the only isolable product. Phenyl chloroformate treatment of **8** in methylene chloride containing pyridine gave phenylcarbonate **9**[10] (red amorphous solid; M^+ obsd 445.1745, calcd for $C_{23}H_{27}O_8N$ 445.1736) in 85% yield. Careful treatment of **9** with methanethiol containing a catalytic amount of boron trichloride etherate at -45 °C afforded hemithioketal **10**[10] (red amorphous solid; M^+ obsd 461.1521, calcd for $C_{23}H_{27}O_7SN$ 461.1508; ^1H NMR ($CDCl_3$) 1.88 (3 H, s), 1.91 (3 H, s), 3.40 (3 H, s), 4.06 ppm (3 H, s)) in 73% yield. The ^1H NMR spectrum indicated that **10** was a single substance; however, its stereochemistry was not established.

The crucial transannular cyclization of **10** was effected by mercuric chloride in methylene chloride containing a small amount of triethylamine. The product (**11**)[10] (purple amorphous solid; M^+ obsd 413.1485, calcd for $C_{22}H_{23}O_7N$ 413.1474) was isolated as about 1:1 mixture[11] of cis-trans isomers by preparative layer chromatography (Merck Al_2O_3 Type T, 1:4 EtOAc-CH_2Cl_2) in 67% yield.[12] Upon contact with weak acid such as a catalytic amount of acetic acid in methylene chloride or thin layer chromatography on silica gel, **11** was smoothly and quantitatively converted to the known indolequinone **12**[9,13] (mp 137–138 °C).

Brief ammonia treatment of **11** (as a 1:1 cis-trans mixture) gave deiminomitomycin A (**13**) in over 90% yield. The ^1H NMR spectrum showed that the initially isolated product was about a 1:1 mixture of cis-trans isomers. The ^1H NMR signal of the 9a methoxy group appears at 3.14 ppm in one isomer, while at 3.32 ppm in the other isomer. The trans stereochemistry was assigned to the isomer with the chemical shift of 3.14 ppm because the 9a methoxy group signal appears at 3.20 ppm in the ^1H NMR spectrum of mitomycins A.[14] During attempted separation of the isomer by preparative layer chromatography (Merck Al_2O_3 Type T, 2:98 CH_3OH-CH_2Cl_2), most of the cis isomer decomposed to the known indolequinone **14**[9,14] (mp 204–206 °C), while the bulk of the trans isomer remained intact. Thus, deiminomitomycin A (**13**)[10] (purple amorphous solid; M^+ obsd 336.1329, calcd for $C_{16}H_{20}O_6N_2$ 336.1321; UV (CH_3OH) 219 nm (log ϵ 4.26), 319 (4.04), 525 (3.18); ^1H NMR ($CDCl_3$) 1.87 (3 H, s), 3.14 (3 H, s), 4.07 ppm (3 H, s)) could be isolated in 30–35% yield from **11**.[12] The observed difference in stability supports the stereochemistry assignment based on the ^1H NMR spectrum. Deiminomitomycin A (**13**) could be quantitatively converted to indolequinone **14** under such weakly acidic conditions as a catalytic amount of acetic acid in methylene chloride or even thin layer chromatography on silica gel. It is interesting to note that deiminomitomycin A is *much less* stable than the naturally occurring mitomycins.

Application of these methods to a total synthesis of the mitomycins is in progress in our laboratories.

Acknowledgment. Financial assistance from National Science Foundation, Milton Fund, and Hoffmann-La Roche Co. is gratefully acknowledged.

References and Notes

(1) See, for example, "The Merck Index 9th Edition, M. Windholz, Ed., Merck & Co. Inc., Rahway, N.J., 1976, p 6060 ff, and references cited therein.
(2) For those synthetic approaches reported before spring, 1974, see G. J. Siuta, R. W. Franck, and R. J. Kempton, *J. Org. Chem.*, **39**, 3739 (1974), and references cited therein; G. Leadbetter, D. L. Fost, N. N. Ekwuribe, and W. A. Remers, *ibid.*, **39**, 3580 (1974); T. Takada, Y. Kosugi, and M. Akiba, *Tetrahedron Lett.*, 3283 (1974); J. W. Lown and T. Itoh, *Can. J. Chem.*, **53**, 960 (1975); T. Kametani, K. Takahashi, M. Ihara, and K. Fukumoto, *J. Chem. Soc., Perkin Trans. 1*, 389 (1976); T. Kametani, T. Ohsawa, K. Takahashi, M. Ihara, and K. Fukumoto, *Heterocycles*, **4**, 1637 (1976); T. Kametani, K. Takahashi, Y. Kigawa, M. Ihara, and K. Fukumoto, *J. Chem. Soc., Perkin Trans. 1*, 28 (1977); D. R. Crump, R. W. Franck, R. Gruska, A. A. Ozorio, M. Pagnotta, G. Suita, and J. G. White, *J. Org. Chem.*, **42**, 105 (1977).
(3) See, for example, S. Kinoshita, K. Uzu, K. Nakano, M. Shimizu, T. Takahashi, and M. Matsui, *J. Med. Chem.*, **14**, 103 (1971).
(4) The structure of mitomycin B including its absolute configuration was recently confirmed by x-ray crystallography: R. Yahashi and I. Matsubara, *J. Antibiot.*, **29**, 104 (1976).
(5) G. O. Morton, G. E. Van Lear, and W. Fulmor, *J. Am. Chem. Soc.*, **92**, 2588 (1970).
(6) R. Royer, P. Demerseman, A.-M. Laval-Jeantet, J.-F. Rossignol, and A. Cheutin, *Bull. Soc. Chim. Fr.*, 1026 (1968).
(7) We considerably improved the overall yield of **1** from 2,6-dimethoxytoluene by the following sequence of reactions, i.e., (1) $Cl_2CHOCH_3/TiCl_4/CH_2Cl_2$, 0 °C, (2) MCPBA/$CH_2Cl_2$, 0 °C, (3) $NaOCH_3$ (0.1 equiv), CH_3OH, 0 °C. The overall yield was 95% yield or better in 100-g scale experiments.
(8) Numbering in this paper corresponds to that of the mitomycins.
(9) Satisfactory spectroscopic and analytical data were obtained for this substance.
(10) Satisfactory spectroscopic data including exact mass spectrum were obtained for this substance.
(11) The transannular cyclization of the acetate (i.e., X = OCH_3; Y = SCH_3; Z = $COCH_3$ in the structure **10**) yielded a mixture of trans (three parts) and cis (two parts) isomers.
(12) This substance was always contaminated with a trace amount of the corresponding indolequinone resulting from decomposition during the work-up.
(13) G. R. Allen, Jr., J. F. Poletto, and M. J. Weiss, *J. Org. Chem.*, **30**, 2897 (1965).
(14) We are indebted to Dr. J. S. Webb, Lederle Laboratories, for providing the spectroscopic data of mitomycin A.

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Stannylation/Destannylation. New Syntheses of Carbonyl Compounds via Organotin Intermediates

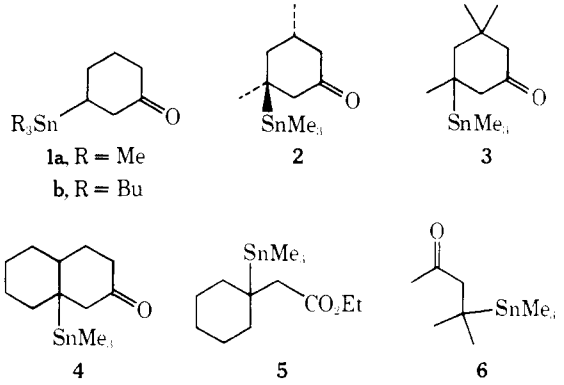
Sir:

Recent experiments in our laboratory indicate that alkyltin compounds are valuable intermediates for organic synthesis.[1] This generalization is based in part on our observations that (1) easily prepared trialkyltin anions undergo high yield conjugate addition[2] to α,β-enones to give useful regiospecific enolates of 3-stannyl ketones; and (2) alkylstannanes are smoothly oxidized by chromic anhydride/pyridine to the corresponding ketones. These two reactions provide a number of useful snythetic transformations. In particular, a dialkylative enone transposition is described and illustrated by a short synthesis of dihydrojasmone.

Trialkylstannyllithium reagents may be conveniently prepared by a procedure similar to the one that we recently reported for the preparation of trimethylsilyllithium.[3,4] Thus, treatment of a tetrahydrofuran solution of hexamethyldistannane or hexabutyldistannane with methyllithium or butyllithium (−20 °C, 15 min) yields the corresponding trialkylstannyllithium and inert tetraalkylstannane in >95% yield.[5] A more economical, but somewhat less convenient procedure, involves titration of ~0.5 M solutions of lithium in liquid ammonia (−70 °C) with a 0.5 M tetrahydrofuran solution of hexaalkyldistannane (yield of R_3SnLi, >95%) or trialkylhalostannane (yield of R_3SnLi, 70–80%).[6]

Regardless of the method of preparation, THF or THF-NH_3 solutions of trialkylstannyllithium react with most α,β-unsaturated carbonyl compounds via the 1,4 mode of addition. Thus 2-cyclohexenone reacts with trimethylstannyllithium or tributylstannyllithium (−78 °C, 5 min) to give 3-stannylcyclohexanones **1a** (96% yield;[7] IR (neat) 1710, 770 cm^{-1}; NMR (δ^{CCl_4}) 0.07 (9 H, s))[8] and **1b** (89% yield; IR (neat) 1710 cm^{-1}), respectively. None of the corresponding 1,2 adduct could be detected. The addition appears to proceed axially with cyclohexenones as evidenced by formation of the *cis*-dimethylcyclonexanone **2** (93% yield) from 3,5-dimethylcyclohexenone.[9] These results parallel our previous observations with trimethylsilyllithium, but the similarities stop here. While trimethylsilyllithium was ineffective at addition to isophorone and $\Delta^1(9)$-2-octalone, trimethylstannyllithium gave the adducts **3** and **4** in 77 and 94% yields, respectively. The success of this reagent at addition to hindered enones is prob-

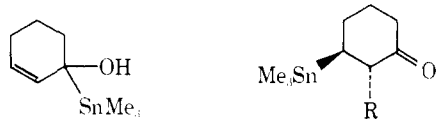
ably due to the great length (~2.2 Å) of the tin-carbon bond and is further illustrated by the observation that even β-disubstituted unsaturated esters react rapidly with trimethylstannyllithium. This ethyl cyclohexylideneacetate gave (THF, −78 °C, 5 min) the corresponding 3-stannyl ester **5** (80% yield; IR (neat) 1728, 770 cm^{-1}; NMR (δ^{CCl_4}) 2.44 (2 H, s), 0.02 (9 H, s)).



1a, R = Me; **b**, R = Bu — **2** — **3**

4 — **5** — **6**

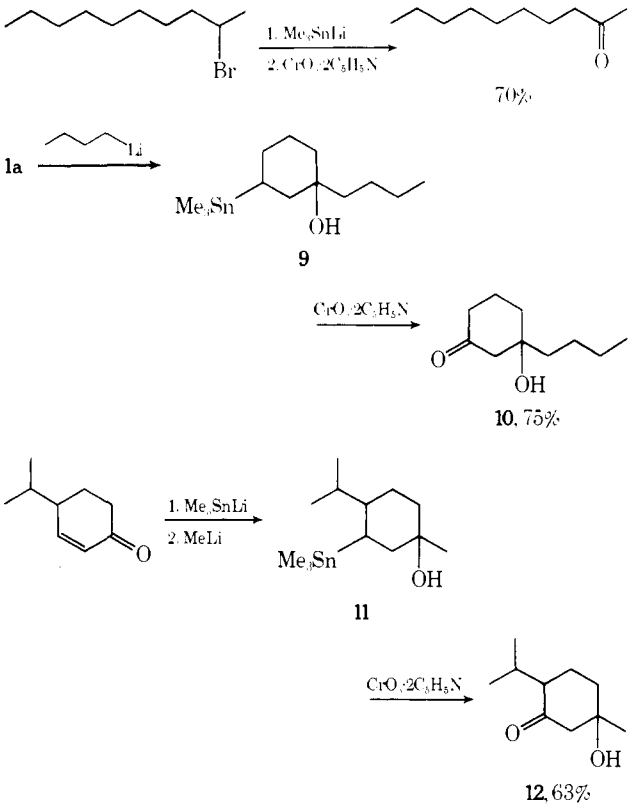
Mesityl oxide is the only enone to which we have observed substantial amounts (~30%) of 1,2 addition with trimethylstannyllithium in THF. It was found, however, that addition of 10% HMPA resulted in exclusive formation of the 1,4 adduct **6** (93% yield). This behavior is consistent with that previously reported for tributylstannylmagnesium bromide[2b] and with the remarkable observation that *ethereal trimethylstannyllithium*[10] *gives at least 90% 1,2 addition to 2-cyclohexenones.* For example, 2-cyclohexenone itself reacts *in diethyl ether* (−78 °C) to produce the rather unstable *gem*-hydroxystannane **7** (IR (neat) 3430, 770 cm^{-1}; NMR (δ^{CCl_4}) 5.82 (1 H, br d, J = 10 Hz), 5.52 (1 H,ddt, J = 10, 4 Hz), 0.09 (9 H, s)) in 80–90% estimated yield (36% isolated).[11] No 3-stannyl ketone **1a** could be detected by TLC or NMR.



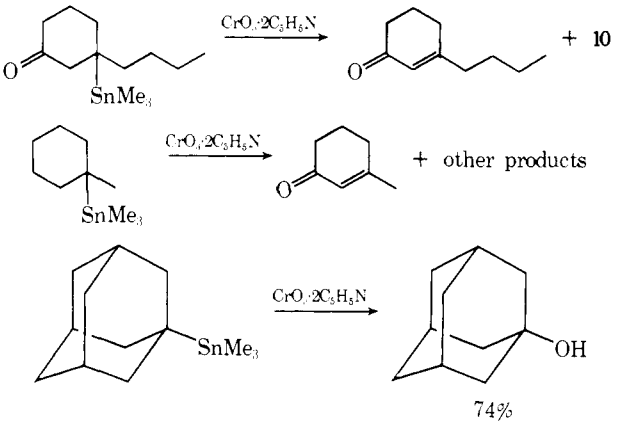
7 — **8a**, R = Me; **b**, R = *n*-Pr

Synthetically, the high yield conjugate addition of trialkylstannyllithium reagents allows a number of useful transformations based on alkylation and oxidation. We have found that the intermediate lithium enolates may be cleanly alkylated with reactive alkyl halides in THF or with primary alkyl iodides in THF-NH_3.[12] For example, sequential addition of 2-cyclohexenone and methyl iodide to trimethylstannyllithium in THF (−78→0 °C) gave the 2-methylcyclohexanone **8a** (IR (neat) 1710, 770 cm^{-1}; NMR (δ^{CCl_4}) 0.95 (3 H, d, J = 6 Hz), 0.11 (9 H, s)) in 95% yield. Preparation of trimethylstannyllithium in 1:2 THF-NH_3 (Li, Me_6Sn_2, −70 °C) followed by addition of 2-cyclohexenone and *n*-propyl iodide yielded (−33 °C, 6 h) **8b** in 89% yield.

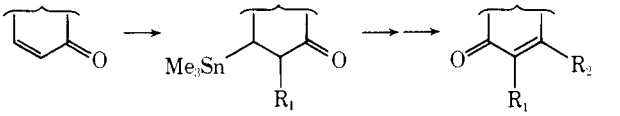
The synthetic utility of the reactions described above depends largely on one's ability to replace tin with some other functionality. We have found that one such transformation is chromic anhydride/pyridine oxidation[13] of a secondary alkyltin moiety to the corresponding carbonyl compound. To illustrate this operation, we have converted 2-bromodecane to 2-decanone by stannylation (1.5 equiv of Me_3SnLi/THF, −20→23 °C, 30 min) and oxidation (15 equiv of $CrO_3 \cdot 2C_5H_5N/CH_2Cl_2$,[14] 23 °C, 22h) in 70% overall yield.[15] Although secondary 3-stannyl ketones are relatively unreactive, 2-stannyl alcohols are smoothly oxidized to the corresponding β-ketols. For example, **9** was oxidized in 75% yield to the crystalline ketol **10** (mp 56–56.5 °C; IR (Nujol) 3375, 1710 cm^{-1}). Dehydration gave 3-*n*-butyl-2-cyclohexenone. A further illustration is provided by the conversion of 4-isopropyl-2-cyclohexenone via hydroxystannane **11** (85% yield) to ketol **12** (63% yield; 10 equiv of $CrO_3 \cdot 2C_5H_5N$, 3 h). Dehydration (I_2/C_6H_6) of **12** led smoothly to (±)-piperitone.



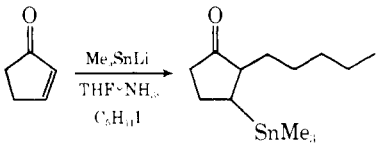
Tertiary alkylstannanes are also oxidized by chromic anhydride/pyridine (10–15 equiv, 5–12 h) but generally yield mixtures of alcohols and elimination products. Thus oxidation (15 equiv of $CrO_3 \cdot 2C_5H_5N$, 18 h) of 3-trimethylstannyl-3-*n*-butylcyclohexanone led to a 1:1 mixture of β-ketol and α,β-enone. Similar oxidation of 1-trimethylstannyl-1-methylcyclohexane gave largely elimination followed by allylic oxidation. As shown by the oxidation of 1-adamantyltrimethylstannane, tertiary alkyltins incapable of elimination give the corresponding alcohols in good yield.



Taken together, the alkylation and oxidation offer an efficient dialkylative enone transposition:[16]



To illustrate this transformation, we have prepared dihydrojasmone by a simple four-step procedure from 2-cyclopentenone. First, addition of trimethylstannyllithium in 1:2 THF-NH_3 and *n*-pentyl iodide gave (−33 °C, 6 h) the alkylated stannyl ketone **13** (IR (neat) 1740, 770 cm^{-1}) in 90% yield. Methyllithium (Et_2O, −78 °C) added to the carbonyl and chromic anhydride/pyridine (15 equiv, 23 °C, 16 h) oxidized the trimethyltin moiety to yield a hydroxy cyclopentanone. Basic dehydration[17] then gave dihydrojasmone[18] **14** in 71% overall yield from **13** (89% conversion).



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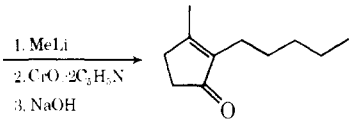

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Acknowledgment. I wish to thank the Petroleum Research Fund, Administered by the American Chemical Society, and the Research Corporation for their generous support of this work.

References and Notes

(1) Other synthetic applications of organotin compounds include E. J. Corey and R. H. Wollenberg, *J. Am. Chem. Soc.*, **96**, 5581 (1974); *J. Org. Chem.*, **40**, 2265, 3788 (1975); E. J. Corey, P. Ulrich, and J. M. Fitzpatrick, *J. Am. Chem. Soc.*, **98**, 222 (1976). For a short review see A. J. Bloodworth and A. G. Davies, *Chem. Ind. (London)*, 490 (1972); P. J. Smith, *ibid.*, 1025 (1976).
(2) (a) Professor H. G. Kuivila of the State University of New York at Albany has independently observed conjugate addition of trimethylstannyllithium to representative α,β-unsaturated ketones: personal communication. (b) Tributylstannylmagnesium bromide reacts with enones to give either 1,2 or 1,4 addition depending on the substitution of the substrate: J.-C. Lahournere and J. Valade, *J. Organomet. Chem.*, **33**, C7 (1971). (c) Stannyl cuprate addition: J. Hudec, *J. Chem. Soc., Perkin Trans 1*, 1020 (1975).
(3) W. C. Still, *J. Org. Chem.*, **41**, 3061 (1976).
(4) Other preparations of R_3SnLi have been reported but are less efficient that the ones described here. These include (a) RLi + $SnCl_2$ (H. Gilman and S. D. Rosenberg, *J. Am. Chem. Soc.*, **75**, 2507 (1953); D. Blake, G. E. Coates, and J. M. Tate, *J. Chem. Soc.*, 618 (1961); W. L. Wells and T. L. Brown, *J. Organomet. Chem.*, **11**, 271 (1968)); (b) R_3SnX or R_6Sn_2 + Li (C. Tamborski, F. E. Ford, and E. J. Soloski, *J. Org. Chem.*, **28**, 237 (1963); H. Gilman, F. K. Cartledge, and S.-Y. Sim, *J. Organomet. Chem.*, **1**, 8 (1963); A. T. Weibel and J. P. Oliver, *ibid.*, **82**, 281 (1974)).
(5) Yields of R_3SnLi were estimated by reaction with 2-cyclohexenone and VPC analysis against an internal standard. These reactions should be conducted with care in an efficient hood since volatile organotin compounds (e.g., Me_4Sn) are toxic.
(6) R_3SnNa has been prepared previously by this method: C. H. W. Jones, R. G. Jones, P. Parington, and R. M. G. Roberts, *J. Organomet. Chem.*, **32**, 201 (1971).
(7) Yields of numbered compounds refer to isolated material after chromatography, distillation or recrystallization.
(8) All new compounds gave satisfactory IR, NMR, and C, H analyses.
(9) Sterochemistry follows from the half-height peak width ($W_{1/2}$ only 0.3 Hz wider than TMS) of the C-3 methyl and the chemical shift (δ 0.03) of protons on the $-SnMe_3$ grouping. Examination of shifts of a large number of 3-trimethylstannylcyclohexanones shows that equatorial $-SnMe_3$ groups absorb at lower field (δ 0.11–0.06); cf. R. K. Boeckman and S. M. Silver, *J. Org. Chem.*, 40, 1755 (1975). See also G. S. Koermer, M. L. Hall, and T. G. Traylor, *J. Am. Chem. Soc.*, **94**, 7205 (1972).
(10) Prepared by addition of MeLi to Me_6Sn_2 in Et_2O (20 °C, 30 min).
(11) Compound **7** underwent substantial decomposition on standing and on silica gel chromatography. Immediate NMR and TLC analysis of the crude product showed **7** to be the major product.
(12) Cf. J. W. Patterson, Jr., and J. H. Fried, *J. Org. Chem.*, **39**, 2506 (1974); E. S. Binkley and C. H. Heathcock, *ibid.*, **40**, 2156 (1975).
(13) Other chromic acid oxidants (Jones reagent, chromic acid/acetic acid) were less effective. Pyridinium chlorochromate may be used, but the rate of oxidation is slower. Chromic acid/acetic acid oxidation of simple alkylstannanes has been studied previously: C. Deblandre, M. Gielen, and J. Nasielski, *Bull. Soc. Chim. Belg.*, **73**, 214 (1964).
(14) R. Ratcliffe and R. Rodehorst, *J. Org. Chem.*, **35**, 4000 (1970).
(15) Other halide → ketone transformations include W. Pritzkow and H. Schaefer, *Chem. Ber.*, **93**, 2151 (1960); V. Franzen and S. Otto, *ibid.*, **94**, 1360 (1961); H. J. Bestmann and O. Kratzer, *ibid.*, **96**, 1899 (1963); D. M. Lemal and A. J. Fry, *Tetrahedron Lett.*, 775 (1961); B. Ganem and R. K. Boeckman, *ibid.*, 719 (1974); K. Baum, C. D. Beard, and V. Grakauskas, *J. Am. Chem. Soc.*, **97**, 267 (1975).
(16) Monoalkylative enone transpositions: B. M. Trost, and J. L. Stanton, *J. Am. Chem. Soc.*, **97**, 4018 (1975); B. M. Trost, K. Hiroi, and N. Holy, *ibid.*, **97**, 5873 (1975); W. Oppolzer, T. Sarkar, and K. K. Mahalanabis, *Helv. Chim. Acta*, **59**, 2012 (1976).
(17) H. Hundsdiecker, *Chem. Ber.*, **75**, 460 (1942).
(18) Jasmone syntheses have been reviewed: T.-L. Ho, *Synth. Commun.*, **4**, 265 (1974).
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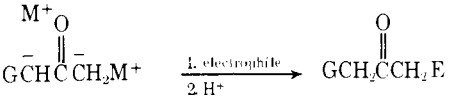
Unusual Mode of Alkylation of Certain Ketone Dianions

Sir:

It has been amply demonstrated[1] that dianions of the general formula **1** react with a variety of electrophiles to give products of structure **2**, resulting from *exclusive* attack at the terminal methylene position. These results have been explained by arguing that the methylene position should bear a higher electron density than the methine site and therefore it should be more reactive.[1,2]



1 2

In the present communication, we wish to report the first examples of electrophilic reactions of ketone dianions which lead to carbon–carbon bond formation *at the methine rather than the methylene site.* Thus, we have observed that reaction of the 1-phenyl-2-propanone dianion **5**, generated as shown in Scheme I, with a variety of alkyl halides led predominately, and in many cases exclusively, to alkylation products at C_1 (structure **8**) rather than at C_3 (structure **9**).

Scheme I