Reactions of Bicyclic α-Keto Triflates with Bases and Nucleophiles

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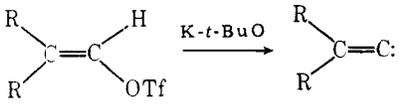
endo-Bicyclo[2.2.1]heptan-2-on-3-yl triflate (**6**) has been found to react with LDA to give products resulting from hydride reduction of the carbonyl group. With LiTMP or potassium *tert*-butoxide β elimination of trifluoromethanesulfinic acid was seen followed by condensation of the norcamphorquinone with the enolate of **6**. No processes corresponding to carbene formation via α elimination of triflic acid from **6** were seen. Reaction of sodium methoxide and deuterium labeled *exo*-bicyclo[2.2.1]heptan-2-on-3-yl triflate (**21**-*5d*) gave a substitution product, methoxy ketone **23**-*6d*, in which the carbonyl group has interchanged positions. This was in line with the suggested methoxy epoxide opening to a zwitterion, hydride migration mechanism and ruled out a direct displacement mechanism. In contrast, the hydride migration mechanism could be ruled out to account for the substitution product in the reaction of cyclohexanon-2-yl triflate with methoxide by a similar labeling study. Reaction of triflates **6** and **21** with nucleophiles which can add reversibly to the carbonyl group gave epoxides when the nucleophile was cyanide and formal displacement products when the nucleophiles were of the polarizable type. With irreversible organometallic reagents, products were derived from addition to the carbonyl followed by loss of triflate involving either migration of the alkyl group, C_1C_7 bond migration, or epoxide formation. Products were a delicate function of stereochemistry of the triflate, stereochemistry of attack on the system, and migratory aptitudes of the attacking reagent.

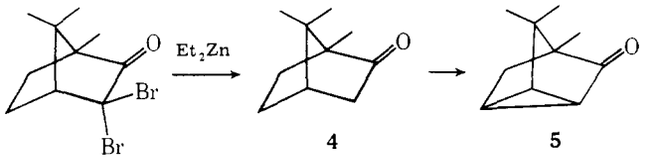
The trifluoromethanesulfonate (triflate) leaving group has assumed increasing importance in organic chemistry over the past ten years. Its high lability has allowed the solvolytic generation of unstable vinyl cations[2] as well as secondary cyclopropyl cations.[3] Stang has also used vinyl triflates **1** as precursors to vinylidene carbenes **2** via an α-elimination



1 2

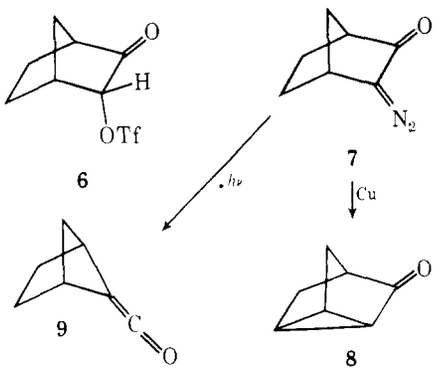
process.[4] We have recently prepared α-keto triflates from the corresponding acyloins.[5a] Vedejs[5b] has prepared certain deactivated triflates from diazo precursors and trifluoromethanesulfonic acid. As part of a study of the reactivity of these triflates, we wanted to determine the viability of generating α-keto carbenes from α-keto triflates by an α-elimination process.

While α-elimination processes are often used to generate certain carbenes (or carbenoids), such processes are rare in the generation of α-keto carbenes. House[5c] has shown that many α-chloro enolates are quite stable, even at room temperature. The only example of α elimination to produce an α-keto carbene that we are aware of is the reported diethylzinc debromination of dibromocamphor **3** in refluxing benzene,



3 4 5

which gave ketone **5**.[6] It was anticipated that the enhanced leaving group ability of triflate would facilitate carbene formation from the corresponding enolate. Triflate **6** was chosen for initial studies since the chemistry of the potential carbene derivable from **6** is well understood. When the carbenoid is generated from diazo ketone **7**, nortricyclanone (**8**) is formed.[7a] Irradiation of **7** gave products derived from ketene **9**.[7b] The intermediate involved in the photolysis is clearly different from that produced in the copper-catalyzed decomposition of **7**. It was therefore of interest to compare the intermediates



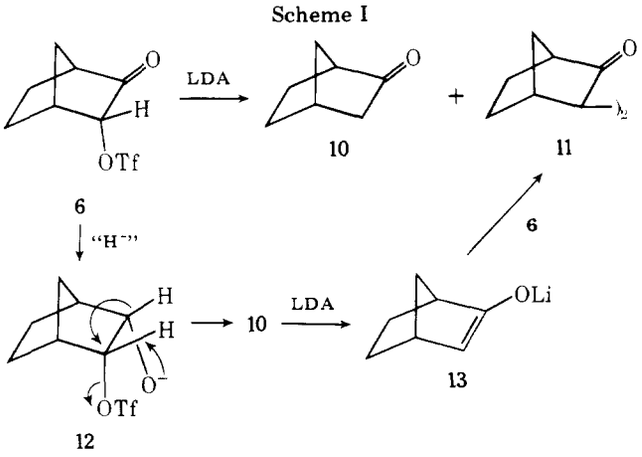
6 7 9 8

from **6** and bases to the intermediates derived from **7**. Reported here are the results of studies of reactions of triflate **6** with bases. Also reported are reactions with other anions as well as reactions of other α-keto triflates.

Results and Discussion

Reaction of *endo*-Bicyclo[2.2.1]heptan-2-on-3-yl Triflate (6) with Lithium Diisopropylamide (LDA). LDA is a widely used base for irreversible enolate formation at low temperatures. Initial attempts at carbene formation from **6** employed this base. When triflate **6** was treated with LDA in ether at −78 °C, norcamphor (**10**) was the major product, along with varying amounts of a dimeric product, ketone **11** (Scheme I). Interestingly, no nortricyclanone could be de-

Scheme I

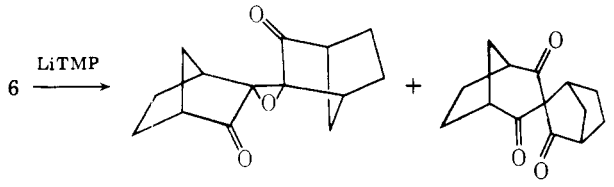


10 11 12 13

0022-3263/79/1944-1798$01.00/0

tected. Ketones **10** and **11** are formally reduction products. Initially these products were difficult to account for mechanistically until the ability of LDA to act as a hydride donor was realized. We have recently found that many enolizable ketones are rapidly reduced with LDA at −78 °C in competition with enolization.[8] Norcamphor (**10**) is suggested to arise from a sequence involving such hydride transfer from LDA to the carbonyl group of **6** followed by intramolecular hydride migration and loss of triflate. Enolization of **10** followed by alkylation with **6** is the suggested origin of the "dimer" **11**. The feasibility of such a sequence was substantiated by the independent formation of norcamphor enolate (**13**) at −78 °C from norcamphor and LDA and treatment with 1 equiv of triflate **6**. Ketone **11** is clearly produced by this sequence. Thus, an apparently complex reaction is readily explained once the hydride donating ability of LDA is realized.

Reaction of Triflate 6 with Lithium Tetramethylpiperidide (LiTMP) and Potassium *tert*-Butoxide. We have found that LiTMP[9] can be used for irreversible enolate formation in cases where reduction by LDA occurs.[8] Triflate **6** reacted with LiTMP to give a product mixture which contained *no* nortricyclanone or products derived from ketene **9**. A mixture of two isomeric products, **14** and **15**, of formula



14 15

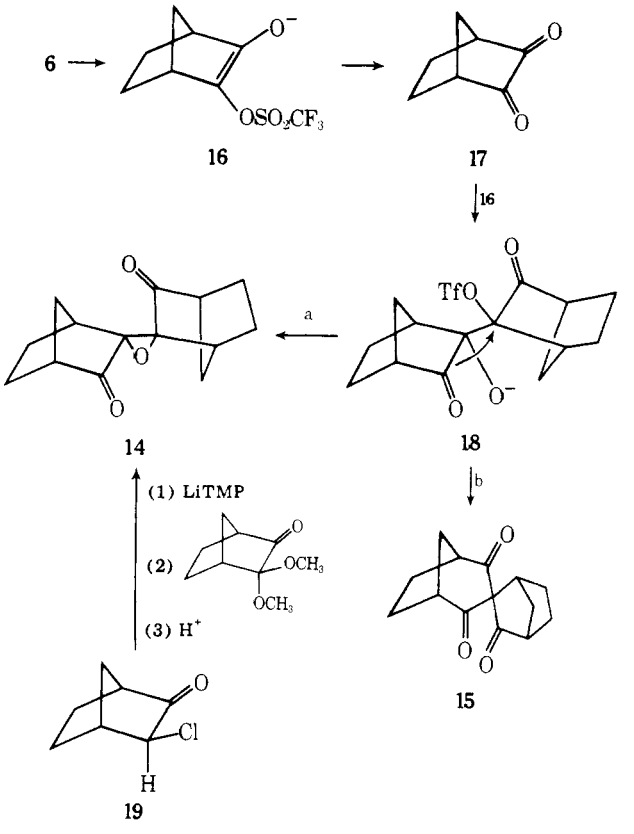
$C_{14}H_{16}O_3$ was produced in comparable amounts which could be separated by silica gel chromatography. The structure of **14** was suggested by its elemental analysis and mass, infrared, ^1H NMR, and ^{13}C NMR spectra. The ^{13}C NMR spectrum of **14** showed 14 distinct carbon atoms, including nonequivalent carbonyl carbons at δ 211.4 and 210.9. Of the six possible isomers of epoxy ketone **14**, the four isomers of higher symmetry can be eliminated by the ^{13}C spectrum. These isomers would show only seven nonequivalent carbon atoms. The other unsymmetrical isomer of **14** was eliminated based on mechanistic considerations.

Product **15** was assigned the structure shown based on its analysis and spectral data. The infrared spectrum showed carbonyl bonds at 5.67 and 5.90 μm. The ^{13}C NMR spectrum showed 14 nonequivalent carbon atoms, including three nonequivalent carbonyl carbons at δ 209.0, 208.6, and 208.4. The other geometric isomer of triketone **15** was eliminated based on the mechanistic considerations discussed below. Triketone **15** rearranged thermally at 185 °C to give an isomeric enone[10] of unknown structure.

Reaction of **6** with potassium *tert*-butoxide in *tert*-butyl alcohol gave only epoxy ketone **14** and none of triketone **15**. Again no "carbene derived" products were observed.

Products **14** and **15** ($C_{14}H_{16}O_3$) both have a molecular formula corresponding to a formal carbene dimer plus one oxygen atom. An apparent oxidation has occurred. A mechanism to account for this "oxidation" is shown in Scheme II. Reaction of **6** with LiTMP (or K-*t*-BuO) generates enolate **16**, which fragments via oxygen–sulfur cleavage (rather than carbene formation) to give norcamphorquinone (**17**) and trifluoromethanesulfinate anion. Capture of enolate **16** by diketone **17** (exo attack on **16** from the exo side of **17**) gives intermediate **18**. Displacement of triflate by oxygen (path a) gives the keto epoxide **14** in a process analogous to the glycidic ester synthesis.[11] The stereochemistry of **14** (exo, endo epoxide, anti carbonyl groups) is controlled by that developed in **18**. Al-

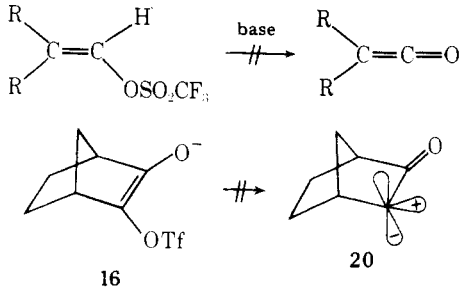
Scheme II



ternatively, **18** could lose triflate with the acyl carbon migrating[12] to the electron deficient center (path b). If these processes are concerted, the triketone product **15** should be produced to the exclusion of the isomeric triketone. This path is apparently not important in *tert*-butyl alcohol with potassium *tert*-butoxide and may be a result of the more nucleophilic nature of oxygen in **18** when the counterion is potassium instead of lithium.

Epoxy ketone **14** could be independently synthesized from *exo*-3-chloronorcamphor (**19**). Condensation of the enolate of **19**, prepared from LiTMP, with 3,3-dimethoxynorcamphor (a norcamphorquinone synthon) in refluxing ether gave a monoketal derivative of **14**. This ketal could be hydrolyzed to give a product identical in all respects with the product **14** derived from **6** and LiTMP or potassium *tert*-butoxide. This sequence completed the structure proof of **14** and demonstrated the viability of diketone **17** in its formation from **6**.

Why are similar processes (elimination of trifluoromethanesulfinate) not seen when vinyl triflates are treated with bases? Undoubtedly relative stabilities of the potential ketene (from the vinyl triflate) vs. the conjugated diketone (from the α-keto triflate) are important factors. Alternatively,

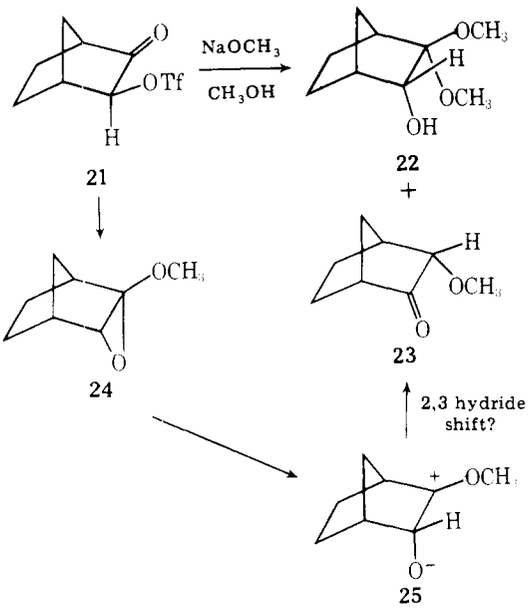


16 20

loss of triflate from **16** could be slow because of the unfavorable carbene state, **20**, that would result. Perhaps with less rigid systems loss of triflate will compete with oxygen–sulfur bond fragmentation.[14]

Reaction of *exo*-Bicyclo[2.2.1]heptan-2-on-3-yl Tri-

Scheme III



flate (21) with Sodium Methoxide. Labeling Studies. When less basic, more nucleophilic alkoxides, such as sodium methoxide, are reacted with triflate **6**, products are derived from attack at the carbonyl group followed by epoxide formation and opening of the epoxide. This reaction of **6** and the epimeric triflate **21** has previously been reported.[5a] Triflate **21** gave ketone **23,** a substitution product, in addition to alcohol **22** (Scheme III). Hydride migration in the zwitterionic intermediate, **25,** appeared to be a reasonable mechanism for the formation of methoxy ketone **23.** However, the origin of **23** was not further investigated and direct displacement of triflate by methoxide remained a possibility. A labeling study was therefore undertaken to determine the origin of **23** in order to better understand the diverse mechanistic processes that α-keto triflates can undergo.

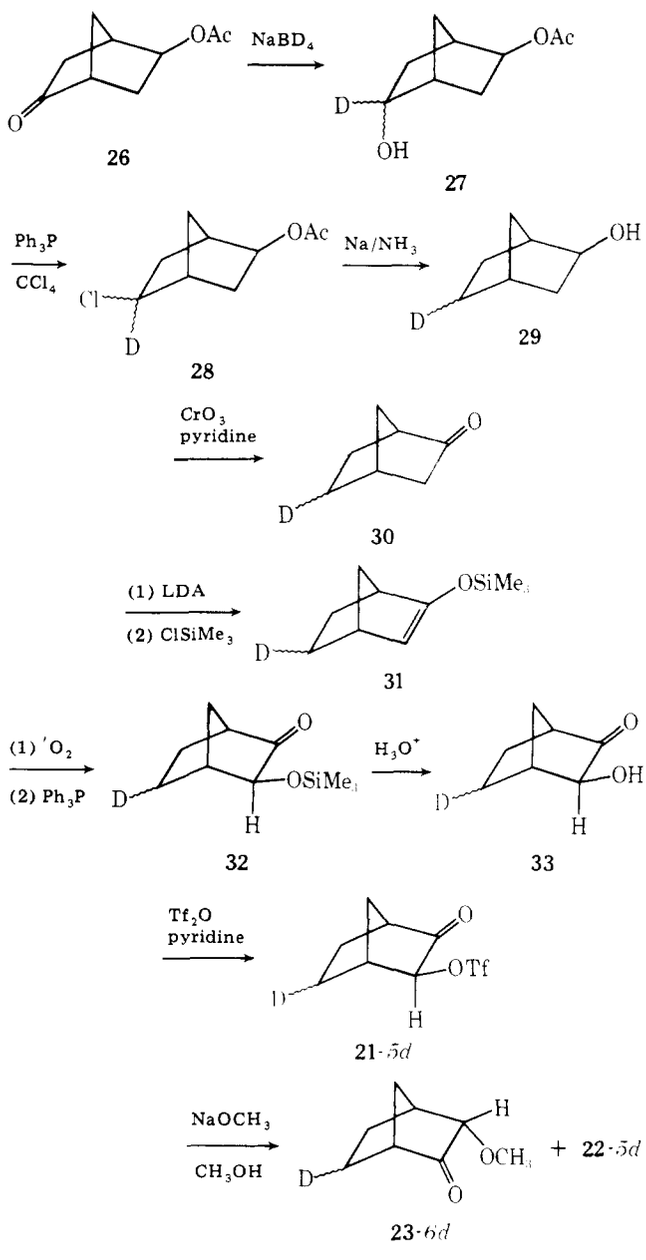
The epoxide, zwitterion, hydride migration mechanism shown predicts that the carbonyl carbons of **21** and **23** interchange positions while carbonyl positions are maintained in a direct displacement mechanism. The labeled triflate **21**-*5d* was therefore prepared as shown in Scheme IV to evaluate the two mechanistic possibilities. Reduction of keto acetate **26** with sodium borodeuteride followed by conversion to the chloride **28,** introduced deuterium in an appropriately functionalized molecule. Treatment with sodium in liquid ammonia dehalogenated and deacetylated **28.** Alcohol **29** was converted in a straightforward manner to silyl enol ether **31.** The recent Jefford procedure,[15] involving reaction of **31** with singlet oxygen, is superior to our previously reported[5a] route for the production of **32.** This route was employed instead of the previous peracid oxidation of **31** to give deuterated **32** which could be converted as previously described[5a] to triflate **21**-*5d*.

Treatment of **21**-*5d* with sodium methoxide in methanol gave substitution product **23**-*6d* and the hydroxy ketal **22**-*5d*. The position of the deuterium label was determined by ^{13}C NMR spectroscopy. The labeled carbon atom of **23**-*6d* appears as a 1:1:1 triplet at δ 26.23. An authentic sample of **23**-*5d* could be prepared as shown in Scheme V. In this case the labeled carbon appears as a 1:1:1 triplet at δ 18.77. The remaining ^{13}C positions of **23**-*6d* and **23**-*5d* are identical with the shifts seen in unlabeled **23.**

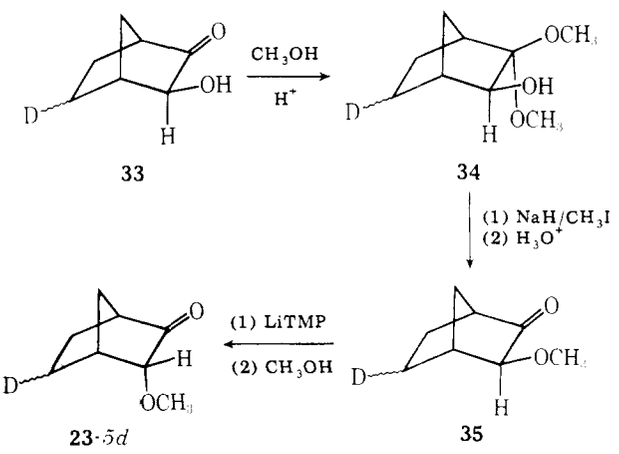
The isolation of **23**-*6d* from reaction of **21**-*5d* rules out the direct displacement mechanism and is completely consistent with the hydride migration mechanism of Scheme III.

We have previously reported[5a] that the triflate derivative

Scheme IV

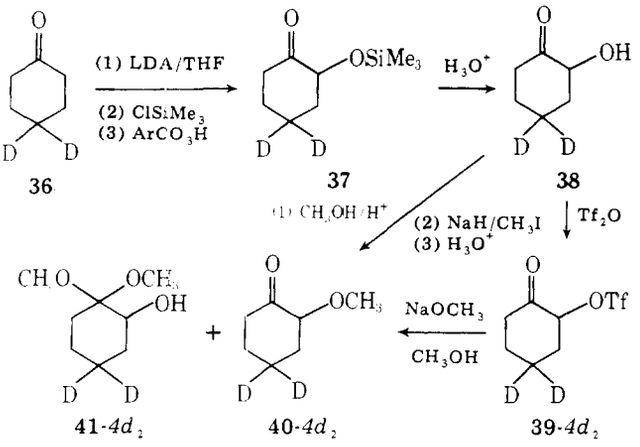


Scheme V

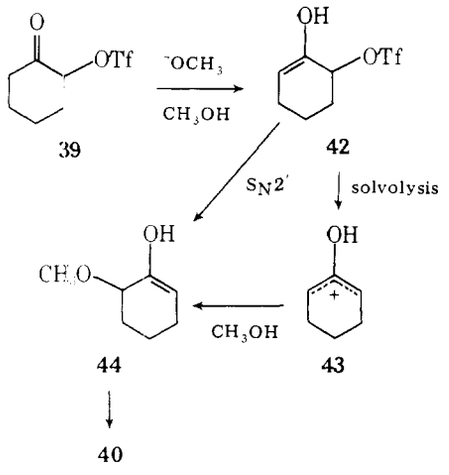


of α-hydroxycyclohexanone (**39**) gave a substitution product, 2-methoxycyclohexanone (**40**), in addition to 2,2-dimethoxycyclohexanol when treated with sodium methoxide. Although it might seem compelling to suggest a hydride migration path,

Scheme VI



Scheme VII

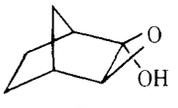


similar to that seen in the formation of **23**, to account for this later substitution product, the appropriate labeling experiment was nonetheless carried out. Deuterated triflate **39**-*4d*$_2$ was prepared as shown in Scheme VI from 4,4-dideuteriocyclohexanone (**36**).

Treatment of **39**-*4d*$_2$ with methoxide gave **40**-*4d*$_2$ as the substitution product. The position of the label was again determined by ^{13}C NMR as well as by infrared spectroscopy. An authentic sample of **40**-*4d*$_2$ could be prepared by ketalization of **38** followed by methylation and hydrolysis of the ketal. The infrared spectrum of authentic **40**-*4d*$_2$ so prepared was identical with that of the product produced from the triflate **39**-*4d*$_2$. Additionally, the ^{13}C NMR spectra of both products were identical with that of unlabeled 2-methoxycyclohexanone, except for the absence of the C_4 signal at δ 23.10. (The unenhanced multiplet due to C_4 is not visible under the spectral conditions.) These results show that the carbonyl carbon has *not* changed position and rule out the epoxide, zwitterion, hydride migration route as the source of 2-methoxycyclohexanone.

The chemistries of triflates **21** and **39** appear, at first glance, to be identical in their reactions with sodium methoxide. However, the labeling studies have shown that the substitution products are formed by completely unrelated processes. Although direct displacement of triflate by methoxide remains a possibility in **39**, mechanisms such as those shown in Scheme VII would also be consistent with the labeling experiment of Scheme VI.[16a] Without further evidence, a clear choice cannot be made between these processes.

Reaction of Bicyclo[2.2.1]heptan-2-on-3-yl Triflates with "Reversible" Nucleophiles. Methoxy epoxides are suggested intermediates in the reaction of triflates **6**, **21**, and **39** with sodium methoxide in methanol.[5a] Certain other halo ketones also give similar intermediates.[16] The tendency of α-keto triflates to give methoxy epoxides appears to be greater than that of the α-halo ketones. With these facts in mind triflates **6** and **21** were reacted with a variety of nucleophiles capable of adding reversibly to the carbonyl group to determine the generality of the epoxide-forming reaction. Table I summarizes the results of this study. The behavior of **6** with hydroxide is believed to be analogous to the reaction with methoxide, despite the fact that a formal displacement product, **45**, is isolated. It is suggested that epoxide **54** is



54

formed, which leads ultimately to **45**. With cyanide, epoxide intermediates **46** and **51** are isolable. The opening of these epoxides is unfavorable because of the cyano substituent. Cyano epoxide **51** is a rare example of an *endo*-norbornyl

Table I. Reaction of α-Keto Triflates with Nucleophiles

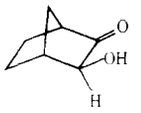
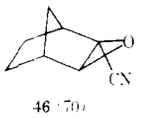
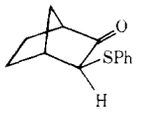
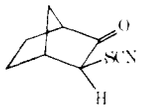
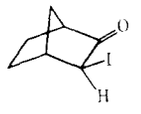
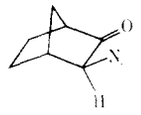
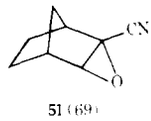
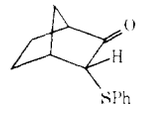
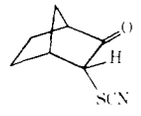
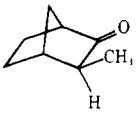
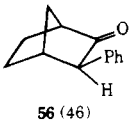
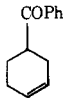
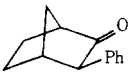
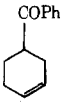
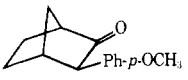
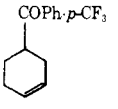
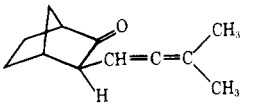
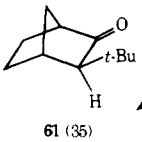
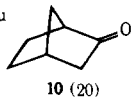
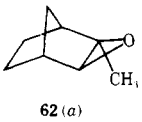
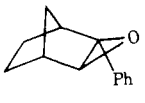
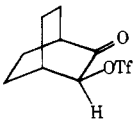
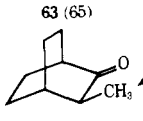
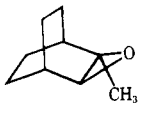
triflate	nucleophile	product (% yield)
6	NaOH	 **45** (79)
6	KCN	 **46** (70)
6	NaSPh	 **47** (86)
6	NaSCN	 **48** (86)
6	NaI	 **49** (83)
6	NaN_3	 **50** (69)
21	KCN	 **51** (69)
21	NaSPh	 **52** (52)
21	NaSCN	 **53** (46)

Table II. Reaction of α-Keto Triflates with Organometallic Reagents

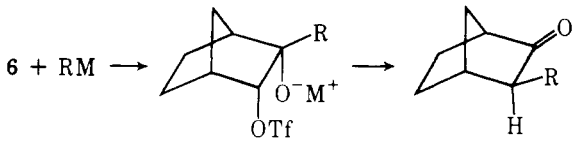
triflate	nucleophile	products (% yield)
	CH_3Li	 55 (83)
6	PhLi	 56 (46)  57 (23)
6	PhMgBr	 56 (a)  57 (a)
6	p-$CH_3OPhMgBr$	 58 (91)
6	p-$CF_3PhMgBr$	 59 (18)
6	$(CH_3)_2C{=}C{=}C(H)Li$	 60 (67)
6	t-BuLi	 61 (35)  10 (20)
21	CH_3Li	 62 (a)
21	PhLi	 63 (65)
	CH_3Li	 64  65 (b)  66 (b)

[a] Absolute yield was not determined; ratio of **56/57** was 2.2.
[b] Ratio of **65/66** was 0.5.

epoxide since oxidations of norbornene derivatives occur predominantly from the exo face.

Thiophenoxide, thiocyanate, iodide, and azide all give products of formal displacement of triflate with inversion of configuration. No epoxides are formed. The products (**49–50, 52,** and **53**) are consistent with either a classical S_N2 displacement or a stepwise addition to the carbonyl followed by intramolecular displacement of triflate. It therefore appears that nucleophiles of high polarizability will give displacement in preference to epoxide formation.

Reaction of Bicyclo[2.2.1]heptan-2-on-3-yl Triflates with "Irreversible" Nucleophiles. A second class of nucleophiles which are known to add irreversibly to the carbonyl group, organolithium reagents and Grignard reagents, was added to α-keto triflates **6** and **21**. The results of these



67 **68**

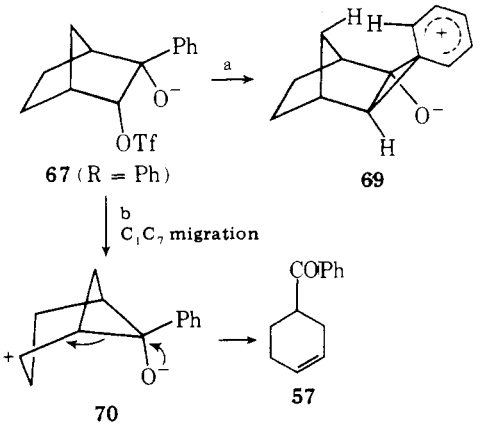
studies are summarized in Table II. Although **55, 56, 58, 60, 61,** and **65** appear to be simple displacement products, the formation of ketone **57** suggests that a more complicated mechanism is operative. The products in Table II can all be accounted for by a mechanism involving addition of the organometallic to the carbonyl group of the triflate to give analogues of **66**. Intramolecular transfer of the group R with loss of triflate generates the substitution product **68** via a stepwise process from **6**. In the reaction of phenyllithium with **6**, a competing process can intervene. It is known the *exo*-2,3-phenyl migration in the norbornyl system is sterically retarded by interaction of the ortho position with the C_7 bridge.[17] The transition state for phenyl migration should resemble **69**. Competing with this process is a pathway which involves loss of triflate with C_7 migration to give **70**. Fragmentation of **70** as shown in Scheme VIII gives the observed minor product **57**.

This type of mechanistic process has precedence. The solvolytic reaction of 3,3-dimethoxybicyclo[2.2.1]heptan-*exo*-2-yl triflate gives a similar mechanistic process,[22] as does the acid-catalyzed decomposition of 3-diazonorcamphor.[7a] In the present case, the mechanistic suggestion in Scheme VIII was tested by changing the migratory aptitude of the aryl group in **67**. In the case of *p*-methoxyphenylmagnesium bromide, only ketone **58** is produced with no trace of the aryl cyclohexenyl ketone product, attesting to the increased migratory aptitude of the *p*-methoxyphenyl group. In contrast, with *p*-(trifluoromethyl)phenylmagnesium bromide the migration is slowed to such an extent that the aryl cyclohexenyl ketone **59** is now the major product. These data therefore support the formation of an intermediate **67** even in the formation of simple substitution products.

Further evidence for the involvement of **66** in the formation of substitution products comes from the independent generation of **67** where R = methyl. Diol **72** could be produced by treatment of **71** with methyllithium and methanolysis of the silylated adduct (Scheme IX). Treatment of **72** with 2 equiv of methyllithium forms the dianion of **72**. Further treatment with triflic anhydride gave **55**, presumably through the intermediacy of **67** (R = CH_3), formed by conversion of the secondary alkoxide to the triflate leaving group. This demonstrates the viability of **67** as an actual intermediate in the formation of **55**.

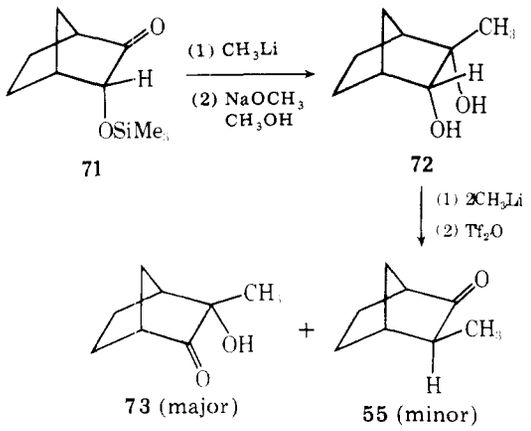
Ketone **55**, however, was only the minor product found in this sequence. The major product was the hydroxy ketone **73**.

Scheme VIII

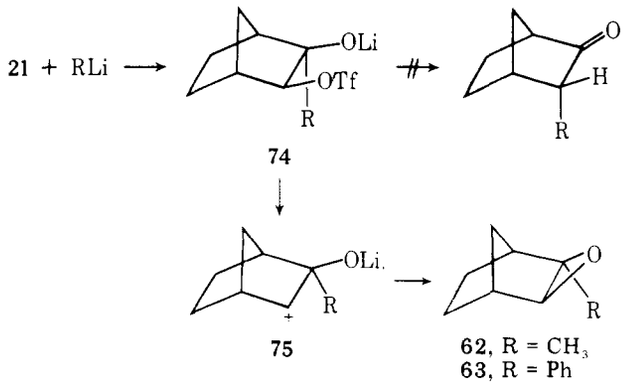


67 (R = Ph) **69**
70 **57**

Scheme IX



Scheme X



The formation of **73** in this reaction represents an oxidation of **72**. Although we are aware of no precedent, a possible origin of this product is hydride transfer from the dianion of **72** to triflic anhydride. This process would be analogous to the Oppenauer oxidation in which triflic anhydride is the hydride acceptor. It is not believed that **67** is involved in the formation of **73**.

The products from reaction of triflate **21** with methyllithium and phenyllithium are *exo*-epoxides **62** and **63**. These structures follow from the NMR and infrared spectra. Additionally, **62** could be independently synthesized by epoxidation of 2-methylnorbornene. These products are suggested to arise by initial addition of the organolithium reagent to the endo face of the carbonyl as in Scheme X. Since migration of groups across the endo side of **74** should be a very difficult process,[18] no simple substitution products are formed. The triflate stabilizing influence of the electronegative carbonyl group has, however, been destroyed, and therefore ionization occurs to give **75** and ultimately **62** and **63**. These products suggest that the exo triflate grouping effectively shields the exo surface of **21** to such an extent that endo attack becomes kinetically favored.[19] The difference between organolithium nucleophiles and nucleophiles such as methoxide and cyanide is that the latter can interact with triflate **21** from the endo direction, but this process is reversible. This reversible behavior of methoxide and cyanide eventually leads to methoxy and cyano epoxides in which the epoxide is endo. With the organolithium reagents, their irreversible nature necessitates products with *endo*-alkyl (-aryl) groups and hence *exo*-epoxides result.

Bicyclo[2.2.2]octan-2-on-3-yl triflate (**64**) reacted with methyllithium to give both a displacement product (**65**) and an epoxide (**66**). The chemistry of α-keto triflates and organometallics therefore appears to be a delicate function of migratory aptitudes in the system vs. the ability of the initially formed tetrahedral adduct to undergo ionization.

Summary

The chemistry of norbornyl α-keto triflates with nonnucleophilic bases does not appear to involve carbene chemistry. With LDA reduction products are seen, while oxidation products are seen with LiTMP. The former can be rationalized by β-hydride donation by LDA, while the later suggests β elimination of trifluoromethanesulfinic acid by LiTMP. Sodium methoxide gives a substitution product with *exo*-bicyclo[2.2.1]heptan-2-on-3-yl triflate which is a result of a rearrangement mechanism and not of a direct displacement of triflate. A similar mechanism is not operative in the formation of 2-methoxycyclohexanone from cyclohexanon-2-yl triflate. The chemistry of bicyclic α-keto triflates and other nucleophiles is largely dependent on the "reversibility" and migratory aptitude of the nucleophile, the stereochemistry of the triflate, the direction of attack on the triflate, and the tendency of the triflate–nucleophile adduct to ionize. These factors control the formation of epoxides vs. substitution products in the reactions of bicyclic α-keto triflates.

Experimental Section

NMR spectra were recorded on a Varian A-60 A or a Varian XL-100 in the Fourier transform mode and are reported in δ (parts per million) relative to tetramethylsilane. 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.

Reaction of *endo*-Bicyclo[2.2.1]heptan-2-on-3-yl Triflate (6) with LDA. Triflate **6** was prepared as previously described.[5a] Triflate **6** (1.50 g) in 6 mL of ether was added dropwise over a 15-min period to a −78 °C solution of LDA prepared from 1.62 g of diisopropylamine in 3 mL of ether and 10.4 mL of 1.4 M methyllithium. After the addition was completed, the mixture was warmed to −40 °C and quenched with water. A standard aqueous workup followed. The yield of norcamphor (**10**) was 31% as determined by gas chromatography vs. an internal standard. Only a trace of ketone **11** could be detected. In a separate run, using 1.1 equiv of LDA prepared from butyllithium per equivalent of **6**, the lower boiling product was separated by distillation. Ketone **11**, which slowly crystallized from the higher boiling fraction, had the following spectral properties: IR (KBr pellet) $\nu_{C=O}$ 5.76 μm; ^{13}C NMR ($CDCl_3$) δ 217.7, 51.9, 50.2, 37.8, 34.4, 27.5, 24.4. The ^{13}C spectrum also showed 13 additional peaks of lesser intensity.

Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.41. Found: C, 77.11; H, 8.16.

Reaction of 6 with Lithium Tetramethylpiperidide. LiTMP[9] was prepared by the addition of methyllithium (4.8 mL of 1.4 M) to a solution of 1.04 g of tetramethylpiperidine in 3 mL of ether under nitrogen. The resulting solution was cooled to −78 °C, and 1.5 g of **6** dissolved in 6 mL of ether was added dropwise. After being stirred at −78 °C for 10 min, the reaction was slowly warmed to 0 °C and ice water was added. The organic layer was extracted with water and saturated sodium chloride and dried (sodium sulfate). The solvent was removed on a rotary evaporator, leaving 0.58 g (86%) of crude **14** and **15**. The ratio of **14**/**15** was 0.90 as determined by gas chromatographic analysis. A portion of this mixture (0.50 g) was chromatographed on 25 g of silica gel and eluted with increasing proportions of ether in petroleum ether. Epoxide **14** (0.24 g) eluted with 16% ether, while triketone **15** (0.26 g) eluted with 65% ether. The compound which eluted first was assigned the structure **14** based on the following data: mp 108–109.5 °C; IR (KBr pellet) $\nu_{C=O}$ 5.71 μm, also a strong band at 13.1 μm; NMR ($DCCl_3$) δ 2.7–3.1 (2 H, m), 1.2–2.3 (6 H, m); ^{13}C NMR ($DCCl_3$) δ 211.4, 210.9, 72.9, 72.6, 49.9, 49.7, 38.0, 35.5, 35.3, 33.7, 26.2, 25.8, 23.2, 22.5; mass spectroscopic molecular weight, 232.1116 (calcd for $C_{14}H_{16}O_3$, 232.1099); mass spectroscopic molecular weight of parent − 16 ion, 216.1143 (calcd for $C_{14}H_{16}O_2$, 216.1150).

Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.65; H, 7.07.

The compound that eluted second, **15**, had the following properties: mp 93–95 °C; IR (KBr pellet) $\nu_{C=O}$ 5.67 and 5.90 μm; NMR ($DCCl_3$) δ 2.85–3.15 (3 H, m), 2.3–2.7 (3 H, m), 1.4–2.3 (10 H, m); ^{13}C NMR ($DCCl_3$) δ 209.0, 208.6, 208.4, 77.4, 49.6, 49.5, 48.9, 47.9, 34.8, 30.1, 27.5, 27.4, 24.6, 23.1.

Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.58; H, 6.76.

Reaction of 6 with Potassium *tert*-Butoxide. Potassium *tert*-butoxide (0.65 g) was dissolved in 10 mL of *tert*-butyl alcohol. A 1-g amount of **6** was added at 0 °C. After the mixture was stirred at room temperature for 2 h, water and ether were added. The organic phase was extracted with water and saturated sodium chloride and dried (sodium sulfate). The solvents were removed on a rotary evaporator and 0.27 g of crude residue remained. The product, which slowly crystallized from the crude oil, was identical in all respects with **14** described above.

Independent Preparation of Epoxy Ketone 14 from *exo*-3-Chloronorcamphor and 3,3-Dimethoxynorcamphor. LiTMP was prepared from 2.93 g of tetramethylpiperidine in 3 mL of ether and 12.8 mL of 1.4 M methyllithium. The mixture was cooled to −78 °C, and 2.0 g of *exo*-3-chloronorcamphor in 3 mL of ether was added dropwise to generate the enolate anion. 3,3-Dimethoxynorcamphor[8] (2.47 g in 7 mL of ether) was added to the mixture at −78 °C. The mixture was warmed to room temperature. Quenching of an aliquot showed unreacted starting materials. The mixture was then refluxed for 8 h, and a standard aqueous workup was followed. After the solvent was removed, the residue was chromatographed on silica gel to give 2.78 g of crude products. Gas chromatographic analysis showed the presence of unreacted 3,3-dimethoxynorcamphor and the monoketal of **14**. A pure sample of this monoketal was isolated by preparative gas chromatography and showed the following spectral characteristics: NMR (CCl_4) δ 3.33 (3 H, s), 3.19 (3 H, s), 2.9–2.4 (4 H, m), 2.2–1.0 (12 H, m).

A solution of 100 mg of the monoketal of **14** obtained above in 1 mL of tetrahydrofuran and 0.5 mL of 1 M HCl was stirred for 2.75 h at room temperature. A standard aqueous workup gave epoxy ketone **14**, which was identical spectrally and by mixture melting point with a sample of **14** obtained by reaction of triflate **6** with LiTMP.

Preparation of 28. The synthesis of keto acetate **26** was accomplished as previously described[20] except for the purification of the intermediate nortricycyl acetate, which was purified by exhaustive ozonolysis of the olefinic byproduct. The sodium borodeuteride reduction of **26** to **27** was as previously described.[20]

Triphenylphosphine (45.1 g) was dissolved in 100 mL of carbon tetrachloride (CCl_4). A 28-g amount of **27**, dissolved in 20 mL of carbon tetrachloride, was added. After the mixture was refluxed on a steam bath for 1 h, most of the solvent was removed through a Vigreux column. Pentane was added, and the solid triphenylphosphine oxide was removed by filtration. The filtrate was concentrated by a rotary evaporator, and the residue was distilled to give 25.17 g (82%) of **28**. A higher boiling fraction which was also collected contained 2.68 g of starting alcohol. The chloro acetate **28** had the following spectral properties: bp 63–65 °C (0.12 mm); IR (neat) $\nu_{C=O}$ 5.75 μm; NMR (CCl_4) δ 4.3–4.6 (1 H, m), 2.25–2.55 (2 H, m), 1.2–2.0 (9 H, m with sharp s at 1.95); mass spectroscopic molecular weight, 189.0646 (calcd for $C_9H_{12}ClDO_2$, 189.0667).

Sodium in Ammonia Reduction of 28. The chloride **28** (25 g) was dissolved in 1.5–2.0 L of liquid ammonia. The reaction vessel was equipped with a dry ice condensor, and small pieces of sodium were added until a blue color persisted. The excess sodium was destroyed by careful addition of ammonium chloride. The dry ice trap was removed, and the ammonia was allowed to evaporate. Ether and water were added. The aqueous phase was extracted with another portion of ether. The combined ether phases were extracted with saturated sodium chloride and dried (sodium sulfate). The solvent was removed through a Vigreux column, and the last traces were removed by a rotary evaporator. The crude semisolid, which weighed 14.6 g, consisted of mostly **29** and a minor amount of 2-acetoxynorbornane. Saponification of the entire residue in aqueous sodium hydroxide–ethanol followed by a standard workup and removal of solvent on a rotary evaporator gave a crude residue which was distilled through a solid distillation head at a pot temperature of 150 °C and a pressure of 140 mm. The yield of **29** was 10.38 g (73%): mp 122–125 °C; IR ν_{O-H} 2.9 μm; NMR (CCl_4) δ 3.6–3.9 (1 H, m), 3.13 (1 H, br s, exchanges with D_2O), 2.0–2.4 (2 H, m), 0.8–1.9 (7 H, m); ^{13}C NMR ($DCCl_3$) δ 74.7, 44.2, 42.2, 35.3, 34.4, 27.8 (triplet, J = 19.7 Hz), 24.4.

Preparation of 30. Sarett oxidation of **29** gave deuterated norcamphor (**30**) as previously described.[21] A total of six extractions with ether was necessary to obtain a 71% yield. Deuterated norcamphor (**30**), which was purified by sublimation, showed a parent peak in the mass spectrum at 111.0773 (calcd for C_7H_9DO, 111.0794).

Preparation of 21-*5d*. Silyl enol ether **31** was prepared from **30** as previously described for the undeuterated analogue.[5a] The Jefford procedure[15] was used for the preparation of **32**. The solvent used was methylene chloride at −10 °C, and the sensitizer was tetraphenylporphyrin. The triflate **21-*5d*** was prepared from **32** as previously described.[5a]

Reaction of 21-*5d* with Sodium Methoxide. The procedure was the same as that previously described.[5a] Deuterated triflate **21-*5d*** reacted with sodium methoxide (0.16 g of sodium dissolved in 10 mL of methanol) to give 0.30 g of products, which were separated by preparative gas chromatography. Both products were stable to the chromatography conditions. The major product was assigned the structure **22-*5d*** and had the following spectral properties: ^{13}C NMR ($DCCl_3$) δ 104.0, 74.2, 50.3, 47.8, 43.8, 41.6, 32.0, 22.4, 18.6 (triplet, J = 20.4 Hz). The minor product was assigned the structure **23-*6d*** and had the following spectral properties: ^{13}C NMR ($DCCl_3$) δ 214.0, 85.1, 58.2, 49.3, 38.2, 31.6, 26.2 (triplet, J = 21.2 Hz), 19.0; NMR (CCl_4) δ 3.3–3.6 (4 H, m with sharp s at 3.51), 2.4–2.9 (2 H, m), 1.2–2.1 (5 H, m); IR (neat) $\nu_{C=O}$ 5.68 μm.

Preparation of 23-*5d*. Hydroxy ketone **33** (1 g), which was prepared by heating the dimer to its melting point, was dissolved in 10 mL of methanol and 1.03 mL of trimethyl orthoformate. Several milligrams of *p*-toluenesulfonic acid were added, and the reaction was stirred at room temperature for 3 h. The acid was neutralized with triethylamine, and the solvents were removed by distillation at 140 mm. The residue was partially distilled to give 0.33 g (24%) of **4**, bp 68–70 °C (0.6 mm). The residue that did not distill was dimeric **33**. Recycling of this dimer as just described gave an additional 0.25 g of **34**. The total yield of **34** was 0.58 g (43%).

Deuterated **34** was converted to **35** by methylation and hydrolysis as previously described for the undeuterated analogue.[5a] Methoxy ketone **35** (0.40 g) was added dropwise to a −78 °C solution of LiTMP, prepared from 0.6 g of tetramethylpiperidine in 3 mL of ether and methyllithium (2.57 mL of 1.6 M). After the mixture was stirred at −78 °C for 15 min, 0.2 mL of methanol in 2 mL of ether was added. The reaction was warmed to room temperature, and water was added. The phases were separated, and the ether phase was extracted with dilute hydrochloric acid to remove the amine, water, and saturated sodium chloride. After being dried (sodium sulfate), the solvent was removed through a Vigreux column and the residue was distilled to give 0.24 g of **23-*5d*** contaminated with only a small amount of the exo isomer by gas chromatographic analysis. Methoxy ketone **23-*5d*** had the following properties: IR (neat) $\nu_{C=O}$ 5.67 μm; NMR (CCl_4) δ 3.3–3.5 (4 H, m with sharp s at 3.55), 2.4–2.9 (2 H, m), 1.1–2.1 (5 H, m); ^{13}C NMR ($DCCl_3$) δ 213.9, 85.1, 58.2, 49.4, 38.1, 31.6, 26.4, 18.8 (triplet, J = 20.6 Hz).

Preparation of 39-*4d*$_2$. 4,4-Dideuteriocyclohexanone (**36**) was prepared by a modified procedure of Green et al.[23] Lithium triethylborodeuteride (Super Deuteride) was used for the tosylate displacement instead of lithium aluminum deuteride. Ketone **36** was converted to **37** via the silyl enol ether using the Rubottom procedure[24] using methylene chloride instead of hexane as solvent. Acid-catalyzed hydrolysis of **37** in ether gave **38**, which was converted to **39-*4d*$_2$** as previously described for undeuterated 2-hydroxycyclohexanone.[5a]

Reaction of 39-*4d*$_2$ with Sodium Methoxide. The crude triflate **39-*4d*$_2$** directly from above was dissolved in 2 mL of 1 M sodium methoxide in methanol. The workup was the same as previously described. The products were collected by preparative gas chromatography. The major product was assigned the structure **41-*4d*$_2$** based on the following spectral data: IR (neat) ν_{O-H} 2.8 μm; ^{13}C NMR ($DCCl_3$) δ 100.5, 68.0, 48.1, 47.4, 28.8, 27.8, 21.9. The minor product was assigned the structure **40-*4d*$_2$** based on the following spectra data: IR (neat) $\nu_{C=O}$ 5.78 μm; ^{13}C NMR ($DDCl_3$) δ 209.6, 84.1, 57.6, 40.4, 34.0, 27.5. The deuterated carbons were not observable in either product.

Reaction of 6 with Sodium Hydroxide. Sodium hydroxide (0.43 g) was dissolved in 7 mL of water and 4 mL of isopropyl alcohol. The triflate **6** (1.99 g) was added dropwise followed by 1 mL of isopropyl alcohol. After being stirred for 30 min, the solution was saturated with sodium chloride and extracted with two portions of ether. The combined ether layers were extracted with saturated sodium chloride and dried (sodium sulfate). The solvent was removed by a rotary evaporator, and the crude residue was sublimed at 1–2 mm to afford 0.71 g (79%) of **45**: IR (neat) $\nu_{C=O}$ 5.78 μm, ν_{O-H} 2.82 μm; NMR δ 3.53 (1 H, d, J = 3 Hz), 2.98 (1 H, br s, exchanges with D_2O), 2.5–2.7 (2 H, m), 1.1–2.4 (6 H, m).

Reaction of Nucleophiles with the Bicyclic α-Keto Triflates. General Procedure. The nucleophile was dissolved or prepared in a given solvent and the triflate was added dropwise, usually at room temperature. After reaction under nitrogen at room temperature or at the reflux temperature of the solvent, ether and water were added and the phases were separated. The ether layer was extracted with water and saturated sodium chloride and dried (sodium sulfate). The solvents were removed on a rotary evaporator or on a steam bath through a Vigreux column. The residue was distilled to give the in-

dicated products.

Reaction of 6 with Potassium Cyanide. Triflate **6** (0.54 g) and 0.19 g of potassium cyanide in 12 mL of methanol reacted at 25 °C for 70 min to give 0.22 g of **46** and undeuterated **34** in a 9:1 ratio. Hydroxy ketal **34** was identified by spectral comparison with an authentic sample. Cyano epoxide **46** had the following spectral properties: IR (neat) $\nu_{C\equiv N}$ 4.41 μm; NMR (CCl_4) δ 3.45 (1 H, d, J = 1 Hz), 2.55–2.85 (2 H, m), 1.2–1.9 (5 H, m), 0.75–1.05 (1 H, m); mass spectroscopic molecular weight, 135.0690 (calcd for C_8H_9NO, 135.0684).

Reaction of 6 with Sodium Thiophenoxide. The addition of 0.07 g of sodium, 0.35 g of thiophenol, and 0.70 g of **6** to methanol at 25 °C in this order gave, after 2 h, 0.51 g (86%) of **47:** bp 123–125 °C (0.05 mm); IR (neat) $\nu_{C=O}$ 5.71 μm; NMR (CCl_4) δ 7.1–7.6 (5 H, m), 3.16 (1 H, d, J = 3 Hz), 2.5–2.7 (2 H, m), 1.3–2.3 (6 H, m); mass spectroscopic molecular weight, 218.0762 (calcd for $C_{13}H_{14}OS$, 218.0765).

Reaction of 6 with Sodium Thiocyanate. Sodium thiocyanate (0.23 g) and 0.7 g of **6** in 18 mL of acetone did not react after 15 h at room temperature. The reaction was refluxed for 38 h. Workup and distillation gave 5% of starting **6** and 0.39 g (86%) of **48:** bp 86–90 °C (0.05 mm); IR (neat) $\nu_{C\equiv N}$ 4.58 μm; $\nu_{C=O}$ 5.69 μm; NMR (CCl_4) δ 3.51 (1 H, d, J = 3 Hz), 2.65–2.95 (2 H, m), 1.3–2.4 (6 H, m); mass spectroscopic molecular weight, 167.0410 (calcd for C_8H_9NOS, 167.0405).

Reaction of 6 with Sodium Iodide. Sodium iodide (1.22 g) and 0.70 g of **6** in 10 mL of acetone gave, after refluxing for 2 h, 0.53 g (83%) of **49:** bp 65–69 °C (0.01 mm); IR (neat) $\nu_{C=O}$ 5.73 μm; NMR (CCl_4) δ 4.15 (1 H, d, J = 3 Hz), 2.5–3.0 (2 H, m), 1.4–2.5 (6 H, m); mass spectroscopic molecular weight, 235.9697 (calcd for C_7H_9IO, 235.9698).

Reaction of 6 with Sodium Azide. Sodium azide (0.19 g) and 0.7 g of **6** in 20 mL of methanol gave no reaction at room temperature. After 19.3 h at reflux and workup, distillation of the residue gave 0.38 g of products, bp 45–65 °C (0.07 mm). Gas chromatographic analysis of the product mixture showed that at least seven compounds were present. The two major products were **50** (75% of the mixture) and recovered **6** (15% of the mixture). None of the other products contained the azide moiety by infrared analysis. The major product **50** had the following spectral properties: IR (neat) $\nu_{N=N=N}$ 4.72 μm, $\nu_{C=O}$ 5.68 μm; NMR (CCl_4) δ 3.31 (1 H, d, J = 3 Hz), 2.3–2.7 (2 H, m), 1.2–2.3 (6 H, m); mass spectroscopic molecular weight, 151.0758 (calcd for $C_7H_9N_3O$, 151.0746).

Reaction of 21 with Potassium Cyanide. Reaction of triflate **21**[5a] (0.25 g) and 0.13 g of potassium cyanide in 7 mL of methanol at 25 °C for 1.5 h gave 0.09 g of **51** and **22**, bp 65–75 °C (0.18 mm). The ratio of cyano epoxide **51**/hydroxy ketal **22** was 5:1. Hydroxy ketal **22** was identified by spectral comparison with an authentic sample. Cyano epoxide **51** had the following spectral properties: IR (neat) $\nu_{C\equiv N}$ 4.41 μm; NMR (CCl_4) δ 4.0 (1 H, d, J = 3 Hz), 2.2–2.8 (2 H, m), 1.2–2.0 (6 H, m); mass spectroscopic molecular weight, 135.0699 (calcd for C_8H_9NO, 135.0684.

Reaction of 21 with Sodium Thiophenoxide. The addition of 0.027 g of sodium, 0.139 g of thiophenol, and 0.25 g of **21** in this order to 3 mL of methanol gave, after reaction at 25 °C for 3 h, 0.11 g of **52:** bp 110–120 °C (0.02 mm); IR (neat) $\nu_{C=O}$ 5.71 μm; NMR (CCl_4) δ 7.0–7.7 (5 H, m), 3.57 (1 H, d, J = 4.5 Hz), 2.4–2.9 (2 H, m), 1.1–2.3 (6 H, m); mass spectroscopic molecular weight, 218.0767 (calcd for $C_{13}H_{14}OS$, 218.0765).

Reaction of 21 with Sodium Thiocyanate. Sodium thiocyanate (0.16 g) and 0.24 g of **21** in 5 mL of acetone gave, after 24 h at 25 °C, 0.12 g of products, bp 80–90 °C (0.08 mm). The product mixture contained at least four components by gas chromatographic analysis. The major product, **53,** was 60% of the mixture and had the following spectral properties: IR (neat) $\nu_{C=O}$ 5.69 μm, $\nu_{C\equiv N}$ 4.59 μm; NMR (CCl_4) δ 4.03 (1 H, d, J = 4.5 Hz), 2.65–3.10 (2 H, m), 1.2–2.4 (6 H, m); mass spectroscopic molecular weight, 167.0561 (calcd for C_8H_9NOS, 167.0405).

Reaction of Bicyclic α-Keto Triflates with Organometallic Reagents. General Procedure. The triflate was dissolved in several milliliters of dry ether, and the solution was cooled to −78 °C. The organometallic reagent was added dropwise, and stirring was continued for 5–10 min. The reaction was slowly warmed to 0 °C, water was added, and the phases were separated. The ether phase was extracted with saturated sodium chloride and dried (sodium sulfate). The solvent was removed on a steam bath through a Vigreux column, and the residue was distilled to give the indicated products.

Reaction of 6 with Methyllithium. Methyllithium (0.93 mL of 1.84 M) and 0.04 g of **6** in 5 mL of ether gave 0.16 g of *exo*-3-methylnorcamphor (**55**), which was identified by spectral comparison with an authentic sample.[25] *exo*-3-Methylnorcamphor (**55**) had the following characteristics: IR (neat) $\nu_{C=O}$ 5.71 μm; NMR ($DCCl_3$) δ 2.2–2.4 (1 H, m), 2.5–2.6 (1 H, m), 1.3–2.0 (6 H, m), 1.05 (3 H, d, J = 7.5 Hz).

Reaction of 6 with Phenyllithium. Phenyllithium (1.42 mL of 1.8 M) and 0.60 g of **6** in 10 mL of ether gave 0.30 g of a 2:1 mixture of **56** and **57,** bp 90–95 °C (0.05 mm). The major product, **56,** had the following spectral properties: IR (neat) $\nu_{C=O}$ 5.71 μm; NMR ($DCCl_3$) δ 7.0–7.6 (5 H, m), 3.12 (1 H, d, J = 3 Hz), 2.5–2.9 (2 H, m), 1.1–2.4 (6 H, m); mass spectroscopic molecular weight, 186.1043 (calcd for $C_{13}H_{14}O$, 186.1021). The minor product was identical with a sample of **57** which was independently synthesized from phenyllithium and cyclohex-3-enecarboxylic acid. Previously reported ketone **56**[26a] had the following spectral characteristics: IR (neat) $\nu_{C=O}$ 5.93 μm; NMR ($DCCl_3$) δ 7.4–7.6 (m), 7.85–8.05 (m), 5.7–5.8 (2 H, m), 3.3–3.7 (m, 1.3–2.5 (m); mass spectroscopic molecular weight, 186.1045 (calcd for $C_{13}H_{14}O$, 186.1021).

Reaction of 6 with Phenylmagnesium Bromide. Phenylmagnesium bromide (2.4 mL of 1.0 M) and 0.60 g of **6** gave a mixture of **56** and **57** in a ratio of 2.2:1 as determined by gas chromatography.

Reaction of 6 with *p*-Methoxyphenylmagnesium Bromide. *p*-Methoxyphenylmagnesium bromide (5.2 mL of 0.414 M) and 0.49 g of **6** gave 0.37 g (91%) of **58,** which was purified by silica gel chromatography. Ketone **58** had the following spectral properties: NMR (CCl_4) δ 6.92 (4 H, AA′BB′ quartet), 3.72 (3 H, s), 2.91 (1 H, d, J = 3.3 Hz), 2.80 (1, H, m), 2.53 (1 H, m), 2.20–1.20 (6 H, m); IR $\nu_{C=O}$ 5.71 μm; mass spectroscopic molecular weight, 216.1156 (calcd for $C_{14}H_{16}O_2$, 216.1150).

Reaction of 6 with *p*-(Trifluoromethyl)phenylmagnesium Bromide. *p*-(Trifluoromethyl)phenylmagnesium bromide (1.5 mL of 1.0 M) and 0.31 g of **6** gave a product mixture that was purified by silica gel chromatography. Ketone **59,** 54 mg (18%), was the only product that eluted. The gas chromatographic analysis of the mixture before silica gel chromatography showed two unidentified minor products of longer retention time in addition to the major product **59.** Ketone **59** had the following spectral properties: IR $\nu_{C=O}$ 5.88 μm; NMR ($CDCl_3$) δ 7.97 (4 H, AA′BB′ quartet), 5.82 (2 H, m), 2.7–1.4 (7 H, m); mass spectroscopic molecular weight, 254.0878 (calcd for $C_{14}H_{13}F_3O$, 254.0918).

Reaction of 6 with 3,3-Dimethylallenyllithium.[28] Methyllithium (1.16 mL of 1.84 M) was added to 0.7 g of 1,1-dimethylallene under nitrogen. Four drops of diisopropylamine were added, and the solution was stirred for 2 h. Triflate **6** (0.54 g), dissolved in 5 mL of ether, was added slowly dropwise to the allenyllithium reagent which had been cooled to −78 °C. The reaction was stirred at −78 °C for 5 min and at 0 °C for 15 min. Water and ether were added. A standard aqueous workup and distillation of the solvent through a Vigreux column left a residue which was distilled to give 0.29 g of a product mixture which consisted of approximately 85% **60** by gas chromatographic analysis. Product **60** had the following spectral properties: IR (neat) $\nu_{C=O}$ 5.71 μm; NMR (CCl_4) δ 4.70–5.05 (1 H, m), 2.4–2.6 (2 H, m), 2.28 (1 H, d of d, J = 3.4 and 5.4 Hz), 1.1–2.1 (12 H, m with a doublet at 1.70, J = 3 Hz); mass spectroscopic molecular weight, 176.1243 (calcd for $C_{12}H_{16}O$, 176.1209).

Reaction of 6 with *tert*-Butyllithium. *tert*-Butyllithium (1.4 mL of 1.5 M in pentane) and 0.50 g of **3** gave a mixture of norcamphor (**10**) and *exo*-3-*tert*-butylnorcamphor (**61**) in 20 and 35% yields, respectively, as determined by gas chromatography. Norcamphor was identified by spectral comparison with an authentic sample. Ketone **61** had the following spectral properties: IR $\nu_{C=O}$ 5.72 μm; NMR ($CDCl_3$) δ 2.9–2.4 (2 H, m), 2.0–1.4 (7 H, m), 1.05 (9 H, s).

Reaction of 21 with Methyllithium. Methyllithium (0.65 mL of 1.84 M) and 0.294 g of **21** gave a 20:1 mixture of **62** and an unidentified product, bp 58–65 °C (13 mm). The major product was identical with a sample of **62** prepared as previously described.[27] Epoxide **62** had the following spectral properties: NMR (CCl_4) δ 2.68 (1 H, br s), 2.25–2.45 (1 H, m), 2.05–2.25 (1 H, m), 1.0–1.7 (8 H, m with sharp s at 1.35), 0.60 (1 H, br d, J = 9 Hz); mass spectroscopic molecular weight, 124.0889 (calcd for $C_8H_{12}O$, 124.0888).

Reaction of 21 with Phenyllithium. Phenyllithium (0.73 mL of 1.75 M) and 0.30 g of **21** gave 0.14 g (65%) of **63:**[26b] bp 88 °C (0.05 mm); NMR (CCl_4) δ 7.1–7.6 (5 H, m), 3.20 (1 H, br s), 2.7–2.9 (1 H, m), 2.40–2.65 (1 H, m), 1.1–1.9 (5 H, m), 0.79 (1 H, br d, J = 9 Hz); mass spectroscopic molecular weight, 186.1043 (calcd for $C_{13}H_{14}O$, 186.1045).

Reaction of Bicyclo[2.2.2]octan-2-on-3-yl Triflate (64) with Methyllithium. Methyllithium (0.37 mL of 1.6 M) and 0.160 g of triflate **64**[5a] gave epoxide **66** and ketone **65** in a ratio of 2:1 as determined by gas chromatography. Ketone **65** was identified by spectral comparison with an authentic sample prepared by methylation of the lithium enolate of bicyclo[2.2.2]octanone. Epoxide **66** had the following spectral properties: NMR (CCl_4) δ 2.87 (1 H, d, J = 4.5 Hz),

2.3–1.4 (10 H, m), 1.30 (3 H, s).

Preparation of Diol 72. Ketone 71[29] (4.32 g) in 10 mL of ether was treated with 15.7 mL of 1.6 M methyllithium at −78 °C. The mixture was then warmed to room temperature and quenched with water. After a standard aqueous workup, the monosilylated diol product was isolated by distillation to give 4.48 g (96%), bp 69–69 °C (1.3 mm). The monosilylated form of **72** (4.0 g) was dissolved in 30 mL of methanol, and 3 mL of 1.0 M sodium methoxide in methanol was added. After 4 h, solvent was removed by a rotary evaporator. The product was isolated by distillation at 0.04 mm. Redistillation gave 1.89 g (71%) of diol **72**, bp 71–72 °C (0.04 mm). Diol **72**, which slowly crystallized, melted at 38–40 °C and had the following spectral properties: NMR ($CDCl_3$) δ 3.53 (1 H, broadened triplet, collapses to doublet, J = 4 Hz, with added D_2O), 3.28 (1 H, d, J = 6 Hz, exchanges with D_2O), 2.88 (1 H, s, exchanges with D_2O), 2.5–1.0 (11 H, m with sharp singlet at 1.25); mass spectroscopic molecular weight, 142.0975 (calcd for $C_8H_{14}O_2$, 142.0994).

Reaction of 72 with Methyllithium and Triflic Anhydride. A solution of 0.35 g of diol **72** in 3 mL of ether was treated with 2.05 mL of 2.4 M methyllithium in ether at room temperature for 15 min. The mixture was then cooled to −78 °C and treated with 0.7 g of triflic anhydride. The mixture was warmed to room temperature, and a standard aqueous workup was followed. Gas chromatographic analysis showed *exo*-3-methylnorcamphor (**55**) and *exo*-3-methyl-3-hydroxynorcamphor (**73**) in 15 and 38% yields, respectively, along with approximately 10% unreacted diol **72**. Samples of **55** and **73** were isolated by preparative gas chromatography and identified by spectral comparison with authentic samples.[30]

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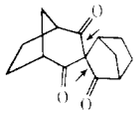

15

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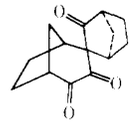

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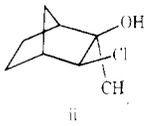

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