CHEMISTRY LETTERS, pp. 331-334, 1980. © The Chemical Society of Japan 1980

# HETEROCONJUGATE ADDITION OF LITHIUM ALKYLS TO SUBSTITUTED HETERO-OLEFINS CONJUGATED WITH SULFUR AND SILICON ATOMS

Minoru ISOBE*, Masato KITAMURA, and Toshio GOTO
Laboratory of Organic Chemistry, Faculty of Agriculture,
Nagoya University, Chikusa, Nagoya 464

Lithium alkyls and a lithiated sulfone carbanion readily added to the substituted hetero-olefins conjugated with silicon and sulfone-sulfur atoms among other combination of the third (or fourth) row hetero atoms, e.g. Si, Se and S.

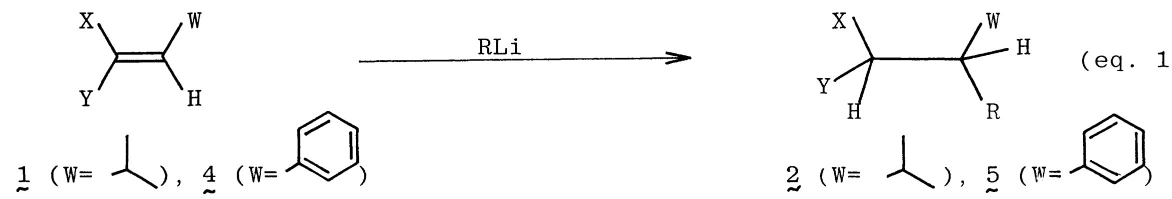
We have recently developed[1] a complete asymmetric induction in heteroconjugate addition on an acyclic system as a new synthetic approach directed toward ansamacrolides. We have defined[1] the term "heteroconjugate addition" to such a reaction that a nucleophile adds to an olefin conjugated with the third (or fourth) row hetero atom(s) such as Si, Se and S. Lithium alkyls are well known to add to the terminal hetero-olefins, X-CH=$CH_2$, where X is $Me_3Si$-[2] or PhSe-[3] resulting the adduct X-$CH_2CH_2R$, but rarely known to add to substituted ones, which are of much synthetic interest for introducing a branched alkyl side chain onto an acyclic carbon chain (see eq. 1). Only a few specialized cases[4] have been reported prior to our previous work[1] of this addition reaction to substituted hetero-olefins.[5] In this communication are described the fundamental results on the heteroconjugate addition of lithium alkyls to substituted hetero-olefins. The substituents W used in this communication are a) isopropyl group as typical bulky alkyl group and b) phenyl group as typical aryl one.

To explore the electrophilic reactivity were prepared from isobutanal the following six olefins (**1a**~**f**) conjugated with two heteroatoms (X/Y): **1a**, $Me_3Si$/$Me_3Si$; **1b**, PhSe/$Me_3Si$; **1c**, PhSe/PhSe; **1d**, $Me_3Si$/PhS; **1e**, $Me_3Si$/PhS(O) and **1f**, $Me_3Si$/PhS$(O)_2$.[6] Each of the olefins was treated with one equivalent of methyl lithium in THF at -78°C (to 0°C) and then the reaction mixture was analyzed.

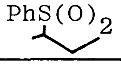
No addition took place in the hetero-olefins **1a** through **1e**; the starting materials (**1a**, **1b** and **1d**) being recovered in high yields. In **1c**, ejection of the phenyl selenyl moiety occurred by direct attack of MeLi onto one of the two selenyls to yield phenylmethylselenide in 68 % as by-product. The sulfoxide in **1e** gave an unidentified mixture with no clear indication of the adduct formation.[4d] Clean addition, however, took place at -78°C in 10 min to the sulfonyl-silyl olefin (**1f**) affording in 97 % yield the adduct **2f**: m/z 298; $\delta_{CDCl_3}$ 0.24s & 0.40s in the ratio of 1:3 (9H), 0.7(6H, m), 1.3(5H, m), 2.8(1H, brs), 7.7(5H, m). The pmr signal at 2.8 ppm disappeared by $D_2O$ addition prior to the work-up, indicating the presence of the intermediate anion capable of further alkylation. When the anion formed in situ was treated with allyl bromide (-78°C to room temp.), the alkylated product (**3**) was indeed obtained in 55 % yield.

Considering the minimum requirement for the substituted sulfonyl-silyl olefins to render heteroconjugate additions, one might suggest that only the sulfonyl group should give enough electrophilicity to its conjugated olefin even without silyl group. However, the silyl moiety was found indispensable, since taking 1-(phenylsulfonyl)-prop-1-ene, for instance, its olefinic proton instead of the silyl was readily removed by treatment with 1 eq. of n-BuLi at -78°C to form a yellow solution. The corresponding anion-formation was proven by quenching it with $D_2O$ and affording 1-(phenylsulfonyl)-1-deuteroprop-1-ene in 70 % yield.[7]

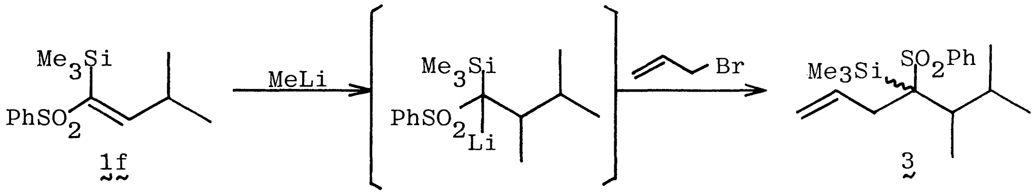
The hetero-olefin substituted with phenyl (**4**) was prepared in 88 % yield by condensation of benzaldehyde with lithium bis(trimethylsilyl)phenylthiomethylide in THF at -78°C[4a,8] followed by oxidation with excess mCPBA. Regioisomers E and Z of **4** were separated by $SiO_2$: E-**4**, mp 85.0°C, $\delta_{CDCl_3}$ 0.02(9H, s), 8.32(1H, s); Z-**4**, mp 89.2°C, $\delta_{CDCl_3}$ 0.49(9H, s), 7.37(1H, s). Addition of MeLi to Z-**4** at -78°C for 30 min gave in 88 % yield the adduct **5a** (entry 8) as a diastereomixture in a ratio of 1:1.2; $\delta_{CDCl_3}$ 0.04(9H, s), 1.58(3H, d, J=7), 3.7(2H, m); and 0.27 (9H, s), 1.70(3H, d, J=7), ca. 3.7(2H). When TMS group was taken off (KF/MeOH/ 60°C/ 10 min), this mixture afforded a single compound **6** (95 % yield): mp 90.5°C $\delta_{CDCl_3-C_6D_6}$ 1.35(3H, d, J=6.5), 3.24(3H, brs), 6.8-7.8(10H).[9] On the other hand, E-**4** isomer, when treated with MeLi at -78°C, gave **5a** in relatively low yield (30-60 %). This was due to elimination of the phenylsulfonyl group (presumably dis-

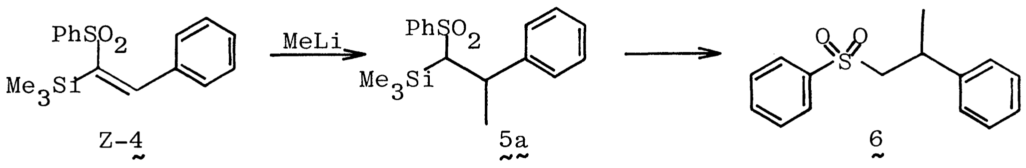


(eq. 1)

| Entry | Compd. No. | W | X | Y | R | Products | Yields(%) |
|---|---|---|---|---|---|---|---|
| 1 | 1a | i-Pro | $\mathrm{Me_3Si}$ | $\mathrm{Me_3Si}$ | Me | SM | - |
| 2 | 1b* | i-Pro | $\mathrm{Me_3Si}$ | PhSe | Me | SM | - |
| 3 | 1c | i-Pro | PhSe | PhSe | Me | $\mathrm{PhSe\text{-}CH{=}CH\text{-}CHMe_3}$ | 68 |
| 4 | 1d | i-Pro | $\mathrm{Me_3Si}$ | PhS | Me | SM | - |
| 5 | 1e | i-Pro | $\mathrm{Me_3Si}$ | PhS(O) | Me | ? | - |
| 6 | 1f | i-Pro | $\mathrm{Me_3Si}$ | $\mathrm{PhS(O)_2}$ | Me | 2a | 97 |
| 7 | 1f | i-Pro | $\mathrm{Me_3Si}$ | $\mathrm{PhS(O)_2}$ | n-Bu | 2b | 79 |
| 8 | Z-4 | Ph | $\mathrm{PhS(O)_2}$ | $\mathrm{Me_3Si}$ | Me | 5a | 88 |
| 9 | E-4 | Ph | $\mathrm{Me_3Si}$ | $\mathrm{PhS(O)_2}$ | Me | 5a + ($\mathrm{PhC{\equiv}CSiMe_3}$) | 54 + (ca.30) |
| 10 | Z-4 | Ph | $\mathrm{PhS(O)_2}$ | $\mathrm{Me_3Si}$ | n-Bu | 5b | 97 |
| 11 | E-4 | Ph | $\mathrm{Me_3Si}$ | $\mathrm{PhS(O)_2}$ | n-Bu | 5b | 77 |
| 12 | Z-4 | Ph | $\mathrm{PhS(O)_2}$ | $\mathrm{Me_3Si}$ | sec-Bu | 5c | 72 |
| 13 | Z-4 | Ph | $\mathrm{PhS(O)_2}$ | $\mathrm{Me_3Si}$ |  $\mathrm{PhS(O)_2}$ | 5d | 90 |

* regiomixtures (E/Z=1)





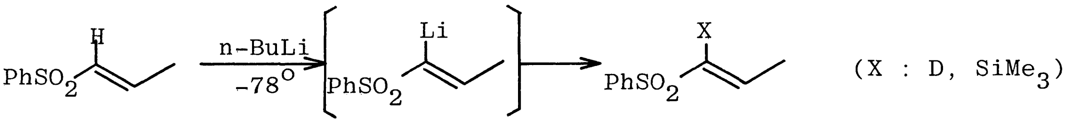
sociation of the vinyl proton of E-4 being involved) to give phenyl(trimethylsilyl)acetylene ($\nu$ 2120 cm$^{-1}$) as a volatile side product. Similarly, addition of n-BuLi to Z and E isomers of 4 yielded 5b in 97% and 77 %, respectively. Even bulkier sec-BuLi added to Z-4 isomer (entry 12). Entry 13 indicated that the α-lithio sulfonyl carbanion also added to Z-4 in high yield.

These methodologies are in progress with further utilization of the heteroatoms in the heteroconjugate adduct, which will be described in detail shortly.

Acknowlegement : Part of this experiment was carried out by Mr. H. Imagawa of this laboratory to whom thanks are due. Financial support on this research was made by MATSUNAGA SCIENCE FOUNDATION.

References and Notes

1. M. Isobe, M. Kitamura and T. Goto, Tetra. Lett., 3465 (1979).
2. a, T. H. Chan, E. Chang and E. Vinokur, Tetra. Lett., 1137 (1970); b, T. H. Chan and E. Chang, J. Org. Chem., 39, 3264 (1974); c, D. Seebach, R. Burstinghaus, B. T. Grobel and M. Kolb, Ann. Chem., 830 (1970); d, G. Stork and B. Ganem, J. Am. Chem. Soc., 95, 6152 (1973).
3. S. Raucher and G. A. Koolpe, J. Org. Chem., 43, 4252 (1978).
4. a, B. T. Grobel and D. Seebach, Chem. Ber., 110, 852 (1977); b, M. van der Leij and B. Zwannenburg, Tetra. Lett., 3383 (1978); c, R. Tanaka, H. Sugihara, K. Tanaka and A. Kaji, Synthesis, 5, 299 (1977); d, H. Sugihara, R. Tanikaga, K. Tanaka and A. Kaji, Bull. Chem. Soc. Japan, 51, 655 (1978).
5. a, B. W. Metcalf and E. Bonilavri, J. C. S. Chem. Comm., 914 (1978); b, B. Cazes and S. Julia, Tetra. Lett., 4065 (1978); c, N. H. Andersen, P. F. Duffy, A. D. Denniston and D. B. Grotjahn, Tetra. Lett., 4315 (1978).
6. Only E isomer of the sulfones was obtainable from a mixture of two regioisomers. On the stereochemistry, see ref. 4a and 8.
7. In addition, trapping of the vinyl-anion with Me$_3$SiCl afforded E-1-(phenylsulfonyl)-1-(trimethylsilyl)-prop-1-ene in only 36 % yield; the lower yield being due to side-reactions between the vinyl-anion and the silylated product.



8. The corresponding sulfides (E and Z isomers) showed pmr signal of the vinyl proton at 6.28 ppm (E isomer) and 6.34 (Z isomer). The signal of the E isomer moved to 8.32 when oxidized into the corresponding sulfone; whereas Z isomer changed into 7.37.
9. Anal. Found, C 68.91, H 6.17; Calcd. C 69.20, H 6.19 for $C_{15}H_{16}O_2S$.

(Received January 8, 1980)