

**REGIO AND STEREOSELECTIVE PREPARATION OF ENOLATES FROM
KETONES BY MEANS OF SODIUM BIS(TRIMETHYLSILYL)-AZIDE**

Marcel GAUDEMAR and Moncef BELLASSOUED

Université Pierre et Marie Curie, Laboratoire de Synthèse Organométallique, 4, Place Jussieu,
75230 - PARIS Cedex 05, France.

Abstract : The deprotonation of some ketones by sodium bis(trimethylsilyl)-azide is regio and stereo-selective. The results are different from those observed with LDA.

Although the preparation of enolates by LiNR_2 or NaNH_2 are classical and much used methods, it is remarkable that very little work has been reported on the deprotonation of ketones by hindered sodium amides. $\text{NaN}(\text{iPr})_2$ does not seem to have been used previously ; however, one finds some references¹⁻⁷ dealing with the use of $\text{NaN}(\text{SiMe}_3)_2$ 1, though the authors were not concerned with regio and stereoselectivity problems.

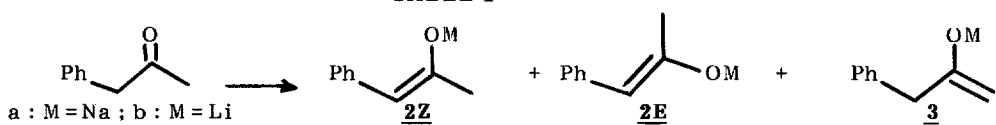
The well known fact that the structures and properties of enolates can widely vary with the methods of preparation and the nature of the counter-ion has prompted us to reexamine the action of hindered sodium amides on ketones.

We have provisionally left aside $\text{NaN}(\text{iPr})_2$, the preparation of which is quite difficult, and rather used reagent 1, easily obtained with an almost quantitative yield according to the method of GOUBEAU et al.^{8,9} : attack of sodium by the amine in the presence of an electron acceptor. The sodium (or lithium) enolates have been trapped with trimethylsilyl chloride.¹⁰ Most of the NMR spectra of trimethylsilyl enolates are known ; when this is not the case, they are easy to interpret.

The deprotonation of phenylacetone (table 1), under kinetic control, by 1 is highly regio and stereoselective in favour of enolate 2a of E configuration. The latter changes spontaneously at room temperature into a pure 2aZ enolate, for which this is an excellent preparation.¹² For comparison, we have repeated these experiments with $\text{LiN}(\text{iPr})_2$, which gives 3b, whereas $\text{LiN}(\text{SiMe}_3)_2$ is superior to 1 for the preparation of the E enolate. However, the pure Z isomer is still inaccessible.

The preparation method of Z sodium enolates can be generalized as shown on table 2.

TABLE 1

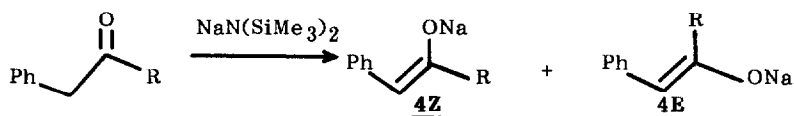


Deprotonation conditions	2Z (%) ^a	2E (%)	3 (%)	Overall yields of trimethylsilyl enolates (%) ^b
NaN(SiMe ₃) ₂ , 15', -100°C	15	85	5	82
" 2h, -60°C	"	"	"	81
" 15', -60°C				86
then 20h, +20°C	100	0	0	
LiN(iPr) ₂ , 30', -70°C	5	35	60	66
" " "				
then 20h, +20°C	15	60	25	68
LiN(SiMe ₃) ₂ 30', -70°C	10	90	0	79
" " "	13 ^c	87	0	80
then 20h, +20°C				

^a Constants and NMR spectra of trimethylsilyl enolates : ref. 11 ; ^b Isolated product yields ;

^c When performing at 0°C with LiN(iPr)₂, HOUSE and al.^{11a} obtained a similar result to that of our last test.

TABLE 2

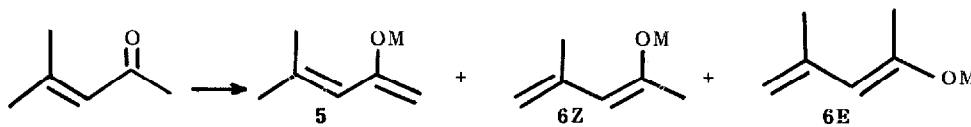


Deprotonation conditions	R	4Z ^a (%)	4E (%)	Overall yields of trimethylsilyl enolates (%)
1 h, -70°C	Et	20	80	94
" "	nPr	"	"	87
1 h, -70°C	Et	100	0	88
then 20 h, +20°C	nPr	"	"	89

^a Constants and NMR spectra of trimethylsilyl enolates : ref. 13. The other enolates are absent or inferior to 5 %.

^b Isolated product yields.

TABLE 3



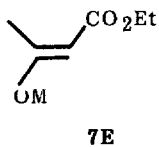
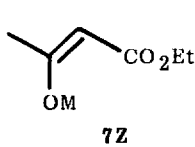
a : M = Na ; b : M = Li

Deprotonation conditions	5 ^a (%)	6Z (%)	6E (%)	Overall yields of trimethylsilyl enolates (%) ^b
NaN(SiMe ₃) ₂ , 5', -70°C	65	35	0	81
" " " then 20h, +20°C	0	95	5	70
LiN(iPr) ₂ , 1h, -70°C	85	15	0	84
" " " then 20h, +20°C	10	55	35	22

^a Constants and NMR spectra of trimethylsilyl enolates : ref. 14.

^b Isolated product yields.

Other examples show the interest of the reagent **1** : it is possible to prepare the practically pure **6aZ** enolate from mesityl oxide (table 3) ; ethyl acetylacetae, treated with **1** at -70°C leads to **7aZ** (yield = 92 % ; Z/E = 95/5) whereas with lithium the ratio Z/E is only 70/30 (NMR : ref. 15).



a : M = Na

b : M = Li

Sodium enolates are more reactive than lithium enolates ; for instance, **2aZ** and **2aE** react instantaneously at -100°C with ClSiMe₃ whereas with the lithium enolates, the reaction only begins at -20°C/-10°C. Furthermore, these sodium enolates are easily convertible into various other enolates by means of metallic bromides in solution ; the reaction can be roughly followed by the precipitation of NaBr ; for example, at -60°C, ZnBr₂ reacts completely with **2aZ** within about one hour.

REFERENCES AND FOOTNOTES

- 1 - R. GOMPPER and K.H. ETZBACH, *Angew. Chem. Int. Ed. Engl.*, **17**, 603, **1978**.
- 2 - A.N. KURKIN and Z.S. NOVIKOVA, *Vest. Mosk. Univ. Khim.*, ser. 2, **19**, 624, **1978**; *C.A.*, **90**, 87583, **1979**.
- 3 - H. HIRSCH, S. HUNIG and H. REIBIG, *Chem. Ber.*, **115**, 3687, **1982**.
- 4 - G. BOCHE, F. HEIDENHAIM, W. THIEL and R. EIBEN, *Chem. Ber.*, **115**, 3167, **1982**.
- 5 - Z.S. NOVIKOVA, A.N. KURKIN and I.F. LUTSENKO, *Zh. Obshch. Khim.*, **55**, 2710, **1985**; *C.A.*, **106**, 18688 x, **1986**.
- 6 - C.R. KRUGER and E. ROCHOW, *J. Organometal. Chem.*, **1**, 476, **1964**.
- 7 - M. TANABE and D.F. CROWE, *Chem. Comm.*, 1498, **1969**.
- 8 - J. GOUBEAU and J. JIMENEZ - BARBERA, *Z. anorg. allg. Chem.*, **303**, 217, **1966**.
- 9 - The experiments are carried out in a mixture of ether-THF (50/50). Either phenanthrene or α -methyl styrene are used as electron acceptors, depending on the trimethylsilyl enolates boiling points. $\text{NaN}(\text{SiMe}_3)_2$, conc. 1.3 N, is soluble at -100°C . For 0.05 at.g of Na, we use 0.045 mol of ketone and 0.055 mol of Me_3SiCl . Then, the precipitate is filtered off, the solvent removed and the chlorotrimethylsilyl enolate distilled.
- 10 - The reactional mixture is always brought back to its initial deprotonation temperature (-100°C or -70°C) before reacting with ClSiMe_3 .
- 11 - a) H.O. HOUSE, L.J. CZUBA, M. GALL and H.O. OLMSTEAD, *J. Org. Chem.*, **34**, 2324, **1969**.
 b) H.O. HOUSE, R.A. AUERBACH, M. GALL and N.P. PEET, *J. Org. Chem.*, **38**, 514, **1973**.
 c) H. EMDE, A. GOTZE, K. KOFMANN and G. SIMCHEN, *Liebigs Ann. Chem.*, 1643, **1981**.
- 12 - H.O. HOUSE et al.^{11a,b} have prepared, by means of NaH (insoluble), a mixture rich in the Z isomer; our method is preferable.
- 13 - The NMR signals (CCl_4 ; ext. ref. TMS; 60 MHz) were assigned by comparison with the spectra^{11a,b} of: $\text{Ph}-\text{CH}=\text{C}(\text{OSiMe}_3)\text{Me}$ and $\text{R}-\text{CH}=\text{C}(\text{OSiMe}_3)\text{Me}$ E and Z, which are very characteristic.
 $\text{Ph}-\text{CH}=\text{C}(\text{OSiMe}_3)\text{Et}$: $\text{Eb}_{0,05} = 60-65^\circ\text{C}$. NMR (δ ppm) Z: 0.11, s, 9H; 1.13, t, 3H; 2.20, q, 2H; 5.45, s, 1H; 7-7.7, m, 5H. E: 0.22, s, 9H; 1.06, t, 3H; 2.24, q, 2H; 5.71, s, 1H; 7.22, s, 5H.
 $\text{Ph}-\text{CH}=\text{C}(\text{OSiMe}_3)\text{nPr}$: $\text{Eb}_{0,05} = 71-75^\circ\text{C}$. NMR (δ ppm) Z: 0.11, s, 9H; 0.98, t, 3H; 1.2-2.4, m, 4H; 5.47, s, 1H; 7-7.7, m, 5H. E: 0.25, s, 9H; 0.92, t, 3H; 1.2-2.4, m, 4H; 5.80, s, 1H; 7.20, s, 5H.
- 14 - S.S.K. WAN, A.C. WEEDON and D.F. WONG, *J. Org. Chem.*, **51**, 3335, **1986**.
- 15 - a) K. KRAGELOH, G. SIMCHEN and K. SCHWEIKER, *Liebigs Ann. Chem.*, 2352, **1985**.
 b) K. SAIGO, H. KURIHARA, H. MIURA, A. HONGU, N. KUBOTA and H. NOHIRA, *Synth. Comm.*, **14**, 787, **1984**.

(Received in France 13 February 1989)