracted in preference to the proton α to the carbonyl group in **30** attests to the low kinetic acidity of this proton. The sulfonyl group activation of the ortho position of **31** is not unexpected. The ortho position in carboxylic acid derivatives such as benzamides,[19] aryloxazolines,[20] and thiobenzamides[21] can be deprotonated with butyllithium. Deprotonation of the aromatic ortho position[31] of **30** can be accomplished by the much weaker amide base LiTMP. This is probably due to the extremely potent electron-withdrawing sulfonyl group. Deprotonation of the aromatic ring in **31** must be more rapid than electron transfer from LiTMP or the enolization process.

Reaction of LiTMP with the triflate, mesylate, acetate, trifluoroacetate, and tosylate derivatives of pivaloin gave no evidence for deprotonation at the α-keto position. We therefore wanted to determine if enolization of *any* pivaloin derivative was possible with LiTMP. Therefore ketone **9** (pK_a = 23.3)[22] and the methyl ether derivative of pivaloin (**36**) were both treated with LiTMP followed



9 13

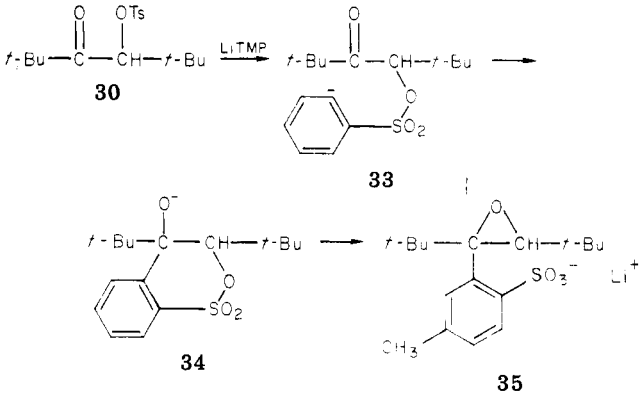


36 37

by chlorotrimethylsilane. While no reaction occurred at low temperature, at room temperature, enolization proceeded smoothly, as evidenced by formation of silyl enol ethers **13** and **37**, respectively. Therefore enolization is possible, albeit slow, with pivaloin derivatives.

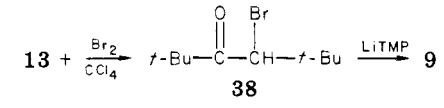
Reaction of LiTMP with Bromo Ketone 38. Bromo ketone **38** could be prepared by addition of bromine to **13**

Scheme VII



30 33 34 35

Scheme VIII



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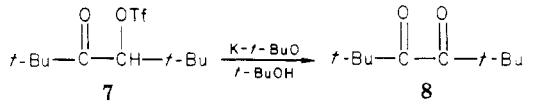
as shown in Scheme VIII. On treatment with LiTMP, a reaction occurs at less than 0 °C giving an 85% yield of the reduced product ketone **9**. This process is formally analogous to the reduction of triflate **7** with LiTMP. However, we cannot rule out a mechanism involving nucleophilic attack by tetramethylpiperidide on halogen with displacement of enolate which would also account for this reduction process.[23] As in the case of triflate **7**, an electron-transfer reduction remains a possibility. In any case, this represents another example of reduction of a formally enolizable ketone with LiTMP.

Reaction of the Triflate Derivatives of Pivaloin and 3-Hydroxycamphor with Potassium *tert*-Butoxide. While the reactions of pivaloin derivatives with LiTMP are of considerable interest from a mechanistic standpoint, we had not achieved either of our original goals, i.e., generation of an α-keto carbene or formation of a stable α-diketone from an α-keto triflate. The latter goal has now been achieved. Treatment of triflate **7** with potassium *tert*-butoxide in *tert*-butyl alcohol gave a 45% yield of diketone **8**. Tosylate **30** also gave **8** on reflux with po-



7 8

tassium *tert*-butoxide in *tert*-butyl alcohol. This β elimination of trifluoromethanesulfinic acid from **7** lends credence to our original suggestion of the intermediacy of norcamphorquinone (**6**) in reaction of triflate **1** with LiTMP or potassium *tert*-butoxide.

Triflate **42** was also prepared as shown in Scheme IX. The silyl enol ether **39** was ozonized in methylene chloride at 78 °C. Heathcock[24] has reported that the ozonolysis of the *tert*-butyldimethylsilyl enol ether of camphor gave the *tert*-butyldimethylsilyl analogue of **40**. Ozonolysis of **39** follows a similar course, giving **40** as a mixture of epimers in 90% yield along with 10% of camphoric anhydride (**41**). Methanolysis of **40** gave **42** which was converted by standard procedures to the triflate mixture **43**. Treatment of **43** with potassium *tert*-butoxide in *tert*-butyl alcohol also results in β elimination of trifluoromethanesulfinic

(19) (a) Puterbaugh, W. H.; Hauser, C. R. *J. Org. Chem.* **1964**, *29*, 853–6. (b) Mao, C. L.; Barnish, J. T.; Hauser, C. R. *J. Heterocycl. Chem.* **1969**, *6*, 475–81.

(20) (a) Gschwend, H. W.; Hamdan, A. *J. Org. Chem.* **1975**, *40*, 2008–9. (b) Meyers, A. I.; Mihelich, E. D. *J. Org. Chem.* **1975**, *40*, 3158–9.

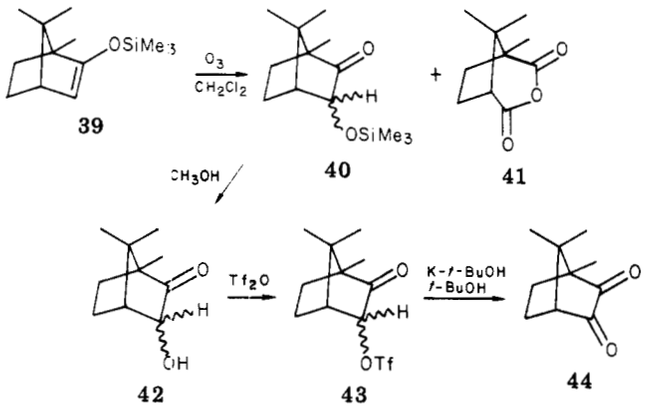
(21) Fitt, J. J.; Gschwend, H. W. *J. Org. Chem.* **1976**, *41*, 4029–31.

(22) Zook, H. D.; Kelly, W. I.; Posey, I. Y. *J. Org. Chem.* **1968**, *33*, 3477–80.

(23) This general type of mechanism has precedent. See: (a) Meisters, A.; Swan, J. M. *Aust. J. Chem.* **1965**, *18*, 163–7. (b) Ziegler, G. R.; Welch, C. A.; Orzech, C. E.; Kikkawa, S.; Miller, S. I. *J. Am. Chem. Soc.* **1963**, *85*, 1648–51.

(24) Clark, R. D.; Heathcock, C. H. *Tetrahedron Lett.* **1974**, 2027–30.

Scheme IX



acid, producing camphorquinone (44) in 92% yield. The isolability of diketones 8 and 44 is attributed to the hindered nature of these substances which prevents further condensation as in the case of the unhindered norcamphorquinone (6).

Experimental Section

NMR spectra were recorded on a Varian A-60 A or Varian XL-100 spectrometer. Data are reported in δ (ppm) relative to Me_4Si. Mass spectra were recorded on an AEI Scientific Apparatus MS 902 spectrometer. Infrared spectra were recorded on a Perkin-Elmer Infracord spectrometer. Elemental analyses were performed by Midwest Microlab, Ltd. Gas-chromatographic analyses were carried out on a Hewlett-Packard Model 5750 chromatograph with a flame-ionization detector using a 5 ft 5% SE-30 on Chromosorb G column. A Varian 920 chromatograph was used for sample isolation.

Reaction of LiTMP with Triflate 7. LiTMP[25] was prepared by the addition of 3.55 mL of 1.4 M methyllithium in ether to 0.70 g of tetramethylpiperidine. The mixture was cooled to −78 °C and a solution of 0.50 g of triflate 7[7] in 2 mL of ether was added. The mixture was brought to 0 °C. Analysis of a small sample by gas chromatography showed largely unreacted 7 at 0 °C. After 2 h at room temperature, an aqueous workup followed. The ether phase was washed with dilute HCl until the aqueous phase remained acidic. The solvent was dried over Na_2SO_4 and removed by distillation through a Vigreux column. The residue was distilled through a short-path condenser at 14 mm. Ketone 9,[26] 0.21 g (81%), was collected and identified by IR and NMR spectral comparison with an authentic sample prepared as described below.

Reaction of Triflate 7 with LiTMP and Chlorotrimethylsilane. LiTMP was prepared from 0.98 g of tetramethylpiperidine and 4.95 mL of 1.4 M methyllithium in ether. A solution of 0.50 g of triflate 7 in 2 mL of ether was added at −78 °C and the mixture was slowly warmed to room temperature. After 2 h at room temperature, 1.00 g of chlorotrimethylsilane was added and the mixture was refluxed for 2 h. The mixture was then diluted with pentane and water was added. The organic phase was washed with a cold solution of $KHSO_4$ and dried over $MgSO_4$. The solvents were removed by rotary evaporation and the residue was distilled at 14 mm. After a small forerun, 0.360 mg (97%) of 13 was collected: ^1H NMR (CCl_4) δ 4.43 (1 H, s), 1.08 (9 H, s), 1.04 (9 H, s), 0.28 (9 H, s); ^{13}C NMR ($CDCl_3$) δ 156.1, 113.9, 36.8, 30.8, 30.5, 29.2, 2.2; mass spectroscopic mol wt 228.1902 (calcd for $C_{13}H_{28}OS$ 228.1909).

Preparation of Pivaloin-d_2 (12-d_2). Sodium (0.55 g) was dissolved in 20 mL of CH_3OD and 2.50 g of pivaloin[27] added followed by 13 mL of D_2O. The mixture was refluxed for 24.5 h. D_2O (25 mL) was then added, and the mixture was extracted with ether. The ether was dried over Na_2SO_4, and the solvent was removed by rotary evaporation. The solid was redissolved in Skelly F and redried over Na_2SO_4. The solvent was removed by rotary evaporation leaving 2.45 g (97%) of pivaloin-d_2. The ^1H NMR spectrum shows greater than 95% deuterium incorporation in the carbinyl position.

In a separate run, treatment of pivaloin under the same conditions for 1 h at room temperature gave complete exchange of the hydroxyl proton and no exchange of the carbinyl proton. Reflux for 8 h gave about 80% exchange of the carbinyl proton.

Preparation of Triflate 7-*d*. The preparation of triflate 7-*d* was completely analogous to the previously described[7] preparation of 7. Reaction of 12-d_2 with triflic anhydride in pyridine for 75 min at room temperature gave 50% of triflate 7-*d*, mp 34–36 °C. The ^1H NMR spectrum of 7-*d* indicates greater than 95% deuterium incorporation as evidenced by the lack of the carbinyl proton at δ 5.37.

Reaction of Triflate 7-*d* with LiTMP and Chlorotrimethylsilane. LiTMP was prepared from 0.98 g of tetramethylpiperidine and 4.95 mL of 1.4 M methyllithium in ether. A solution of 0.50 g of triflate 7-*d* in 2 mL of ether was added to the solution at −78 °C. The remainder of the procedure was identical with that used for the unlabeled triflate 7. Distillation gave 0.36 g (96%) of 13-*d*, bp 80–88 °C (14 mm). The ^1H NMR spectrum of 13-*d* was identical with that of 13 except for the absence of the olefinic proton at δ 4.43; ^{13}C NMR ($CDCl_3$) δ 36.8, 30.8, 30.5, 29.2, 2.2. The olefinic carbon atoms were not visible under the spectral conditions.

Preparation of Mesylate 16. A solution of 1.0 g of pivaloin and 1.17 g of triethylamine in 10 mL of methylene chloride was cooled to −10 °C and 0.89 g of mesyl chloride was added dropwise. After about 5 min at 15 °C, the mixture was taken up into ether and water. The ether extract was washed with dilute HCl and saturated NaCl solution and dried over $MgSO_4$. After filtration, the solvents were removed by rotary evaporation. The solid which formed was slurried with cold pentane and collected, giving 1.25 g (86%) of mesylate 16: 89–90 °C; ^1H NMR ($CDCl_3$) δ 5.30 (1 H, s), 3.00 (3 H, s), 1.25 (9 H, s), 1.05 (9 H, s); ^{13}C NMR ($CDCl_3$) δ 211.9, 81.4, 44.7, 38.9, 35.1, 27.5, 26.2.

Anal. Calcd for $C_{11}H_{22}O_4S$: C, 52.77; H, 8.86. Found: C, 52.91; H, 8.99.

Reaction of Mesylate 16 with LiTMP at Room Temperature. LiTMP was prepared from 1.19 g of tetramethylpiperidine and 6 mL of 1.4 M methyllithium in ether. The solution was cooled to −40 °C and a mixture of 0.59 g of 16 in 11 mL of ether was added. The mixture was stirred at room temperature for 4.25 h. Water was then added and a standard aqueous workup followed. Solvent was removed by distillation through a Vigreux column and distillation at 2 mm gave 0.13 g (33%) of enones 17 and 18 in a 3.7:1 ratio as determined by gas chromatography. Pure samples of 17 and 18 were isolated by preparative gas chromatography. About 0.26 g of relatively nonvolatile residue remained after distillation of 17 and 18. Gas chromatography of the residue showed the presence of a small amount of sultone 19 and a major unidentified product. A sample of this unidentified product was isolated by preparative gas chromatography. Mass spectrometry showed a molecular ion at *m/e* 336.3011 which corresponds to $C_{22}H_{40}O_2$ (calcd *m/e* 336.3028), a formal dimer of 17 (or 18): IR (CCl_4) 5.86, 5.94 μm; NMR ($CDCl_3$) δ 0.80 (9 H, s), 1.03 (9 H, s), 1.19 (9 H, s), 1.22 (9 H, s), 2.6–2.2 (1 H, m), 3.3–2.9 (2 H, m), 5.15 (1 H, s). Enones 17 and 18 were identified by comparison with previously reported IR and NMR spectral data.[28] 17: NMR (CCl_4) δ 6.85 and 6.38 (2 H, AB q, J = 15.5 Hz), 1.12 (9 H, s), 1.10 (9 H, s). 18: NMR (CCl_4) δ 6.05 and 5.82 (2 H, AB q, J = 13.5 Hz), 1.12 (18 H, s).

Reaction of Mesylate 16 with LiTMP at Low Temperature. LiTMP was prepared from 0.79 g of tetramethylpiperidine and 4.0 mL of 1.4 M methyllithium. A solution of 0.40 g of mesylate 16 in 7 mL of ether was added at −50 °C and the mixture was warmed to 0 °C. Gas-chromatographic analysis showed no unreacted 16. After 5 min at room temperature, water was added

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and a standard aqueous workup followed. Gas-chromatographic analysis showed a small amount of **18** and a large peak corresponding to sultone **19**. After being dried over $MgSO_4$, the solvent was removed by rotary evaporation. The solid residue was slurried with cold pentane and collected, giving 0.32 g (80%) of sultone **19**: mp 126–127 °C; ^1H NMR ($CDCl_3$) δ 4.43 (1 H, s), 3.77 and 3.42 (2 H, AB q, J = 15 Hz), 2.27 (1 H, br s), 1.20 (9 H, s), 1.07 (9 H, s); ^{13}C NMR ($CDCl_3$) δ 94.3, 85.7, 54.7, 39.3, 36.9, 27.5, 24.6; IR ($CDCl_3$) ν_{OH} 2.76, 2.82 μm.

Anal. Calcd for $C_{11}H_{22}O_4S$: C, 52.77; H, 8.86. Found: C, 53.27; H, 8.78.

Preparation of Acetate 26. A solution of 1.0 g of pivaloin in 5 mL of THF was cooled to −78 °C and 4.36 mL of 1.4 M methyllithium was added at −78 °C. The mixture was warmed to room temperature and recooled to −20 °C. Acetic anhydride (1.35 g) was added. After 15 min at room temperature the mixture was refluxed for 15 min. A standard aqueous workup followed. After being dried over $MgSO_4$, solvents were removed by rotary evaporation. Gas-chromatographic analysis showed about 20% unreacted pivaloin. The residue was chromatographed on 45 g of silica gel and eluted with 3% ether in Skelly F. The pivaloin remained on the column. The chromatographed acetate **26** was distilled to give 0.87 g (70%) of pure **26**: bp 64 °C (1.1 mm); NMR (CCl_4) δ 5.29 (1 H, s), 2.05 (3 H, s), 1.18 (9 H, s), 0.99 (9 H, s).

Anal. Calcd for $C_{12}H_{22}O_3$: C, 67.26; H, 10.35. Found: C, 66.98; H, 10.32.

Reaction of LiTMP with Acetate 26. LiTMP was prepared from 0.50 g of tetramethylpiperidine and 2.53 mL of 1.4 M methyllithium. A solution of 0.30 g of acetate **26** in 1 mL of ether was added at −78 °C. The mixture was warmed to 0 °C and gas-chromatographic analysis of a small sample showed no remaining **26**. After 15 min at room temperature, a standard aqueous workup followed. Solvents were removed by rotary evaporation, giving 0.30 g (100%) of crude hydroxy lactone **27**. An analytical sample, mp 109–111 °C, was purified by sublimation: NMR ($CDCl_3$) δ 4.18 (1 H, s), 2.77 (2 H, br s), 1.92 (1 H, br s), 1.13 (9 H, s), 1.01 (9 H, s).

Anal. Calcd for $C_{12}H_{22}O_3$: C, 67.26; H, 10.35. Found: C, 67.19; H, 10.56.

Preparation of Trifluoroacetate 28. A solution of 1.00 g of pivaloin in 10 mL of pyridine was cooled to 0 °C and 2.44 g of trifluoroacetic anhydride was added dropwise. After 45 min at room temperature, a standard aqueous workup followed. After being dried over $MgSO_4$, ether solvent was removed by rotary evaporation. Distillation of the residue gave 1.45 g (93%) of trifluoroacetate **28**: bp 78–80 °C (14 mm); NMR (CCl_4) δ 5.47 (1 H, s), 1.18 (9 H, s), 1.04 (9 H, s).

Anal. Calcd for $C_{12}H_{19}F_3O_3$: C, 53.73; H, 7.14. Found: C, 53.71; H, 7.19.

Reaction of Trifluoroacetate 28 with LiTMP. LiTMP was prepared from 0.92 g of tetramethylpiperidine and 4.65 mL of 1.4 M methyllithium. The mixture was cooled to −78 °C and a solution of 0.50 g of trifluoroacetate **28** in 2.5 mL of ether was added. The mixture was warmed to room temperature. Gas-chromatographic analysis showed the presence of pivaloin (**12**) and amide **29**. After 5 h at room temperature, a standard aqueous workup followed. Solvents were removed by rotary evaporation and samples of **12** and **29** were isolated by preparative gas chromatography. Pivaloin (**12**) was identified by mass, infrared, and NMR spectral comparison with an authentic sample. Amide **29** was identified by means of mass, infrared, and NMR spectral data: IR $\nu_{C=O}$ 5.96 μm; NMR (CCl_4) δ 1.80 (6 H, s), 1.46 (12 H, s). An analytical sample of **29**, mp 45–47 °C, was prepared by sublimation.

Anal. Calcd for $C_{11}H_{18}F_3NO$: C, 55.68; H, 7.65. Found: C, 55.62; H, 7.49.

Preparation of Tosylate 30. A solution of 1.72 g of pivaloin in 10 mL of THF was cooled to −78 °C and 7.60 mL of 1.4 M methyllithium was added. The solution was warmed to room temperature and 2.00 g of *p*-toluenesulfonyl chloride was added. The reaction (exothermic) was cooled in a water bath. After 1 h at room temperature, a standard aqueous workup followed. After the solution was dried over $MgSO_4$, solvents were removed by rotary evaporation, leaving 3.06 g (94%) of crude tosylate **30**. The crude product was slurried with pentane and collected, giving 2.10 g of pure tosylate **30**: mp 83–84 °C; NMR ($CDCl_3$) δ 7.95–7.20 (4 H, AA'BB' q), 5.26 (1 H, s), 2.45 (3 H, s), 1.22 (9 H, s), 0.98 (9 H, s).

Anal. Calcd for $C_{17}H_{26}O_4S$: C, 62.55; H, 8.03. Found: C, 62.82; H, 8.08.

Reaction of LiTMP with Tosylate 30. LiTMP was prepared from 0.69 g of tetramethylpiperidine and 3.49 mL of 1.4 M methyllithium. A solution of 0.79 g of tosylate **30** in 7 mL of ether was added at −78 °C and the mixture was warmed to room temperature. After 20 min, the mixture was cooled to about −30 °C and water was added followed by 15 mL of methylene chloride (to prevent crystallization of **31**). A solution of 1.10 g of $KHSO_4$ was then added and the mixture was transferred to a separatory funnel with the aid of about 20 mL of methylene chloride. Enough water was added to dissolve the salts which crystallized. The organic phase was washed with saturated NaCl solution and dried over $MgSO_4$. Solvents were removed by rotary evaporation leaving 1.14 g (100%) of **31**. The product **31**, mp >250 °C, was slurried in pentane and collected: ^1H NMR ($CDCl_3$) δ 7.88 (1 H, d, J = 8 Hz), 7.48 (1 H, br s), 7.07 (1 H, d of br s, J = 8 Hz), 3.28 (1 H, s), 2.36 (3 H, s), 1.62 (6 H, s), 1.49 (12 H, s), 2.93 (9 H, s), 2.86 (9 H, s); ^{13}C NMR ($CDCl_3$) δ 143.4, 139.2, 138.4, 130.0, 126.9, 126.8, 75.3, 73.6, 56.5, 34.7, 33.8, 32.7, 31.2, 29.3, 27.3, 21.2, 16.4.

Anal. Calcd for $C_{26}H_{45}NO_4S$: C, 66.77; H, 9.70; N, 2.99; S, 6.86. Found: C, 66.59; H, 9.39; N, 3.07; S, 7.21.

Preparation of 2,2,5,5-Tetramethyl-3-hexanone. (9). A solution of 4.75 g of pivaloin in 15 mL of ether was added dropwise to a solution of 0.50 g of lithium in 200 mL of liquid ammonia. The blue color was completely discharged when the last of the pivaloin was added. Ammonium chloride was added and the ammonia was allowed to evaporate. A standard aqueous workup followed. Gas-chromatographic analysis showed a mixture of ketone **9** and the reduced ketone 2,2,5,5-tetramethyl-3-hexanol along with unchanged pivaloin as the major component. After solvent removal by rotary evaporation, the residue was distilled through a Vigreux column at 15 mm. A mixture of ketone **9** and 2,2,5,5-tetramethyl-3-hexanol (1.43 g) was collected. This mixture was dissolved in 10 mL of acetone and Jones reagent was added until the orange color was no longer discharged. After an aqueous workup and solvent removal by rotary evaporation, ketone **9**, 1.2 g, was isolated by distillation at 15 mm. Previously reported ketone **9**[25] showed the following: NMR ($CDCl_3$) δ 2.37 (2 H, s), 1.11 (9 H, s), 1.02 (9 H, s).

Reactions of Ketone 9 with LiTMP and Chlorotrimethylsilane. LiTMP was prepared from 0.54 g of tetramethylpiperidine and 2.73 mL of 1.4 M methyllithium. Ketone **9** (0.30 g) was added and the mixture was refluxed for 90 min. Chlorotrimethylsilane (0.46 g) was then added and reflux was continued for 45 min. After the mixture was stirred for an additional 3 h at room temperature, pentane was added and a standard aqueous workup followed. Tetramethylpiperidine was removed by washing the organic phase with cold dilute $KHSO_4$ solution. After solvent removal by rotary evaporation, the residue was distilled through a short-path condenser at 14 mm. Silyl enol ether **13** (0.35 g, 80%) was collected after a small forerun of starting ketone **9**. The spectral properties of **13** prepared in this manner were identical with those of the product produced from triflate **7**, LiTMP, and chlorotrimethylsilane.

Preparation of Methyl Ether 36. Sodium hydride (0.28 g) was added to a solution of 1.70 g of pivaloin in 10 mL of THF. After the solution was refluxed for 5 min, 2.2 g of methyl iodide was added and the mixture was refluxed for 2.25 h. A standard aqueous workup followed. Gas-chromatographic analysis showed about 35% unreacted pivaloin. After solvent removal by rotary evaporation, the crude products weighed 1.90 g. One-half of this mixture was chromatographed on 20 g of silica gel and eluted with 4% ether in Skelly F which completely separated the pivaloin. After removal of solvents, the crude chromatographed **36** was distilled, giving 0.55 g, bp 84–85 °C (14 mm). The overall yield of **36** was 60%: NMR (CCl_4) δ 3.73 (1 H, s), 3.34 (3 H, s), 1.17 (9 H, s), 0.96 (9 H, s).

Anal. Calcd for $C_{11}H_{22}O_2$: C, 70.92; H, 11.90. Found: C, 71.10; H, 11.79.

Reaction of 36 with LiTMP and Chlorotrimethylsilane. LiTMP was prepared from 0.98 g of tetramethylpiperidine and 4.95 mL of 1.4 M methyllithium. Ketone **36** (0.42 g) was added at about −50 °C. The mixture was stirred at room temperature

for 1.5 h and refluxed for 30 min. Chlorotrimethylsilane (1.00 g) was added and the mixture was refluxed for 3 h. Skelly F was then added and a standard aqueous workup followed. The organic phase was washed with cold dilute $KHSO_4$ and dried over $MgSO_4$. The solvent was removed by rotary evaporation. Distillation of the residue gave, after a small forerun, 0.55 g (95%) of silyl enol ether **37**: ^1H NMR (CCl_4) δ 3.48 (3 H, s), 1.17 (18 H, s), 0.28 (9 H, s); mass spectroscopic mol wt 258.2004 (calcd for $C_{14}H_{30}O_2Si$ 258.2015).

Preparation of Bromo Ketone 38. A solution of 0.30 g of silyl enol ether **13** in 2 mL of CCl_4 was cooled to −30 °C and 0.21 g of bromine in 0.5 mL of CCl_4 was added. Solvent was removed by aspirator and the residue was distilled, giving 0.25 g (82%) of bromo ketone **38**, bp 63 °C (1.1 mm). Previously reported[26b] bromo ketone **38** had the following: NMR (CCl_4) δ 4.40 (1 H, s), 1.25 (9 H, s), 1.14 (9 H, s).

Reaction of LiTMP with Bromo Ketone 38. LiTMP was prepared from 0.29 g of tetramethylpiperidine and 1.46 mL of 1.4 M methyllithium. The mixture was cooled to −60 °C and 158 mg of bromo ketone **38** was added. The mixture was warmed to room temperature and stirring was continued for 50 min. A standard aqueous workup followed. After solvent removal by distillation through a Vigreux column, the residue was distilled to give 93 mg (88%) of ketone **9** which was identified by IR and NMR comparison with an authentic sample.

Reaction of Triflate 7 with Potassium *tert*-Butoxide. A 0.51 M solution of potassium *tert*-butoxide in *tert*-butyl alcohol (2.6 mL, prepared by dissolving 0.40 g of potassium in 20 mL of anhydrous *tert*-butyl alcohol) was cooled to 15 °C and 0.20 g of triflate **7** was added. After 2.5 h at room temperature, a standard aqueous workup followed. Gas-chromatographic analysis showed diketone **8** along with about 10% pivaloin. After distillation of the solvent through a Vigreux column, the residue was distilled, giving 0.05 g (45%) of diketone **8** which was identified by IR and NMR spectral comparison with an authentic sample.[27b]

Reaction of Tosylate 30 with Potassium *tert*-Butoxide. Tosylate **30** (0.25 g) was added to 3 mL of a 0.51 M solution of potassium *tert*-butoxide in *tert*-butyl alcohol. The mixture was refluxed for 1 h and a standard aqueous workup followed. Gas chromatographic analysis showed diketone **8** along with about 10% pivaloin. Distillation gave 0.044 g (34%) of diketone **8** which was identified by IR and NMR spectral comparison with an authentic sample.[27b]

Preparation of Alcohols 41. A solution of 490 mg of silyl enol ether **39**[29] in 5 mL of methylene chloride was cooled to −78 °C and ozonized until a blue color appeared. Gas-chromatographic analysis showed the presence of siloxy ketones **40** as well as camphoric anhydride (**41**). Solvent was removed by rotary evaporation. The NMR of the residue shows an *exo*-siloxy:*endo*-siloxy ratio of 1.5 in the mixture. The exo proton of **40** appears as a doublet, J = 5 Hz, at δ 4.08. The endo proton in **40** appears as a broad singlet at δ 3.58. The crude residue was dissolved in 5 mL of methanol and after 5 min, the solvent was removed by rotary evaporation. The residue was taken up into Skelly F. Camphoric anhydride (**41**), which did not dissolve, was separated by decanting the liquid. The yield of **41** was 40 mg (10%). Anhydride **41** was identified by spectral comparison with an authentic sample. After evaporation of the Skelly F by rotary evaporation, the residue was further purified by sublimation at 1 mm. The NMR of **42** showed an *exo*-hydroxy:*endo*-hydroxy ratio of 1.5. The exo proton of **42** appears as a doublet (after exchange of the hydroxyl proton with D_2O), J = 5 Hz, at δ 4.17. The endo proton of **42** appears as a broad singlet at δ 3.70. The preparation of hydroxy ketones **42** by alternate routes has been reported.[30]

Preparation of Triflates 43. Triflic anhydride (2.20 g) was dissolved in 8 mL of pyridine at 0 °C and a solution of 1.00 g of the mixture of alcohols **42** in 4 mL of pyridine was added at 0 °C. After 18 min at 0 °C, the mixture was taken up into ether and extracted with cold water. After a standard aqueous workup with HCl washing to remove pyridine, the solution was dried over $MgSO_4$. About one-half of the solvent was removed by a steam bath and the remainder of the ether was removed by rotary evaporation. The crude mixture of triflates **43**, 1.33 g (74%), was used directly in the next reaction. The NMR of the triflate mixture showed an exo-triflate:endo-triflate ratio of 0.7. The exo proton (α to the carbonyl group) in the mixture appeared as a doublet, J = 5 Hz, at δ 5.06. The endo proton appeared as a broad singlet at δ 4.62.

Reaction of Triflate 43 with Potassium *tert*-Butoxide. A 0.42 M solution of potassium *tert*-butoxide in *tert*-butyl alcohol (6.3 mL) was cooled to about 15 °C and 0.51 g of triflates **43** was added. After 5 min at room temperature, a standard aqueous workup followed. The organic extract was dried over $MgSO_4$ and solvents were removed by rotary evaporation, leaving 0.26 g (92%) of crude camphorquinone, mp 194–196 °C, which was identified by spectral comparison with an authentic sample.

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Registry No. **7**, 71341-17-8; **7-*d***, 73333-50-3; **8**, 4388-88-9; **9**, 868-91-7; **12**, 815-66-7; **12-d_2**, 73333-51-4; **13**, 73333-52-5; **13-*d***, 73333-53-6; **16**, 68505-99-7; **17**, 20859-13-6; **18**, 29569-89-9; **19**, 73333-54-7; **26**, 73333-55-8; **27**, 73333-56-9; **28**, 73333-57-0; **29**, 73333-58-1; **30**, 14775-42-9; **31**, 73333-60-5; **36**, 73333-61-6; **37**, 73333-62-7; **38**, 55073-87-5; **39**, 56613-17-3; *endo*-**40**, 68546-51-0; *exo*-**40**, 68546-50-9; **41**, 76-32-4; *endo*-**42**, 21488-68-6; *exo*-**42**, 22759-33-7; *endo*-**43**, 73333-63-8; *exo*-**43**, 73333-64-9; **44**, 465-29-2; LiTMP, 38227-87-1; 2,2,5,5-tetramethyl-3-hexanol, 55073-86-4.

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Reaction of Diphenyl- and Difluorocarbenes with 3,7-Dimethylenebicyclo[3.3.1]nonane[1]

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Both difluorocarbene and diphenylcarbene add to 3,7-dimethylenebicyclo[3.3.1]nonane to give mono- and diadducts. Products of abstraction–recombination are produced from diphenylcarbene, but neither carbene gives products of conjugate addition.

Attempts to find conjugate or 1,4-addition reactions of carbenes almost invariably fail.[3] We know of only three successes: one is the addition of triplet dicyanocarbene to cyclooctatetraene;[4] another involves the general class

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