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A NOVEL SYNTHESIS OF CYCLOPENTENONES AND CYCLOHEXENONES VIA CYCLIACYLATION OF LITHIOALKENYLCARBOXAMIDES[1]

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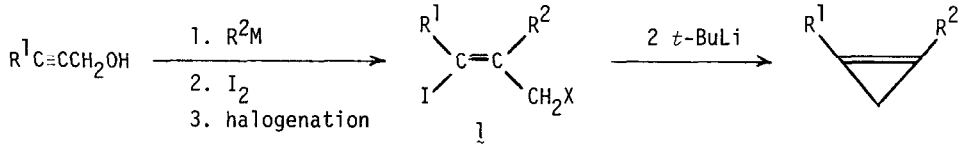
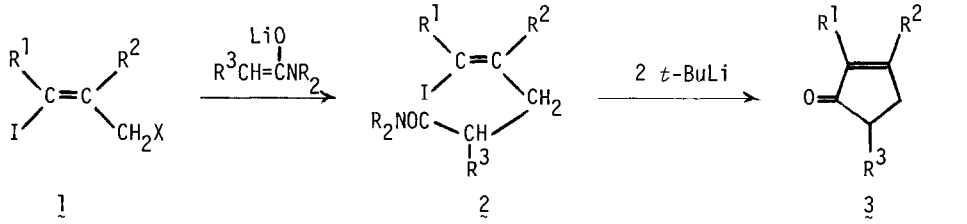
SUMMARY: The reaction of 1-iodo-3-bromopropene derivatives (1) with lithium enolates of *N*,*N*-dialkylcarboxamides followed by treatment of the allylation product (2) with two equiv of *t*-BuLi cleanly provides cyclopentenones in high yields, while the corresponding cycliacylation reaction of 6-iodo-5-hexenamides provides cyclohexenones.

1-Iodo-3-halopropene derivatives (1), readily obtainable via hydrometalation[3] or carbometalation[4] of propargylic alcohols appear attractive as three-carbon synthons for the synthesis of cycloalkenes. Although some reports have described their use in the synthesis of butyrolactones,[5] little, if any, appeared to be known about their use in the synthesis of carbocycles. We recently reported a mild and selective method for converting 1 into cyclopropenes[6] (eq 1).



1 (1)

We now report that the reaction of 1 with lithium enolates of *N*,*N*-dialkylamides followed by treatment of the allylation products (2) with 2 equiv of *t*-BuLi cleanly provides cyclopentenones (3) in high yields (eq 2).



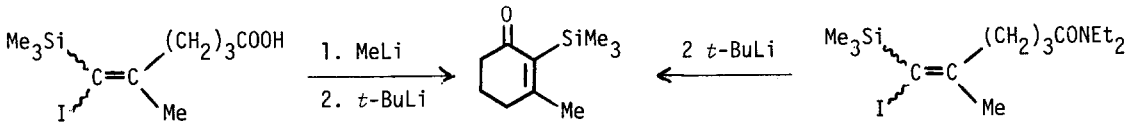
1 2 3 (2)

R^1 = H, C, or Si group. R^2 = H or C group. X = Br.

The cycliacylation reaction of alkenyllithiums with carboxamides appears to be unprecedented, although the corresponding reaction of aryllithiums is known.[7] Besides being reasonably general and expeditious, the present method provides an attractive route to certain cyclopentenones not readily accessible by the conventional aldol route, such as α-silylcyclopentenones.[8]

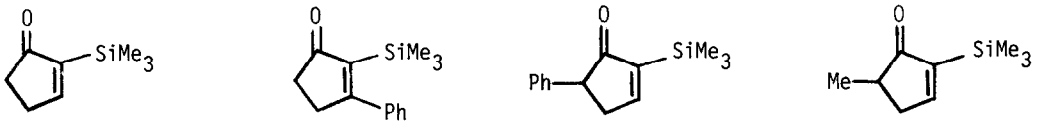
We recently reported a cycliacylation reaction involving successive treatment of iodo alkenecarboxylic acids with MeLi and *t*-BuLi.[9] Unfortunately, however, its application to the

conversion of 4[10] into 5 led to a disappointingly low yield (35%) of 5. On the other hand, treatment of the corresponding *N*,*N*-diethylcarboxamide[10] (6) with 2 equiv of *t*-BuLi in ether at -78°C followed by warming to room temperature gave 5 in 78% yield, while the use of 1 equiv of *n*-BuLi led to an yield of 48%.

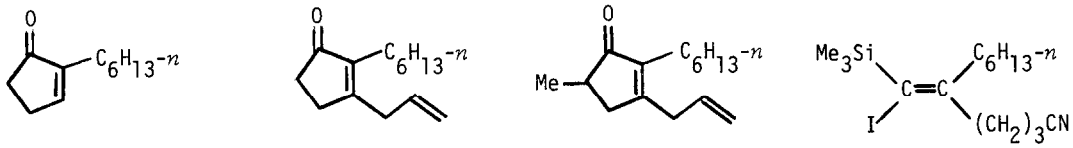


4 5 6

It then occurred to us that, if allylation of carboxamide enolates with 1 should proceed well, this and the cycliacylation procedure described above would combine to provide an expeditious route to cyclopentenones. We have indeed found that both of these steps proceed well, as indicated by the results summarized in Table.



7 8 9 10



11 12 13 14

The following features of the reaction should be noted. First, the method is indeed well suited for the preparation of 2-silyl-substituted cycloalkenones, i.e., 5 and 7-10. Second, there is no difficulty in accommodating substituents, such as Me and Ph, in the 5-position of cyclopentenones through the use of carboxamide enolates that are substituted with appropriate R^3 groups, as indicated by the preparation of 9, 10, and 13. Since introduction of an unsaturated group, such as Ph, in a position alpha to the carbonyl group via enolates is often problematical,[11] the method herein described offers a viable alternative. On the other hand, our attempts to incorporate substituents in the 4-position of cyclopentenones via the reaction of carboxamide enolates with 3-alkyl substituted 1-iodo-3-halopropenes led only to β-elimination of the latter. Based on the data at hand, we tentatively judge that the cycliacylation step is general with respect to substituents in cyclopentenones and cyclohexenones and that the scope is mainly limited by the availability of the required precursor 2. Third, it is striking that, whereas the carboxamide 6 readily cyclizes, a similarly structured nitrile 14[12] does not yield the desired cyclohexenone or any other monomeric product, although 14 was totally consumed. The reaction must have therefore produced polymeric products. Molecular models suggest that, in the (*E*)-lithio derivative of 14, the Li-C bond cannot

readily be parallel with the C≡N bond, whereas the Li-C and C=O bonds in the (*E*)-lithio derivative of 6 can readily be parallel with each other. Fourth, the use of *t*-BuLi (2 equiv) generally leads to considerably higher yields than that of *n*-BuLi (1 equiv).

The following procedure for preparing 9 is representative. (*Z*)-3-(Trimethylsilyl)-3-iodo-2-propen-1-ol was treated with 2 equiv each of CBr_4 and PPh_3[13] in ether at 0 to 25°C for 2 h to provide (*Z*)-1-(trimethylsilyl)-1-iodo-3-bromo-1-propene in 78% yield. To a solution of lithium disopropylamide (3.4 mmol) in THF at 0°C were sequentially added *N*,*N*-diethylphenylacetamide (0.68 g, 3.6 mmol, 0°C, 20 min) and (*Z*)-1-(trimethylsilyl)-1-iodo-3-bromo-1-propene in THF (1.01 g, 3.2 mmol, -78°C, 60 min). The reaction mixture was quenched with aqueous $NaHCO_3$, and the ether extract was dried over $MgSO_4$, concentrated, and chromatographed (silica gel, 4:1 hexane-ether) to provide 0.81 g (60%) of (*Z*)-*N*,*N*-diethyl-2-phenyl-5-iodo-5-(trimethylsilyl)-4-pentenamide. To 0.77 g (1.8 mmol) of the above-obtained amide in ether was added at -78°C *t*-BuLi (1.7 M, 2.1 mL, 3.6 mmol) in pentane. After 40 min, the mixture was poured into acqueous NH_4Cl. The organic extract was dried ($MgSO_4$), concentrated, and distilled (100-110°C at 0.2 mm Hg, Kugelrohr) to give 0.33 g (80%) of 9: IR (neat) 1700 (s), 1580 (m), 1273 (m), 1247 (m), 843 (s), 753 (m), 697 (m) cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 0.20 (s, 9 H), 2.6-3.6 (m, 3 H), 7.0-7.4 (m, 5 H), 7.87 (t, *J* = 3 Hz, 1 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ -2.20, 39.61, 51.49, 124.09, 126.19, 126.72, 127.16, 128.23, 139.65, 145.87, 170.65, 211.37. High resolution MS Calcd for $C_{14}H_{18}OSi$: 230.1127. Found: 230.1135.

We are currently investigating the synthetic use of α-silylcycloalkenones.

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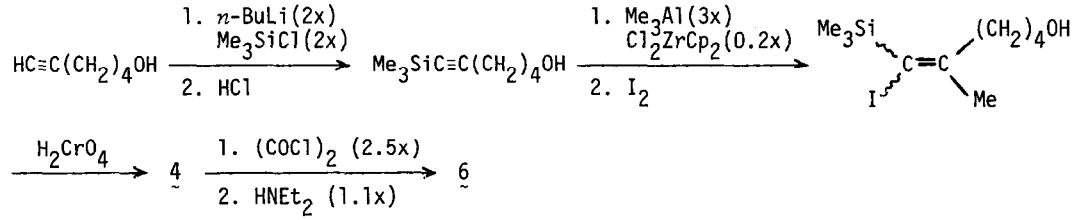
(8) Cyclopentenones may, however, be silylated by a multi-step procedure [Guaciaro, M. A.; Workulich, P. M.; Smith, A. B. *Tetrahedron Lett.* 1978, 4661].

(9) Negishi, E.; Miller, J. A. *J. Am. Chem. Soc.* 1983, *105*, 6761.

(10) The compound 4 and 6 were prepared by the following sequence.



(11) For a successful α-arylation of ketones, however, see Rossi, R. A.; Bunnett, J. F. *J. Am. Chem. Soc.* 1972, *94*, 638.

(12) The compound 14 was prepared by the following sequence.

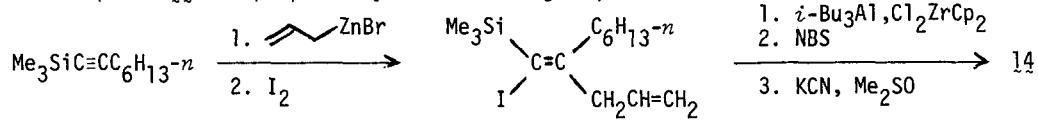


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Table. Preparation of Cycloalkenones by the Reaction of *N*,*N*-Diethyliodoalkenamides with Butyllithium.[a]

Cycloalkenone	BuLi[b]	Yield (%) Isolated	Yield (%) GLC
7	*t*	53	89
7	*n*	—	48
8	*t*	83	>90
8	*n*	—	62
9	*t*	50	—
10	*t*	80	—
11	*t*	—	81
11	*n*	73	87
12	*t*	71	—
13	*t*	79	—
5[c]	*t*	57	78
5[c]	*n*	—	48
5[d]	MeLi and *t*-BuLi	—	35

[a]The reactions were run according to the representative procedure described in the text. [b]Either 2 equiv of *t*-BuLi or 1 equiv of *n*-BuLi was used. [c]Prepared from 6. [d]Prepared from 4.

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