CHEMISTRY LETTERS, pp. 1453-1456, 1989.

Diastereoselective Water Quenching of the 1:2 Michael Adducts of Grignard Reagents with Methyl 2-(Trimethylsilyl)acrylate

Junji TANAKA,* Shuji KANEMASA,* Hiroshi KOBAYASHI,
and Otohiko TSUGE
Institute of Advanced Material Study, and Department of
Molecular Science and Technology, Interdisciplinary
Graduate School of Engineering Sciences, Kyushu University,
Kasugakoen, Kasuga 816

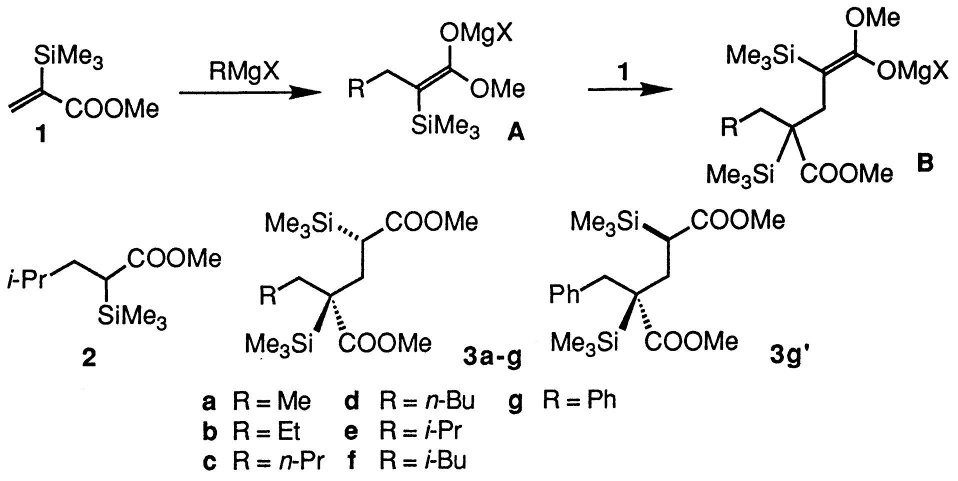
Reactions of alkyl Grignard reagents with methyl 2-(trimethylsilyl)acrylate produce, after quenching with water, 1:2 adducts in most cases as single diastereomers. Tight chelation working in the 1:2 adduct anions would be responsible for such high chemo- and diastereoselectivities.

Methyl 2-(trimethylsilyl)acrylate (1) is known to serve as highly reactive and base-stable acceptor in Michael additions with organometallics; the resulting adduct anions can be utilized in situ for subsequent condensation with carbonyl compounds producing 2,3-disubstituted acrylates.1) Use of methylmagnesium iodide as a donor leads to an unusual formation of the condensation product derived from 1:2 adduct anion.

During our investigation on Michael additions between 2-silylacrylate 1 and alkyl Grignard reagents, we have found that 1:2 adducts are produced as sole or major products after quenching the adduct anions with water and they are single diastereomers. This communication briefly describes our preliminary results.

Michael addition of 1 with methylmagnesium iodide and subsequent quenching with water were investigated: An equimolar mixture of 1 and the Grignard reagent was allowed to react in the presence of a catalytic amount of copper(I) chloride (0.5 mol%) in diethyl ether at -15 °C for 1 h to afford, after water quenching at the same temperature, dimethyl 2-ethyl-2,4-bis(trimethylsilyl)glutarate (3a) as a sole product and a single diastereomer in 71% yield (Scheme 1 and Entry 1). Diester 3a corresponds to the product derived from the repeated Michael addition of 1:1 adduct anion A onto 1 and subsequent diastereoselective protonation of the resulting 1:2 adduct anion B (R = Me, X = I for both A and B). Any sign of formation of either the 1:1 adduct or other products involving more than two equivalents of 1 was not observed.2) 2R*,4R*-Stereostructure of diester 3a and E-geometry of the enolate intermediates A and B were assigned by analogy with the structural assignment of 3g and on the basis of the proposed stereochemical course of this type of reaction, respectively, which will be discussed below.

Under similar reaction conditions, primary alkyl Grignard reagents such as



Scheme 1.

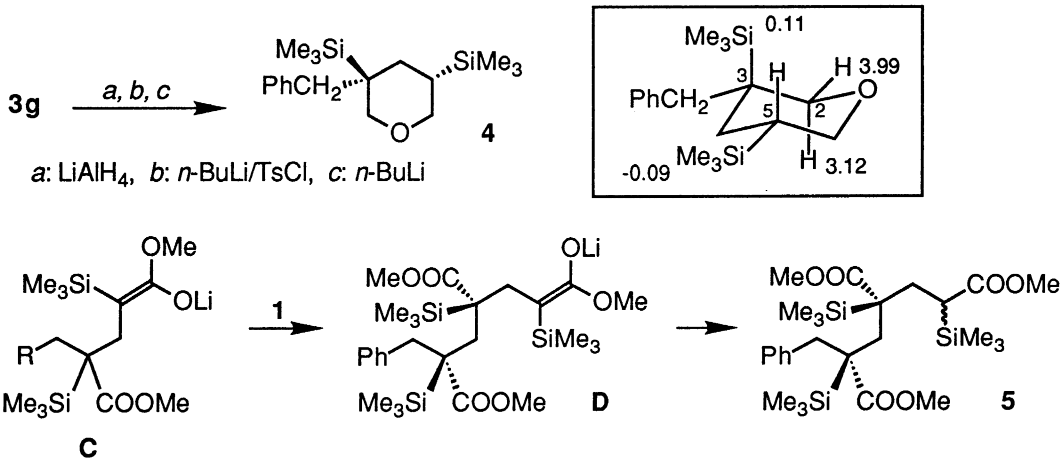
ethyl-, propyl-, butyl-, and i-butylmagnesium bromides produced dimethyl 2-alkyl-2,4-bis(trimethylsilyl)glutarates 3b-d and 3f all as sole products and also single diastereomers (Entries 2-5). In contrast with the exclusive chemoselectivity in favor for the formation of 1:2 adducts 3, however, the reaction of 1 with i-propylmagnesium bromide furnished 1:1 adduct 2 and 1:2 adduct 3e in 36% and 19% yields, respectively. The latter 3e was again diastereomerically pure.

Table 1. Michael Additions of Methyl 2-(Trimethylsilyl)acrylate **1**

Entry	Donor (equiv.)	Catalyst (mol%)	Solvent	Reaction conditions		Products (yield/%)$^{a)}$		
				Temp/°C	Time/h	2	3a-g	4
1	MeMgI (1)	CuCl (0.5)	Et_2O	-15	1	0	$71^{b)}$	-
2	EtMgBr (1)	CuCl (0.5)	Et_2O	-15	1	0	$73^{b)}$	-
3	*n*-PrMgBr (1)	CuCl (0.5)	Et_2O	-15	1	0	$67^{b)}$	-
4	*n*-BuMgBr (1)	CuCl (0.5)	Et_2O	-15	1	0	$65^{b)}$	-
5	*i*-BuMgBr (1)	CuCl (0.5)	Et_2O	-15	1	0	$62^{b)}$	-
6	*i*-PrMgBr (1)	CuCl (0.5)	Et_2O	-15	1	36	$19^{b)}$	-
7	PhMgBr (0.5)	None	Et_2O	-15	1	0	$87^{b)}$	0
8	PhMgBr (0.5)	None	THF	-15	1	0	$63^{c)}$	0
9	PhLi (0.3)	None	THF	-78	1	0	$65^{d)}$	$17^{e)}$
10	PhLi (0.3)	None	THF	-78	20	0	$37^{d)}$	$47^{f)}$

a) Yield of isolated products. b) Obtained as a single diastereomer (^{1}H NMR). c, d) Obtained as inseparable mixtures of two diastereomers **3g** and **3g'** whose ratio was determined on the basis of ^{1}H NMR spectra: c) **3g**:**3g'** = 3:2, d) **3g**:**3g'** = 2:3. e) No ratio was given. f) Ratio of two diastereomers was 7:1. The major diastereomer was separated in a pure form by crystallization.

It was previously reported that the reaction of 1 with an equimolar amount of phenylmagnesium bromide or phenyllithium led to 1:1 adduct 2g as a far major or sole product.[1,3] However, use of two equivalents of the acceptor 1 to phenylmagnesium bromide in the absence of copper catalyst exclusively produced 1:2 adduct 3g after water quenching.[4] It should be emphasized that the 1:2 adduct 3g given in 87% yield by the reaction in diethyl ether was a single diastereomer (Entry 7), while a 3:2 mixture of two diastereomeric 1:2 adducts, 3g and 3g', was obtained in 63% yield by the reaction in tetrahydrofuran (THF) (Entry 8).[5]



Scheme 2.

In order to assign its stereostructure, diester 3g was converted into tetrahydropyran 4 in a total yield of 55% through three step transformation as shown in Scheme 2.[6] On the basis of the NOE difference spectrum of 4,[7] 3,5-trans stereostructure of 4, and hence 2R*,4R*-configuration of 3g, was determined. By analogy of the stereochemical course of the reiterative Michael addition of 1, 3a-f must also have 2R*,4R*-structures.

In the reaction of phenyllithium with three equivalents of 1 in THF, 1:3 adduct 5 was given newly together with 1:2 adducts 3g and 3g' (Scheme 2 and Entries 9 and 10). Diastereomer ratio of the 1:2 adducts was again poor (3g:3g' = 2:3) in these cases. Among four possible diastereomers for 1:3 adduct 5, only two of them were actually produced in a 7:1 ratio (Entry 10). It is most likely that two diastereomers of 5 have been formed on water quenching of the diastereomerically pure 1:3 adduct anion D resulting from the diastereoface-selective Michael addition of 1:2 adduct anion C.

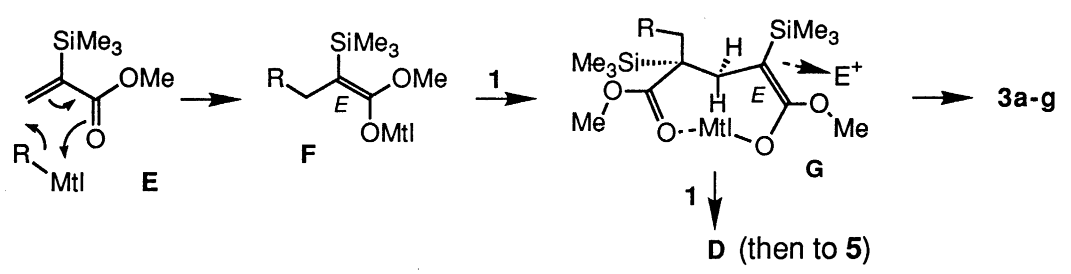


Fig. 1. Diastereoselective quenching of the 1:2 Michael adduct anions **G** with water leading to **3a-g** (and/or **3g'**) or with 2-silylacrylate **1** leading to the 1:3 adduct **5**.

E-Geometry was proposed to the intermediate enolate F (or throughout A to D), which was presumably constructed via an approach E.[8] The 1:2 adduct anion G formed by a similar approach can be stabilized as a tight eight-membered chelation. If this chelation is strong enough to survive on water quenching, protonation will take place diastereoselectively from the outside of the enolate plane of G. Magnesium enolate G (Mtl = MgX) is the case, whereas lithium enolate G (Mtl = Li) is less stable so that the chelation collapses on quenching. The lithium chelation G (Mtl = Li), although fragile under hydrolytic conditions, can be diastereoselectively trapped with the third molecule of acceptor 1 to form the 1:3 adduct anion D, and then protonated giving 5. THF having a stronger solvation ability destabilizes this chelation G to lower the diastereoselectivity.

As there is few example known for absolutely diastereoselective protonation of enolates,[9,10] more study in detail is now in progress on these stereoselective formation of Michael adducts of enolate types and on their diastereoselective trapping with other electrophiles.

References

1) O. Tsuge, S. Kanemasa, and Y. Ninomiya, Chem. Lett., 1984, 1993.

2) Grignard reagent-induced dimerization of 2-alkylacrylates produces 1:2 Michael adducts as 10:1 to 4:1 mixtures of two diastereomers (M. Yamaguchi, Y. Kurasawa, and K. Yokota, The 55th National Meeting of the Chemical Society of Japan, Preprint II, 4V08, p. 736 (1987) and the private information).

3) Phenyllithium shows a better chemoselectivity in favor for the 1:1 adduct formation than phenylmagnesium bromide.

4) Kinetic control of this type of reaction has been discussed, which will be soon reported elsewhere.

5) In the reaction of 1 with lithium enolates, THF is the solvent which favors the formation of 1:2 adducts rather than 1:1 adducts (Our unpublished results).

6) M. Yamaguchi, M. Tsukamoto, S. Tanaka, and I. Hirao, Tetrahedron Lett., 25, 5661 (1984).

7) The Me_3Si at $\delta = 0.11$ was confirmed to attach to the 3-position because of a strong NOE with $3\text{-}PhCH_2$. This Me_3Si showed another NOE with a doublet proton at 3.99 ($2\text{-}H_{eq}$). Since $5\text{-}Me_3Si$ must occupy an equatorial position regardless of the configuration of 3-position, stereostructure of 3g was determined as shown in Scheme 2.

8) The linear transition state has been recently proposed to the Michael additions of lithium enolates with α,β-unsaturated esters or ketones (C. H. Heathcock and D. A. Oare, J. Org. Chem., 50, 3022 (1985); M. Yamaguchi, K. Hasebe, S. Tanaka, and T. Minami, Tetrahedron Lett., 27, 959 (1986)).

9) As a review: L. Duhamel, P. Duhamel, J. C. Launay, and J. C. Plaquevent, Bull. Soc. Chim. Fr., 1984, 412.

10) U. Schöllkopf, D. Pettig, and U. Busse, Synthesis, 1986, 737.

(Received June 2, 1989)