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CONJUGATE ADDITION REACTION OF TRIMETHYLSILYLACETONITRILE WITH α,β-UNSATURATED CARBONYL COMPOUNDS. SYNTHETIC STUDIES TOWARD SESBANIMIDE

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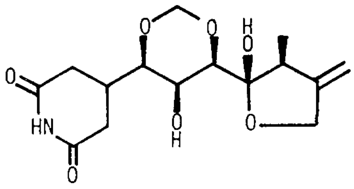
Summary: Lithiated trimethylsilylacetonitrile was allowed to react with some α,β-unsaturated carbonyl compounds to give the corresponding conjugate addition products.

Conjugate addition reaction of the carbanions with α,β-unsaturated carbonyl compounds constitutes a fundamental procedure for the carbon-carbon bond forming reactions.[1] Lithiated acetonitrile derivatives having alkoxy,[2] phenylseleno,[3] diethylphosphoro,[4] phenylthio,[5] aromatic,[6] and dialkylamino[7] α-substituents have been reported to undergo the conjugate addition reactions. However, none has been known about the conjugate addition reaction of the lithiated acetonitrile having trimethylsilyl substituent, while Peterson-type olefinations have been well documented.[8] Here we report the conjugate addition reactions of the lithiated trimethylsilylacetonitrile with some α,β-unsaturated carbonyl compounds.

In connection with our studies toward the total synthesis of sesbanimide 1,[9] we had an oppotunity to develop the conjugate 1,4-addition reaction of the acetonitrile carbanion 3 with 2.[10] The reaction of 2 with 3 in THF at -78°C gave the mixture of the 1,4-addition product 5 (25%) and 1,2-addition product 6 (50%).[11] Regioselectivity was greatly improved by using 4[8b,c] having trimethylsilyl substituent (THF, -78°C) to give exclusively 7 in a quantitative yield. Protodesilylation of 7 with CsF (0.1 eq) in aq. CH_3CN (rt, 1 h) cleanly afforded 5 in 94% yield. Activation of the lithium enolate, the intermediary formed by 1,4-addition of 4, by adding HMPA (3 eq) in the THF solvent also effected the direct protodesilylation to give 5 in 72% yield along with 7 (8%). 5 was then converted into the imide 8, the left half of 1, by the subsequent treatment with H_2O_2-NaOH in aq. EtOH at 50°C, then with t-BuOK at 200°C in 47% yield. Thus, lithium trimethylsilylacetonitrile was found to be the acetonitrile anion equivalent working as the good Michael donor.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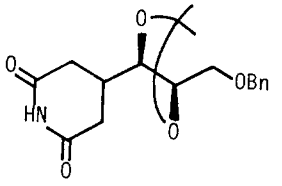
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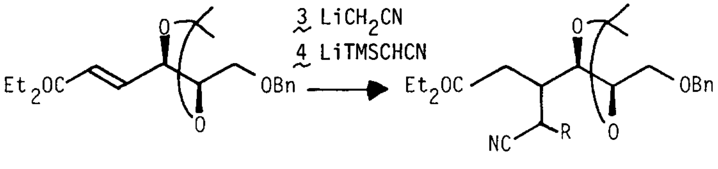
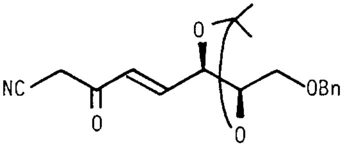


2

5 R=H
7 R=TMS



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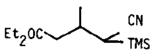
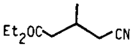
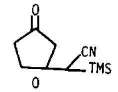
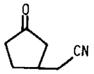
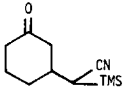
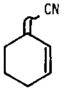
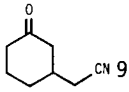
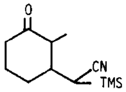
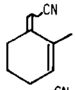
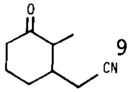
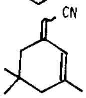
Further studies to explore the reaction of 4 with some α,β-unsaturated carbonyl compounds were carried out and some of the results are summarized in the Table. The reaction of 4 with ethyl crotonate followed by protodesilylation afforded the corresponding nitrile in 81% yield. The reaction of 4 with cyclopentenone and cyclohexenone also gave the corresponding 1,4-addition products, while the reactions of 3 with the same enones have been reported to give exclusively 1,2-addition products.[12] Substitution at C2 or C3 of the enones, however, prevented the 1,4-addition and 1,2-addition followed by Peterson olefination became the major contribution as shown in the reactions with 2-methylcyclohexenone and isophorone.[13]

Table. Reactions of 4 with α,β-unsaturated carbonyl compounds

Carbonyl compounds	Products(%)[a]				Products(%)[b]	
	1,4-Addition		1,2-Addition			
ethyl crotonate		c		d		81
cyclopentenone		97		d		99
cyclohexenone		81		17		96
2-methylcyclohexenone		27		53		99
isophorone		d		88		

a) Isolated yields. b) Yields from the TMS derivatives. c) Protodesilylated without any purification. d) Only a trace amount of the product was detected.

References and Notes

1. H. O. House, "Modern Synthetic Reactions," W. A. Benjamin, INC., 1972.
2. G. Stork and L. Maldonado, J. Am. Chem. Soc., 96, 5272(1974).
3. P. A. Grieco and Y. Yokoyama, J. Am. Chem. Soc., 99, 5210(1977).
4. B. Deschamps, Tetrahedron, 24, 2009(1978).
5. N. Wang, S. Su, and L. Tsai, Tetrahedron Letters, 1121(1979).
6. L. Wartski, M. El Bouz, and J. Seyden-Penne, Tetrahedron Letters, 1543(1979).
7. T. Wakamatsu, S. Hobara, and Y. Ban, Heterocycles, 19, 1395(1982).
8. a) I. Ojima and M. Kumagai, Tetrahedron Letters, 4005(1974); b) I. Matsuda, S. Murata, and Y. Ishii, J. Chem. Soc. Perkin I, 26(1979); c) R. Haruta, M. Ishiguro, K. Furuta, A. Mori, N. Ikeda, and H. Yamamoto, Chemistry Letters, 1093(1982).
9. R. G. Powell, C. R. Smith, Jr., D. Weisleder, G. K. Matsumoto, J. Clardy, and J. Kozlowsky, J. Am. Chem. Soc., 105, 3739(1983).
10. The ester 2 (E/Z=7/3) was prepared by the reaction of the corresponding aldehyde with $Ph_3P=CHCO_2Et$ in refluxing benzene. The aldehyde was prepared from D-tartaric acid according to the reported procedure for the optical antipode. T. Mukaiyama, K. Suzuki, and T. Yamada, Chemistry Letters, 929(1982).
11. Satisfactory spectral and analytical data were obtained for all compounds.
12. R. Sauvetre, M.-C. Roux-Schmitt, and J. Seyden-Penne, Tetrahedron Letters, 24, 2135(1978).
13. The following experimental procedure provides details of a typical reaction. A solution of 2 (3.2 g, 10 mmol) in THF (10 ml) was added to a solution of 4 (14 mmol) in THF (35 ml). The mixture was stirred at -78°C for 1 h and was added by satd. aq. NH_4Cl. Extraction with ether and concentration gave the crude 7. A solution of the crude 7 and CsF (151 mg, 1 mmol) in 10% aq. CH_3CN (11 ml) was stirred at rt for 1 h and was added by satd. aq. $NaHCO_3$. Extraction with ether and purification by column chromatography (SiO_2, AcOEt/hexane=1/4) gave 5 in 94% yield.

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