# Fluoride-Mediated Reactions of Enol Silyl Ethers. Regiospecific Monoalkylation of Ketones

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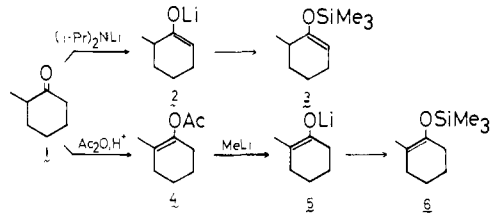
**Abstract:** Treatment of enol silyl ethers with alkyl halides in the presence of benzyltrimethylammonium fluoride and molecular sieves at room temperature gives the corresponding monoalkylated products with high regiospecificity. In most cases no polyalkylated products formed in the reaction. The alkylation reaction is highly chemospecific: esters, epoxides, and even ketones survive the reaction conditions. The reactions of various cyclohexanone derivatives proceed with the preferential axial attack of the electrophile.

It has been a difficult synthetic problem to perform $\alpha$-alkylation of ketones in a highly controlled manner. It can be achieved only when the enolate anion generated regiospecifically is allowed to react with an alkylating agent before the enolate anion undergoes equilibration via proton transfer. Polyalkylation and nonregioselective alkylation often accompany the desired reaction. Self-condensation of the ketone can also be a cause of trouble. The conventional solution has been the introduction of blocking and activating groups.[1] In the last decade, synthetic chemists, utilizing newly developing chemistry of strong bases, have devised ways to generate regiospecific (lithium) enolates without recourse to such extraneous groups.[2] Generation of isomeric lithium enolates **2** and **5**[3] illustrates such a methodology. Utilization of enol silyl ethers,[4] e.g., **3** or **6**, as precursors of enolate anions is also a good alternative approach.




Problems remained to be solved, however. Although the alkylation of lithium enolates with reactive halides usually gives satisfactory results,[5] the reactions with relatively unreactive ones, e.g., butyl iodide, do not. Because the alkylation reaction is now slow as compared to the proton transfer, the desired products are obtained in moderate yields.

Among some conceptual approaches to accomplish the highly regiospecific reaction, one involves retardation of the undesirable proton transfer by using a metal enolate with a relatively covalent metal–oxygen bond.[6] This, however, has not yet proven too successful. The Friedel–Crafts-like reaction of enol silyl ethers reported recently is a new class of reactions in enolate chemistry,[7] opening a new horizon, e.g., alkylation with tertiary alkyl halides.

Table I. Methylation of 7[a]

| entry | molecular,[b] sieves (4A) | solvn | temp, °C | time, h | % yield 1 | % yield 8 | % material balance |
|---|---|---|---|---|---|---|---|
| 1 | − | THF | 0 | 24 | 33 | 57 | 90 |
| 2 | + | THF | 0 | 6 | 90 | 10 | 100 |
| 3 | + | THF | 25 | 1 | 87 | 3 | 97 |
| 4 | + | DME | 0 | 8 | 90 | 10 | 100 |
| 5 | + | DME | room temp | 23 | 70 | 9 | 79 |

[a] For the standard reaction conditions, see Experimental Section. [b] The reaction was performed with (+) or without (−) molecular sieves.

In principle, there would be another approach of employing a "naked enolate anion", which involves entirely an ionic oxygen–cation bonding: acceleration of the alkylation reaction would remove the difficulties.[8] A quaternary ammonium enolate, an ideal candidate in this sense, may, in turn, suffer accelerated proton-transfer reaction. We considered a metathesis between an enol silyl ether and a tetraalkylammonium fluoride as the means to generate this enolate species. Because of the high affinity of fluorine and silicon atoms, the fluoride anion was expected to attack the silicon atom in preference to other carbon electrophiles. In fact, the fluoride anion, unique among other halide and alkoxide anions,[11] effected the desired reaction of enol silyl ethers and alkyl halides. The reaction could (only, vide infra) be carried out by generating the enolate anion in the presence of an alkylating agent; thus the undersirable proton-transfer reaction was cut down to a negligible level. Here we record the full details of this fluoride-mediated reaction,[12] which only rivals the reaction of lithium enolates in terms of the yield problem mentioned above, yet more importantly proceeds with remarkable cleanliness and mildness.

(1) Cf. House, H. O. "Modern Synthetic Reactions"; W. A. Benjamin: Menlo Park, CA, 1972; Chapter 9.
(2) Cf. D'Angelo, *Tetrahedron* **1976**, *32*, 2979.
(3) House, H. O.; Czuba, L. J.; Gall, M.; Olmstead, H. D. *J. Org. Chem.* **1969**, *34*, 2324.
(4) (a) Stork, G.; Hudrlik, P. F. *J. Am. Chem. Soc.* **1968**, *90*, 4462, 4464. (b) Review: Rasmussen, J. K. *Synthesis* **1977**, *91*.
(5) For instance: (a) House, H. O.; Gall, M.; Olmstead, H. D. *J. Org. Chem.* **1971**, *36*, 2361. Gall, M.; House, H. O. *Org. Synth.* **1972**, *52*, 39. (b) Borowitz, I. J.; Casper, E. W. R.; Crouch, R. K.; Yee, K. C. *Ibid.* **1972**, *37*, 3873.
(6) Tardella, P. A. *Tetrahedron Lett.* **1969**, 1117. Odic, Y.; Pereyre, M. *J. Organomet. Chem.* **1973**, *55*, 273.
(7) (a) Hashimoto, S.; Itoh, A.; Kitagawa, Y.; Yamamoto, H.; Nozaki, H. *J. Am. Chem. Soc.* **1977**, *99*, 4192. (b) Chan, T. H.; Paterson, I.; Pinsonnault, J. *Tetrahedron Lett.* **1977**, 4183. (c) Reetz, M. T.; Maier, W. F. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 48.
(8) (a) For the acceleration of the alkylation of enolate anions with ammonium salts: Zook, H. D.; Gumby, W. L. *J. Am. Chem. Soc.* **1960**, *82*, 1386. Review: Jackmam, L. M.; Lange, B. C. *Tetrahedron* **1977**, *33*, 2737. (b) Preparation and reactions of "naked" enolate anions of active methylene compounds: Brandström, A.; Gustvii, K. *Acta Chem. Scand.* **1969**, *23*, 1215.
(9) Noyori convincingly showed the formation of a "naked" enolate anion in such a metathesis by replacing the ammonium cation with a more stable sulfonium cation: Noyori, R.; Nishida, I.; Sakata, J.; Nishizawa, M. *J. Am. Chem. Soc.* **1980**, *102*, 1223. (b) Alkylation of the enolate generated in situ: Noyori, R.; Nishida, I.; Sakata, J. *Tetrahedron Lett.* **1980**, 2085. (c) Aldol reaction: Noyori, R.; Nishida, I.; Sakata, J. *J. Am. Chem. Soc.* **1981**, *103*, 2106.
(10) For the use of fluoride anion for the protonolysis of silyl ethers: Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 2549.
(11) Alkoxide anion can also effect the reaction, while halides except fluoride are ineffective. The reaction of the silyl ether **5** and butyl iodide (1.5 equiv) in the presence of potassium methoxide and 18-crown-6 (0.5 equiv) gave 2-butylcyclohexanone in 31% yield, yet the apparently higher reactivities of alkoxide anions than those of fluoride anion rendered this approach unattractive.
(12) For the preliminary communication, Kuwajima, I.; Nakamura, E. *J. Am. Chem. Soc.* **1975**, *97*, 3257.

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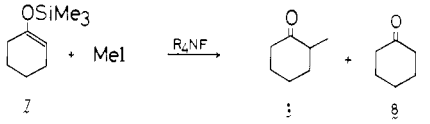
Table II. Effect of Miscellaneous Conditions[a]

| entry | $R_4NF$ | RX (equiv) | molecular,[b] sieves (4A) | solv | % yield 1 | % yield 8 | % material balance |
|---|---|---|---|---|---|---|---|
| 1 | BTAF | MeI (1.0) | –[c] | THF | 23 | 66 | 89 |
| 2 | | MeI (3.0) | + | THF | 91 | 9 | 100 |
| 3 | | MeOTs (1.0) | + | THF | 0 | 81 | 81 |
| 4 | | MeI (1.0) | – | $CH_3CN$ | 32 | 68 | 100 |
| 5 | | MeI (1.0) | + (3A) | $CH_3CN$ | 38 | 62 | 100 |
| 6 | | MeI (1.0) | + (4A) | $CH_3CN$ | 37 | 63 | 100 |
| 7 | BTAF | MeI (1.0) | + | THF | 36 | 51 | 87 |
| 8 | KF–crown[d] | MeI (1.0) | – | THF | 20 | 24 | *e* |

[a] See note a in Table I. The reaction temperature was initially 0 °C and was then raised to room temperature. [b] See note b in Table I. [c] BTAF was finely pulverized by stirring overnight with glass beads. [d] KF (2 equiv)–dicyclohexyl-18-crown-6 (0.1 equiv) for 7 days at room temperature. [e] Not determined. About 50% of the enol silyl ether remained.

**Optimum Reaction Conditions.** Tetraalkylammonium fluorides are very hygroscopic compounds. Since the alkylation reaction requires the use of 1 equiv of the fluoride under anhydrous conditions, complete removal of water from the fluoride was desirable. We employed the reaction of enol silyl ether **7** and methyl iodide as a standard reaction with a stoichiometry of **7**: $MeI:F^- = 1:1:1.1–1.2$ in order to determine the optimum conditions.




7 1 8

Tetramethylammonium, tetraethylammonium, tetrabutylammonium (TBAF), cetyltrimethylammonium, and benzyltrimethylammonium fluorides (BTAF) were prepared by neutralization of the corresponding commerical hydroxides (10–40% aqueous or methanolic solution) with dilute aqueous hydrogen fluoride. Preliminary experiments indicated that BTAF (readily available from commercial Triton B) is most suitable for the purpose.

Search of the literature showed that none of the "anhydrous" tetraalkylammonium fluoride had any convincing proof of its purity.[13] We examined a variety of conditions to remove water from BTAF by performing the methylation reaction in acetonitrile where BTAF makes a nearly homogeneous mixture. The first trial consisted of a simple and direct method: BTAF was heated under reduced pressure. Heating at an elevated temperature (above 100 °C) caused noticeable decomposition of BTAF. The decomposition accompanied the loss of weight and the lowering of the pH value of the fluoride. Below 90 °C, however, the decomposition was reasonably slow, and the material dried at 90 °C (ca. 0.1 mm) for 48 h yielded 36% of the monomethylation product (**1**) together with 60% yield of cyclohexanone (**8**). BTAF dried at 30 °C (ca. 0.1 mm) to a constant weight (2 days) gave constant results of methylation (ca. 30% yield). BTAF thus obtained was a clean white solid. There was found no marked solvent effects among acetonitrile, dioxane, and THF (cf. Table I, entry 1). Azeotropic removal of water (benzene, Dean–Stark apparatus) made no improvement.

The use of inorganic drying agents was precluded, because the fluoride anion readily reacts with metal cations to form stable metal fluorides. Molecular sieves, however, brought about a dramatic improvement (Table I). Stirring BTAF with 4A molecular sieves overnight in THF improved the yield of **1** from 33% (Table I, entry 1) to 90% (entries 2 and 4). Even when molecular sieves were employed, the drying conditions for BTAF were still crucial. They should remain in a certain optimum range (30 °C, 2 days–50 °C, 1 day at ca. 0.1 mm). BTAF was normally stirred overnight with molecular sieves, and the alkylation reaction was performed by addition of a mixture of **7** and methyl iodide into the resulting pasty suspension of BTAF and molecular sieves. It is noteworthy that no byproducts other than cyclohexanone formed in these methylation reactions (Table I).

(13) Cf. Kent, P. W.; Young, R. C. *Tetrahedron* **1971**, *27*, 4057.

Table III. Solvent Effects in Benzylation of 7[a]

| solvent | % yield[b] 20 min | % yield[b] 1 h |
|---|---|---|
| DME | *c* | 63[d] |
| THF | 44 | 56 |
| benzene | 21 | 49 |
| hexane | 9 | 17 |
| acetone | 25 | 27 |

[a] The reaction was performed at ca. 25 °C with molecular sieves in a 0.3 M solution with a molar ratio of reagents; BTAF:7:benzyl bromide = 1.2:1.1:1.0. [b] Yields refer to GLC yields, unless otherwise noted. [c] Not determined. [d] Isolated yield.

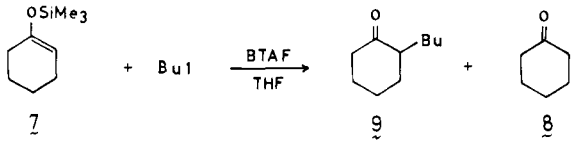
Solvents exercise great influence on the yield and the reaction rate (Tables II and III). DME and THF are the most suitable for this reaction, whereas they form heterogeneous reaction mixture. The relatively low reaction rate (30 min in DME) compared with the alkylation of rate of lithium enolates (less than 10 min in DME)[5a] may be due to heterogenuity of the mixture. Longer reaction in DME tended to cause a decrease of both the product yield and the material balance (Table I, entry 5), but such effects were not observed in THF (entry 3). Reactions in these media were exothermic and cooling (<0 °C) at the beginning of the reaction considerably improved the material balance. It should be noted that the reaction proceeds even at –30 °C, and after 96 h, methylcyclohexanone was obtained in 79% yield. The reaction was not completed at this point, and approximately 5% of **7** was recovered. Brief examination of HMPA indicated that it is not a suitable solvent. It is interesting to note that, in acetonitrile, the effect of the molecular sieves (either 4A or 3A) was scarely observed (Table II, entries 4–6). In halomethanes, the fluoride anion lost its activity during stirring with molecular sieves.

The source of the fluoride anion was reinvestigated briefly. TBAF, which is a good catalyst in the related catalyzed reactions,[14] gave poor results even in the presence of molecular sieves (Table II, entry 7). The reason is not clear, however. As for the stability of the fluoride, BTAF was reasonably stable to heating and to the reaction conditions. The formation of aromatic amines which would have formed by base-catalyzed decomposition[15] was not detected in any crude reaction mixture. Combination of KF/dicyclohexyl-18-crown-6 in acetonitrile[16] effected only very slow reactions at ca. 25 °C; an admixture of KF (2 equiv) and crown ether (0.1 equiv) in THF brought about only ca. 50% conversion of the enol silyl ether **7** after 7 days of stirring (Table II, entry 8).

In an attempt to examine the generation of the free enolate anion for further studies, we treated **7** initially with BTAF and then with methyl iodide. The experiments, either with or without sieves, invariably gave back **8**, indicating protonation of the anion before alkylation.

Effects of excess reagents were investigated with respect to both the enol silyl ether and the alkyl halide. The methylation reaction of **7** which gave an excellent yield even with 1 equiv of methyl iodide was not greatly affected by the use of excess alkyl halide (Table II, entry 2). However, the use of excess reagent improved the situation for butylation (eq 1). The use of 10 equiv of butyl iodide increased the yield approximately 1.5 times, but further excess did not give better results. As in the methylation reaction, excellent material balance of cyclohexanone was observed in every

(14) For instance: (a) Nakamura, E.; Murofushi, T.; Shimizu, M.; Kuwajima, I. *J. Am. Chem. Soc.* **1976**, *98*, 2346. (b) Noyori, R.; Yokoyama, K.; Sakata, J.; Kuwajima, I.; Nakamura, E.; Shimizu, M. *Ibid.* **1977**, *99*, 1265. (c) Nakamura, E.; Hashimoto, K.; Kuwajima, I. *Tetrahedron Lett.* **1978**, 2079. (d) *Bull. Chem. Soc. Jpn.* **1980**, *54*, 804.
(15) Pine, S. H. *Org. React.* **1970**, *18*, 403.
(16) Liotta, C. L.; Harris, H. P. *J. Am. Chem. Soc.* **1974**, *96*, 2250.

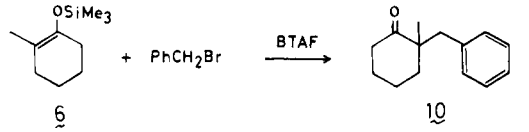


(1)

| equiv | | | % yield | |
|---|---|---|---|---|
| 1.0 | 1.0 | 1.1 | 30 | 70 |
| 1.0 | 10 | 1.1 | 50 | 50 |
| 1.0 | 30 | 1.1 | 45 | 48 |

run of the butylation reaction. Since the reaction of the fluoride anion with an excess alkyl halide would result in the loss of the fluoride anion,[17] i.e., the decrease of the reactive species, these results indicate the chemospecific attack of the anion onto the silyl ether. Alkyl bromide, chloride, and tosylate (Table II, entry 3) and tetraalkylammonium salt, e.g., BTAF, did not serve as the alkylating agents.

The use of an excess enol ether also increased the yield of the monoalkylated product (eq 2). For instance, the yield of **10** in



(2)

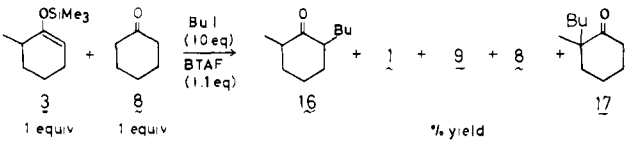
| equiv | | | % yield |
|---|---|---|---|
| 1.0 | 1.0 | 1.1 | 37 |
| 2.0 | 1.0 | 2.2 | 59 |

the reaction of **6** was substantially increased by 100% excess of **6**. These results crucially depend upon the fact that the quaternary ammonium fluoride does not cause aldol reaction between an enol silyl ether and a ketone.[14b]

Alkylation of several representative ketones were examined to establish the generality of the procedure, and the results are summarized in Table IV. The reactions were carried out under a standard set of conditions: BTAF was used with molecular sieves at 0–30 °C in THF or DME. All cases except the reaction of cyclopentene **15** proceeded with complete regiospecificity and produced neither polyalkylation nor O-alkylation products; the cyclopentanone case where the enolate anion is very susceptible to isomerization[18] gave a small amount (up to 10%) of dialkylated products. The results in Table IV demonstrate that the reaction is applicable to ketones of a wide spectrum of substitution patterns.

**Equilibration of Enolate.** The regiospecificity of the present reaction is much higher than that of lithium enolates in ethereal solvents.[5]

Even the reactions with unreactive alkyl halides take place before the enolate species undergoes equilibration. In order to gain more insight into the problem of equilibration, butylation of enol silyl ether **3** was carried out in the presence of cyclohexanone (**8**) (eq 3). In the reaction mixture was found a small



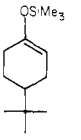
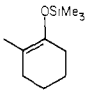
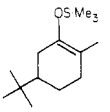
| % yield | | | | |
|---|---|---|---|---|
| 28 | 72 | 5 | 95 | 0 |

c:t = 36:64

(3)

amount of 2-butylcyclohexanone (**9**) together with the expected compound **16**, showing occurrence of proton-transfer reactions. The butylated product **16** was a cis–trans mixture in a ratio of 36:64. The cis–trans ratio was not influenced by the presence of

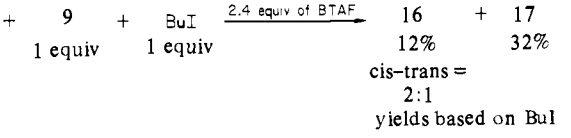
Table IV. Regiospecific Monoalkylation of Ketones

| enol silyl ether | RX | % yield[a] |
|---|---|---|
|  7 | MeI | (87–91) |
| | $PhCH_2Br$ | 66–69 |
| | $BrCH_2COOMe$ | 72–80 |
| | BuI | (50) |
|  11 | MeI | (74) |
|  3 | $PhCH_2Br$ | 72–74 |
| | $PhCH{=}CHCH_2Br$ | 78 |
| | $BrCH_2COOMe$ | 78 |
| | BuI | 40 (46) |
|  6 | $PhCH_2Br$ | 59 |
| | $BrCH_2COOMe$ | 42 |
| | BuI | 37 |
|  12 | $CD_3I$ | (76) |
|  13 | $BrCH_2COOMe$ | 64 |
|  14 | $BrCH_2COOMe$ | 76 |
|  15 | $PhCH_2Br$ | 59–67[b] |

[a] Isolated yield. GLC yield in parentheses. [b] About 10% of dialkylated product formed.

cyclohexanone (vide infra). Predominant formation of the thermodynamically unstable trans isomer, however, indicates the absence of any significant proton transfer involving the butylated product **16**. 2-Butyl-2-methylcyclohexanone **17**, the regioisomer of **16**, was not detected. The perfect material balance of both cyclohexanone and 2-methylcyclohexanone indicates the absence of any side reactions besides the proton-transfer reactions.

Competitive alkylation of a pair of isomeric enol ethers, **3** and **6**, with butyl iodide revealed that the silyl ether **6** alkylates faster than the other.[19] The formation of more *cis*-**16** than *trans*-[16] indicates the occurrence of proton transfer under these particular conditions.



This seemingly unreasonably sluggishness of proton transfer would be reconciled to the mode of the reaction, namely, the in situ generation of the enolate anion under a mobile equilibri-

(17) Sharts, C. M.; Sheppard, W. A. *Org. React.* **1974**, *21*, 125.

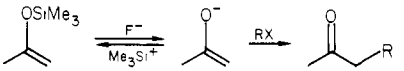
(18) Cf. (a) Posner, G. H.; Sterling, J. J.; Whitten, C. E.; Lentz, C. M.; Brunelle, D. J. *J. Am. Chem. Soc.* **1975**, *97*, 107. (b) Patterson, J. W.; Fried, J. H. *J. Org. Chem.* **1974**, *39*, 2506.

(19) Since the cleavage of Si–O bond by fluoride anion is very fast (cf. ref 14b), this result probably reflects the reactivities of the two regioisomers of the ammonium enolates: cf. Caine, D.; Huff, B. J. L. *Tetrahedron Lett.* **1966**, 4695. Johnson, F. *Chem. Rev.* **1968**, *68*, 375.

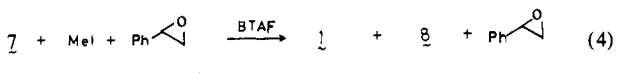
Table V. Stereochemistry of the Alkylation of Silyl Ether 3

| alkyl halide (equiv) | % *trans*-6-alkyl-2-methylcyclohexanone |
|---|---|
| $PhCH_2Br$ (0.9) | 76–78 |
| $PhCH{=}CHCH_2Br$ (1.0) | 62 |
| $BrCH_2COOMe$ (0.9) | 68 |
| BuI (10) | 63–67 |

um,[9c,14c,d] which is driven to the right by the subsequent irreversible alkylation reaction.



**Chemospecificity.** A variety of functional groups survive the conditions of this reaction. The mild reactivity of the fluoride anion[20] is primarily responsible for the specificity. The fluoride anion shows high specificity toward the silicon atom of enol silyl ethers but is almost inert to carbonyl compounds.[14b] Epoxides (eq 4) and ketones (eq 5) remain unattacked in the present reaction. Ester groups are also tolerable. Such reactivities are consistent with the properties expected for "naked" enolate anions.[9,14]



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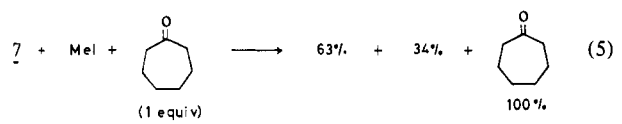


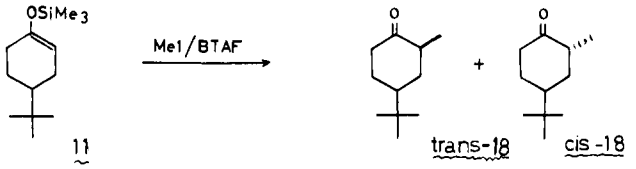
(5)

**Sterochemistry.** The stereochemical outcomes of the reaction of enol silyl ethers **3**, **11**, and **12** were investigated. The reactions of **3** and **11** represent the alkylation reaction in which the product is susceptible to epimerization at the alkylated carbon. It was of primary interest to investigate the sterochemistry of the alkylation of these substrates, since there have not been any pertinent reports about the direct kinetic results of the sterochemistry in the alkylation of this type of enolate anions. Namely, the formation of regioisomers or polyalkylated products frequently encountered in the alkylation of lithium enolates indicates the perturbation of the initial stereochemical results by the subsequent proton-transfer reactions.[5,18,24]

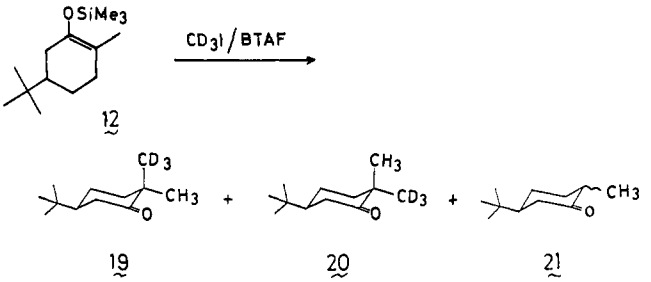
Alkylation of 2-methylcyclohexanone was performed by allowing the enol silyl ether **3** to react at 0 °C–room temperature with alkyl-6-methylcyclohexanone than the cis isomer (Table V). The observed cis–trans ratios were quite reproducible.

The alkylation reaction of conformationally stable ketone was then investigated. Methylation of **11** with excess methyl iodide gave 2-methyl-4-*ter*-butylcyclohexanone (**18**)[12] in 74% yield together with the parent ketone (26% yield). The cis–trans ratio was 3:7.

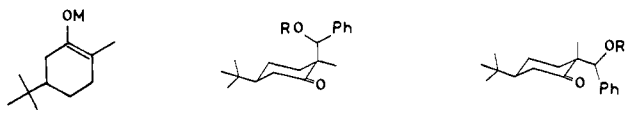
The isomer ratios obtained here should mostly represent the kinetic pathway of these alkylation reactions, as judged by the following facts: (1) slow proton-transfer reactions between ketones and the enolates as proven by eq 3 and 5 and the general absence of polyalkylated ketones or products with the wrong regiochemistry; (2) the cis–trans ratios are rather insensitive either to the kind of alkylating agent or the substituents on the ring.



The stereochemistry of the alkylation of the enol silyl ether **13** was also examined, since this type of enolates has already been studied carefully by House.[22] Alkylation of **12** with trideuteriomethyl iodide at 0 °C to room temperature gave the alkylated product in 76% yield together with the parent ketone **21** (22% yield). The ratio of two steroisomers, **19** and **20**, was 4:1.



This result poses an interesing problem about the role of the countercation in determining the stereochemical course of the reactions of enolate anions; the deuteriomethylation of the lithium enolate **22b** occurs predominantly (83%) via axial attack of the reagent;[22] the isomeric ratio is essentially the same as the one obtained in the present study. Michael reaction of the potassium enolate **22a** also results in the axial introduction (82–86%) of the substituent on reacting with methyl acrylate.[22] Though the alkylation reactions appear rather insensitive to the nature of the cation, aldol reactions are very sensitive to it. The zinc enolate **22c** gives the axial aldol **23a** in preference (67–70%) to the equatorial isomer **24a**.[23] The TBAF-mediated aldol reaction of **12** at −35 °C gives the axial aldol **23b** and none of the equatorial one **24b**.[14b]



## Conclusion

Methods currently available for alkylation of ketones fall into two classes: one starts from the enolate anion of the parent ketone and the other from some suitable precursor. The former category is simple and straightforward. The present approach for the alkylation is included in the latter one. Though such a procedure needs preparation of the required enol silyl ethers, this is not necessarily disadvantageous, for, in many cases, isomerically pure enol silyl ethers are obtained not from the parent carbonyl compounds but from other compounds, e.g., via rearrangement etc. This suggests a notable possibility of the fluoride-catalyzed method in intramolecular reactions, because, once we set up a suitable array of functional groups, selective activation of the enol silyl ether moiety in the presence of suitable groups would result in cyclization or other intramolecular reactions.

## Experimental Section

**General Data.** Boiling points are uncorrected. Infrared spectra (IR) were recorded on a Hitachi EPI-G3 spectrometer; absorptions are reported in reciprocal centimeters. Proton nuclear magnetic resonance spectra (NMR) were obtained on a Varian Associate Model T-60 spec-

(20) Cf. Kuwajima, I; Murofushi, T.; Nakamura, E. *Synthesis* **1976**, 602.
(21) House H. O.; Terfertiller, B. A.; Olmstead, H. D. *J. Org. Chem.* **1968**, *33*, 935. Huff, B. J. L.; Tuller, F. N.; Caine, D. *Ibid.* **1969**, *34*, 3070.
(22) House, H. O.; Umen, M. J. *J. Org. Chem.* **1973**, *38*, 1000.
(23) House, H. O.; Crumrine, D. S.; Teranishi, A. Y.; Olmstead, H. D. *J. Am. Chem. Soc.* **1973**, *95*, 3310.
(24) Distinctive axial attack of reagents onto related cyclohexene derivatives. (a) Lithio hydrazone and related species Corey, E. J.; Enders, D. *Tetrahedron Lett.* **1976**, *3*. Fraser, R. R.; Dhawan, K. L. *J. Chem. Soc., Chem. Commun.* **1976**, *674*. (b) π-Allyl palladium complex: Trost, B. M.; Strege, P. E. *J. Am. Chem. Soc.* **1975**, *97*, 2534.
(25) (a) The scope of the alkylation reaction of lithium enolates in liquid ammonia has been to a highly practical level; broadened recently Binkley, E. S.; Heathcock, C. H. *J. Org. Chem.* **1975**, *40*, 2156. See also ref 18b. Cf. Stork, G.; Rosen, P.; Goldman, N.; Coombs, R. V.; Tsuji, J. *J. Am. Chem. Soc.* **1965**, *87*, 275. (b) Rathke, M. W.; Lindert, A. *Synth. Commun.* **1978**, *8*, 9.

trometer; the chemical shifts ($\delta$) are expressed in parts per million downfield from internal tetramethylsilane. Analytical gas liquid chromatography (GLC) was performed on a Hitachi 063 instrument with flame ionization detector and nitrogen carrier gas. Columns A, B, C, D, and E refer respectively to the following: 10% QF-1 on Diasolid L, 3 mm × 2 m; 20% QF-1 on Diasolid L, 3 mm × 6 m; 20% Reoplex 400 on Chromosorb W (AW), 3 mm × 6 m; and 5% XE-60 on Chromosorb P (AW), 3 mm × 1 m; 10% SE-30 on Diasolid L, 3 mm × 2 m. Preparative gas liquid chromatography was performed on a JEOL 810 instrument with helium gas. Column F was employed for preparative GLC: 20% SE-30 (30–60 mesh) on Diasolid L, 10 mm × 2 m. Analytical thin-layer chromatography (TLC) was carried out by using Merk-precoated, glass-backed Kieselgel 60 $F_{254}$ plates. Preparative thin-layer chromatography was performed on glass plates (20 × 20 cm) coated with Merk Kiesel gel $PF_{254}$ (1 mm thick). Column chromatography was performed on Wakogel C-200 silica gel. Mass spectra were determined on Hitachi RMU-7M spectrometer at 70-eV ionizing irradiation. Microanalyses were performed on Perkin-Elmer 240 at Microanalytical Laboratory, Tokyo Institute of Technology.

The alkylation reaction was carried out in a simple glass-sealed tube with a magnetic stirring bar (glass or Teflon coated) under nitrogen. Solid samples were placed in the reaction vessel in a drybox and liquid reagents were introduced with the aid of a hypodermic syringe through a rubber septum. Concentration of organic solutions was usually achieved on a rotary evaporator under aspirator pressure, and bulb-to-bulb distillation was performed with a Kugelrohr apparatus.

**Material.** 1-Trimethylsiloxycyclohexene (**7**), 4-*tert*-butyl-1-(trimethylsiloxy)cyclohexene (**11**), and 1-(trimethylsiloxy)cyclopentene (**15**) were prepared either by the House method A[3] or by silylation with ethyl (trimethylsilyl)acetate.[14a] 6-Methyl-1-(trimethylsiloxy)cyclohexene (**3**) was prepared according to the House method B,[3] and about 99% was isomerically pure. 2-Methyl-1-(trimethylsiloxy)cyclohexene (**6**) was prepared by treating the lithium enolate **5** generated from 2-methyl-1-acetoxycyclohexene (**4**)[22] with chlorotrimethylsilane and was of 98% isomeric purity. 5-*tert*-Butyl-2-methyl-1-(trimethylsiloxy)cyclohexene (12) was prepared from the corresponding ketone (**21**)[22] in the same manner. 3-Methyl-2-(trimethylsiloxy)-1-butene (**14**) was prepared by ethyl (trimethylsilyl)acetate[14a] and was of 99.5% isomeric purity. 3-Methyl-1-(trimethylsiloxy)cyclohexene (**13**) was prepared by the conjugate addition of $Me_2CuLi$.

Tetraalkylammonium hydroxides were obtained from Tokyo Kasei Co. TBAF[20] was supplied by Fluka AG. Potassium fluoride was dried at 100 °C, ca. 0.1 mm overnight over phosphorus pentoxide. Molecular sieves were activated at 320 °C for 6 h and stored under nitrogen.

Butyl iodide and methyl iodide were dried over calcium chloride, distilled from phosphorus pentoxide, and stored over copper powder. $CD_3I$ (Fluka) was used without purification. Commercial benzyl bromide, methyl bromoacetate, phenyloxilane, cyclohexanone, and cycloheptanone were distilled before use. Dicyclohexyl-18-crown-6 (Aldrich) was used without purification.

Tetrahydrofuran (THF), DME (dimethoxyethane), and dioxane were distilled from sodium benzophenone ketyl in a recycling still. Acetonitrile was distilled successively from phosphorus pentoxide and potassium carbonate under nitrogen, and this procedure was repeated once; dry acetonitrile was stored over molecular sieves under nitrogen. Benzene and hexane was distilled from sodium wire. HMPA (hexamethylphosphoramide) was distilled from calcium hydride and stored over molecular sieves.

**Benzyltrimethylammonium Fluoride (BTAF).** A 40% methanolic solution of Triton B (benzyltrimethylammonium hydroxide, 10 mL) was neutralized with ca. 4.7% aqueous HF (ca. 8.6 mL) until the pH value of the solution reached 8–7. After removal of the solvent at ca. 1 mm, the residue was dried at 50 °C (0.5 mm) for 20 h with the aid of an oil pump protected by a liquid $N_2$ trap. The resulting highly hydroscopic mass (3.50 g) was pulverized and stored over phorphorus pentoxide.

**General Procedure for the Fluoride-Mediated Reaction of Enol Silyl Ether and Alkyl Halide.** BTAF (1–3 mmol) and molecular sieves (1 g/mmol) were placed under nitrogen in a sealed tube, and 1–2 mL/mmol of THF (unless otherwise noted) was added. The suspension was stirred overnight at room temperature.[26] The resulting fine suspension was cooled to 0 °C, and a solution of an enol silyl ether (1–3 mmol) and an alkyl halide (1–10 mmol) in the same solvent (1–2 mL/mmol of the silyl ether) was added to it. The mixture was stirred for 10 min at 0 °C and then for several hours at the temperature individually indicated. The reaction mixture was diluted with 20 mL of hexane and filtered through a pad of Hyflo Super Cell. The crude product was in most cases a mixture of the monoalkylated ketone and the parent ketone.

**Methylation of Cyclohexanone: 2-Methylcyclohexanone (1).** 1-(Trimethylsiloxy)cyclohexene (**7**) (230 mg, 1.35 mmol), methyl iodide (0.125 mL, 1.35 mmol), and BTAF (274 mg, 1.62 mmol) in 3 mL of DME were allowed to react at −78 °C for 5 min and at 0 °C for 6 h. After filtration, tetralin was added to the filtrate as an internal standard. The mixture was analyzed by GLC (column A, 60 °C) and proved to have only two components, 2-methylcyclohexanone (90% yield) and cyclohexanone (10% yield). Typical retention times were 9.3 and 10.1 min, respectively. Experiments to determine the optimum conditions were carried out in essentially the same manner as described here.

**2-(Methoxycarbonyl)methylcyclohexanone.** Finely pulvelized BTAF (21.2 g, 0.125 mol) and 4A molecular sieves (50 g) were suspended in 50 mL of THF, and the suspension was stirred for 14 h at room temperature. A solution of methyl bromoacetate (16.0 g, 0.105 mmol) and 1-(trimethylsiloxy)cyclohexene (**7**) (19.5 g, 0.115 mol) in 50 mL of THF was added to the suspension during a 10-min period at 0 °C. After being stirred for 10 min, the mixture was stirred at room temperature for 11 h. Filtration of the mixture through Celite followed by evaporation of the solvent gave an oil (24.0 g), which was distilled to afford the title ketoester (12.8 g, 72%): 90–100 °C (1.2 mm); IR (neat) 1740 (vs), 1710 (vs) $cm^{-1}$; NMR ($CCl_4$) 0.8–3.1 (m, 11 H), 3.60 (s, 3 H); mass spectrum, *m/e* (relative %) 170 ($M^+$, 15), 139 (46), 138 (87), 127 (19), 97 (38), 74 (35), 55 (100); high-resolution mass spectrum 170.0941 (calcd for $C_9H_{14}O_3$, 170.0941).

**2-Benzylcyclohexanone.** 1-(Trimethylsiloxy)cyclohexene (**7**) (233 mg, 1.37 mmol), benzyl bromide (213 mg, 1.25 mmol), and BTAF (253 mg, 1.49 mmol) were allowed to react at 0 °C for 14 h and at 25 °C for 4 h. After routine workup, 234 mp of a crude oil was obtained. Purification by preparative TLC (5% ether in hexane) afforded 161 mg of the title compound (69%). A duplicate experiment carried out initially at 0 °C and then at 20 °C for 9 h gas a 66% yield. Bulb-to-bulb distillation gave an analytically pure sample, which showed spectral properties in complete accordance with those reported in the literature;[5a] bp 105 °C (0.06 mm).

Anal. ($C_{13}H_{16}O$): C, H.

**2-Butylcyclohexanone (9).** 1-(Trimethylsiloxy)cyclohexene (**7**) (246 mg, 1.45 mmol), butyl iodide (2.67 g, 14.5 mmol), and BTAF (294 mg, 1.74 mmol) were allowed to react at room temperature for 24 h. GLC analysis performed with tetralin as an internal standard (column A, 100 °C) indicated the presence of 2-butylcyclohexanone (50% yield) and cyclohexanone (50% yield). Typical retention times were 20.5 and 7.3 min, respectively. The title compound was identified by comparative GLC analysis and by isolation with TLC. The ketone exhibited IR, NMR, and mass spectra the same as those reported in the literature:[25a] bp 120 °C (bath temperature) (55 mm) (lit.[6c] 89–92 °C (12 mm)); mass spectrum, *m/e* (relative %) 154.1385 (calcd for $C_{10}H_{18}O$, 154.1357 ($M^+$, 4)), 98 (100), 70 (18), 55 (18).

**Reaction of 4-*tert*-Butyl-1-(trimethylsiloxy)cyclohexene (11) and Methyl Iodide.** The silyl ether (**11**) (401 mg, 1.78 mmol), methyl iodide (0.83 mL, 8.88 mmol), and BTAF (360 mg, 2.13 mmol) were allowed to react at 0 °C for 2 h. GLC analysis (column C, 140 °C) of the crude mixture with tetralin as an internal standard indicated the formation of 4-*tert*-butylcyclohexanone (26% yield) and 4-*tert*-butyl-2-methylcyclohexanone (74% yield). The stereochemistry of the methylated product was determined on the basis of the NMR spectrum of the product mixture and that of the authentic cis–trans mixture.[21] The spectrum ($CCl_4$) of the product exhibited only one methyl doublet at $\delta$ 1.10, indicating the predominance of the trans isomer. The signal underwent a typical solvent-induced shift of the axial methyl group (6-Hz upfield shift in benzene), further suporting the assignment. The cis–trans ratio was determined by a praseodymium(III)-induced shift of the methyl group signal. Addition of 10 mol % of $Pr(fod)_3$ to the product mixture shifted the axial methyl doublet 304 Hz ($J$ = 7 Hz) and the equatorial one 336 Hz ($J$ = 6 Hz). Integration of these signals indicated the cis–trans ratio to be 3:7.

**2-Benzyl-6-methylcyclohexanone.** 6-Methyl-1-(trimethylsiloxy)cyclohexene (**3**) (290 mg, 1.58 mmol), benzyl bromide (245 mg, 1.43 mmol), and BTAF (291 mg, 1.72 mmol) were allowed to react initially at 0 °C and then at 20 °C for 8 h. The routine workup gave an oily product (302 mg), whose NMR spectrum exhibited no trace of the characterisitc singlet ($\delta$ 2.78) of the regioisomer **10**. Purification on preparative TLC (5% ether in hexane) afforded 46 mg of the cis ketone (16%) and 167 mg of the trans isomer (58%). The assignment of the stereochemistry was confirmed by basic equilibration (MeOK, MeOH).

Cis isomer: IR (neat) 1710 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 0.97 (d, $J$ = 6 Hz, equatorial methyl), 1.1–2.7 (m, 8 H), 2.7–3.4 (m, 2 H), 7.07 (s, 5 H).

Anal. ($C_{14}H_{18}O$): C, H.

Trans isomer: IR (neat) 1710 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 1.05 (d, $J$ = 7 Hz, axial methyl), 1.2–3.2 (m, 10 H), 7.05 (s, 5 H).

(26) In order to obtain the optimum results, effeicient stirring appeared crucial. Since BTAF loses most of its activity after several days under these conditions, the pretreatment of BTAF should not be longer than about 10 h.

Anal. ($C_{14}H_{18}O$): C, H.

**6-Methyl-2-(3-phenyl-2-propenyl)cyclohexanone.** 6-Methyl-1-trimethylsiloxy)cyclohexene (**3**) (282 mg, 1.53 mmol), cinnamyl bromide (315 mg, 1.53 mmol), and BTAF (284 mg, 1.68 mmol) were allowed to react at room temperature for 1 h. After the routine workup, purification on preparative TLC (20% ether in hexane) gave 105 mg of the cis isomer of the title compound (30%) and 172 mg of the trans isomer (49%).

Cis isomer: $R_f$ 0.75; IR (neat) 1708 (s), 965 (m) $cm^{-1}$; NMR ($CCl_4$) $\delta$ 0.98 (d, $J$ = 5 Hz, 3 H), 1.1–2.7 (m, 10 H), 5.7–6.5 (m, 2 H), 7.16 (s, 5 H).

Anal. ($C_{16}H_{20}O$): C, H.

Trans isomer: $R_f$ 0.6; IR (neat) 1709 (s), 965 (m) $cm^{-1}$; NMR ($CCl_4$) $\delta$ 1.05 (d, $J$ = 6 Hz, 3 H), 1.3–2.8 (m, 10 H), 5.7–6.5 (m, 2 H), 7.16 (s, 5 H).

Anal. ($C_{16}H_{20}O$): C, H.

**2-((Methoxycarbonyl)methyl)-6-methylcyclohexanone.** 6-Methyl-1-(trimethylsiloxy)cyclohexene (**3**) (282 mg, 1.54 mmol), methyl bromoacetate (214 mg, 1.40 mmol), and BTAF (283 mg, 1.67 mmol) were allowed to react initially at 0 °C and for 8 h at room temperature, and the routine workup gave an oily product (259 mg), from which 189 mg of the title compound was isolated with the aid of preparative TLC (73%). GCL analysis (column A, 110 °C) indicated the cis–trans ratio to be 32:68. Typical retention times were 18.6 and 21.1 min, respectively: bp 75–80 °C (bath temperature) (0.1 mm); IR (neat) 1740 (vs), 1710 (vs) $cm^{-1}$; NMR ($CCl_4$) $\delta$ 0.95 (d, 0.9 H, $J$ = 7 Hz, equatorial $CH_3$), 1.17 (d, 2.1 H, $J$ = 8 Hz, axial $CH_3$), 1.1–3.2 (m, 10 H), 3.67 (s, 3 H); mass spectrum, $m/e$ (relative %) 184 ($M^+$, 18), 153 (41), 152 (100), 111 (23), 74 (28), 69 (45), 55 (94); high-resolution mass spectrum 184.1076 (calcd for $C_{10}H_{16}O$:184.1097).

**2-Butyl-6-methylcyclohexanone (16).** 6-Methyl-1-(trimethylsiloxy)-cyclohexene (**3**) (226 mg, 1.23 mmol), butyl iodide (2.26 g, 12.3 mmol), and BTAF (249 mg, 1.47 mmol) were allowed to react initially at 0 °C and for 24 h at room temperature. GLC analysis of the reaction mixture with tetralin as an internal standard (column A, 80 °C) showed the presence of *cis*-**16** (17%) and *trans*-**16** (29% yield). The absence of the positional isomer was established by GLC with column B (150 °C, where *cis*-2,6-, *trans*-2,6-, 2,2-dialkyl isomers had retention times of 35, 42.5, and 44 min, respectively.

In another run, the cyclohexene **3** (403 mg, 2.19 mmol), butyl iodide (4.02 g, 21.9 mmol), BTAF (407 mg, 2.41 mmol) were allowed to react at 20 °C for 21 h. After the routine workup, the crude mixture was purified on column chromatography (20 g of silica gel, hexane followed by hexane/ether) to afford 147 mg of the title ketone (40%): bp 105–110 °C (bath temperature) (28.5 mm) (lit.[5b] 85 °C (2.5 mm)); IR (neat) 1710 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 0.63–2.73; mass spectrum, $m/e$ (relative %) 168 ($M^+$, 5), 112 (100), 84 (18), 70 (16), high-resolution mass spectrum 168.1481 (calcd for $C_{11}H_{20}O$, 168.1512).

The NMR spectrum of the butylated product showed two doublets. One was centered at $\delta$ 1.00 ($J$ = 7 Hz), which disappeared after basic equilibration, and was assigned to the methyl group of the trans isomer. Another centered at $\delta$ 0.93 ($J$ = 6 Hz) was assigned to that of the cis isomer.[18a]

**2-Benzyl-2-methylcyclohexanone (10).** 2-Methyl-1-trimethylsiloxy)-cyclohexene (**6**) (432 mg, 2.34 mmol), benzyl bromide (200 mg, 1.17 mmol), and BTAF (396 mg, 2.34 mmol) were allowed to react at 20 °C for 1 h. After the routine workup, purification on preparative TLC gave 140 mg of the title ketone (59%), which showed spectral properties in accordance with the assigned structure, and proved to contain no regioisomer.[5a]

Anal. ($C_{14}H_{18}O$); C, H.

**2-Methyl-2-((methoxycarbonyl)methyl)cyclohexanone.** 2-Methyl-1-(trimethylsiloxy)cyclohexene (6) (306 mg, 1.39 mmol), methyl bromoacetate (206 mg, 1.39 mmol), and BTAF (287 mg, 1.70 mmol) were allowed to react at 20 °C for 1 h. After the routine workup, the crude mixture was purified by bulb-to-bulb distillation to give 108 mg of the title ketone (42%). Comparable GLC analysis revealed the absence of the regioisomer (column D, 120 °C). The isomeric purity was further established by a sharp singlet of the high field methyl group on the NMR spectrum: bp 70–75 °C (bath temperature) (0.1 mm); IR (neat) 1739 (s), 1710 (s) $cm^{-1}$; NMR ($CCl_4$) $\delta$ 1.17 (s, 3 H), 1.5–2.6 (m, 10 H), 3.60 (s, 3 H).

**2-Butyl-2-methylcyclohexanone (17).** 1-Methyl-1-(trimethylsiloxy)-cyclohexene (**6**) (342 mg, 1.86 mmol), butyl iodide (1.03 g, 5.6 mmol), and BTAF (345 mg, 2.04 mmol) were allowed to react at 20 °C for 1 h. The crude mixture obtained by the routine workup proved to contain to regioisomer (GLC by column B, 130 °C). Purification on column chromatography (15 g silica gel, hexane/ether) afforded the title ketone (116 mg, 37%), which was identified by comparative GLC analysis with the authentic sample. The purified material exhibited a sharp singlet at $\delta$ 0.98 on the NMR spectrum.

**Reaction of 4-*tert*-Butyl-1-methyl-2-(trimethylsiloxy)cyclohexene (12) and Methyl-$d_3$ Iodide.** The silyl ether (**12**) (332 mg, 1.39 mmol), methyl-$d_3$ iodide (0.263 mL, 2.77 mmol), and BTAF (281 mg, 1.66 mmol) were allowed to react initially at 0 °C and at room temperature for 2 h. GLC analysis (column, E, 110 °C) of the crude mixture (240 mg) indicated the formation of 5-*tert*-butyl-2-methyl-$d_3$-2-methylcyclohexenone (76% yield) and 5-*tert*-butyl-2-methylcyclohexanone (22%). Typical retention times were 15.1 and 13.4 min, respectively. The separation of the methylated products was achieved by preparative GLC (colum F), and the cis–trans ratio (**19–20**) was determined to be 79:21 with the aid of the NMR spectrum (benzene) by examination of the relative intensities of the methyl signals:[22] IR (neat) 1705 (s) $cm^{-1}$ NMR ($C_6H_6$) $\delta$ 0.73 (s, 9 H, *tert*-butyl), 0.75–1.5 (m, 10 H, including sharp s at 0.90 and 1.05); mass spectrum, $m/e$ (relative %) 185 ($M^+$, 9), 141 (26), 128 (28), 100 (27), 97 (6), 73 (11), 72 (9), 69 (20), 57 (100), 55 (48).

**2-((Methyoxycarbonyl)methyl)-3-methylcyclohexanone.** 3-Methyl-1-(trimethylsiloxy)cyclohexene (**13**) (233 mg, 1.26 mmol), methyl bromoacetate (176 mg, 1.15 mmol), and BTAF (233 mg, 1.38 mmol) were allowed to react at 20 °C for 3 h. After the routine workup, purification of the crude product (164 mg) on preparative TLC gave the title ketoester (135 mg, 64%): bp 75 °C (bath temperature) (0.06 mm); IR (neat) 1740 (vs), 1715 (vs) $cm^{-1}$; NMR (CCl) $\delta$ 0.9–1.2 (m, 3 H), 1.2–2.8 (m, 10 H), 3.67 (s, 3 H); mass spectrum, $m/e$ (relative %) 184 ($M^+$, 3), 153 (19), 111 (100), 74 (17), 69 (23); high-resolution mass spectrum 184.1088 (calcd for $C_{10}H_{16}O_3$, 184.1097).

**Methyl 5-Methyl-4-oxohexanoate.** 3-Methyl-2-(trimethylsiloxy)-1-butene (**14**) (146 mg, 0.93 mmol), methyl bromoacetate (170 mg, 1.11 mmol), and BTAF (188 mg, 1.10 mmol) were allowed to react at 0 °C for 5 min and for 17 h at room temperature. After the routine workup, the crude product (133 mg) afforded, on preparative TLC, the title ketone (113 mg, 76%): bp 60–65 °C (bath temperature) (0.13 mm); IR (neat) 1745 (vs), 1715 (s) $cm^{-1}$; NMR ($CCl_4$) $\delta$ 1.01 (d, $J$ = 7 Hz, 6 H), 2.3–2.9 (m, 5 H), 5.00 (s, 3 H); mass spectrum, $m/e$ (relative %) 158 ($M^+$, 1), 127 (15), 115 (100), 99 (7), 87 (19), 71 (15), 59 (26), 55 (51), 43 (65); high-resolution mass spectrum 158.0932 (calcd for $C_8H_{14}O_3$, 158.0942).

**2-Benzylcyclopentanone.** 1-(Trimethylsiloxy)cyclopentene (**15**) (267 mg, 1.71 mmol), benzyl bromide (643 mg, 3.76 mmol), and BTAF (318 mg, 1.88 mmol) were allowed to react at 20 °C for 1 h. The crude product obtained after the routine workup and preparative TLC gave 199 mg of the title ketone (67%). Bulb-to-bulb distillation gave an analytical sample: bp 100 °C (bath temperature) (0.12 mm); IR (neat 1738 (s) $cm^{-1}$; NMR ($CCl_4$) $\delta$ 1.2–3.3 (m, 9 H), 7.20 (s, 5 H).

Anal. ($C_{12}H_{14}O$): C, H.

**Acknowledgment.** we thank Fluka AG for generous supplies of some reagents. This research was partly supported by a grant from the Ministry of Education.

**Registry No. 1**, 583-60-8; **3**, 19980-33-7; **4**, 1196-73-2; **6**, 19980-35-9; **7**, 6651-36-1; **8**, 108-94-1; **9**, 1126-18-7; **11**, 19980-19-9; **12**, 62572-34-3; **13**, 55373-58-5; **14**, 17510-45-1; **15**, 19980-43-9; *cis*-**16**, 50299-69-9; *trans*-**16**, 50299-71-3; **17**, 1197-78-0; *cis*-**18**, 3211-27-6; *trans*-**18**, 3211-26-5; **19**, 37786-88-2; **20**, 37786-89-3; **21**, 56569-76-7; **22a**, 80287-76-9; **22b**, 80287-77-0; **22c**, 80287-78-1; **23a**, 56084-18-5; ethyl (trimethylsiloxy)acetate, 80287-79-2; benzyltrimethylammonium fluoride, 329-97-5; methyl iodide, 74-88-4; methyl bromoacetate, 96-32-2; 2-(methoxycarbonylmethyl)cyclohexanone, 13672-64-5; 2-benzylcyclohexanone, 946-33-8; benzyl bromide, 100-39-0; butyl iodide, 542-69-8; 4-*tert*-butylcyclohexanone, 98-53-3; cinnamyl bromide, 4392-24-9; *cis*-6-methyl-2-(3-phenyl-2-propenyl)cyclohexanone, 80300-94-3; *trans*-6-methyl-2-(3-phenyl-2-propenyl)cyclohexanone, 80300-95-4; *cis*-2-((methoxycarbonyl)methyl)-6-methylcyclohexanone, 80287-80-5; *trans*-2-((methoxycarbonyl)methyl)-6-methylcyclohexanone, 80287-81-6; 2-((methoxycarbonyl)methyl)-3-methylcyclohexanone, 80287-82-7; methyl 5-methyl-4-oxohexanoate, 2177-83-5; *cis*-2-benzyl-6-methylcyclohexanone, 29478-34-0; *trans*-2-benzyl-6-methylcyclohexanone, 29478-35-1.