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WATER-INDUCED FORMATION OF AZOMETHINE YLIDE 1,3-DIPOLE. STEREOSPECIFIC AND REGIOSELECTIVE CYCLOADDITION REACTIONS

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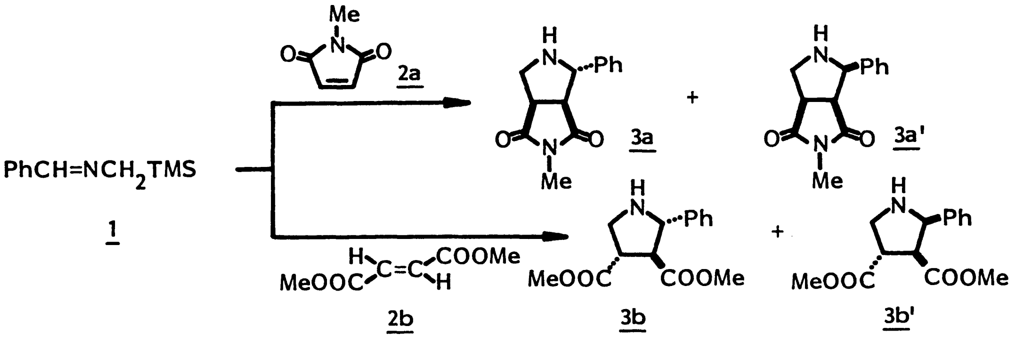
An N-(trimethylsilylmethyl)imine generates the azomethine ylide 1,3-dipole of nonstabilized type, when treated with water, which cycloadds to olefinic dipolarophiles in a stereospecific and regioselective manner.

The recent rapid growth of N-ylide chemistry owes much to the simple compound, N-(trimethylsilylmethyl)imminium salts that are accessible by either the quaternalization of N-(trimethylsilylmethyl)imines$^{1)}$ or the alkylation of imines with trimethylsilylmethyl triflate.$^{2)}$ The former method seems more sensible at this moment because a convenient and general synthesis for a variety of the N-silylmethylimines has been recently reported.$^{3)}$ The quaternalization of N-silylmethylimines with such electrophiles as acyl halides, alkyl halides, and trimethylsilyl triflate is often followed by a spontaneous desilylation forming nonstabilized azomethine ylides.$^{1)}$ In the course of our study on the desilylation of N-(trimethylsilylmethyl)imines, we have come across a novel desilylation reaction.

We wish to report here the water-induced formation of azomethine ylide 1,3-dipole and its stereospecific and regioselective cycloadditions to olefinic dipolarophiles.

The reaction of N-benzylidene(trimethylsilylmethyl)amine 1 with N-methylmaleimide 2a gave a mixture of two isomeric [3+2] cycloadducts 3a and 3a', while



Scheme 1.

Table 1. The reactions of 1 with 2a and 2b under various conditions

Entry	Reaction[a]	Reaction conditions				Product[d]	Recovered		Polymer
		Solvent[b]	Additive[c]	Temp	Time/h	3+3'	1	2	of 2
1	1 + 2a	distil. HMPA	CsF	R.T.	24	-	100	-	100
2		distil. HMPA		R.T.	24	-	100	-	100
3		comm. HMPA		R.T.	24	60	40	-	40
4		distil. HMPA	H_2O	R.T.	24	100	-	-	-
5		distil. THF		R.T.	24	+	100	100	-
6		distil. THF	H_2O	R.T.	24	40	60	60	-
7	1 + 2b	distil. HMPA		R.T.	24	30	70	70	-
8		distil. HMPA		75 °C	24	100	-	-	-
9		distil. HMPA	H_2O	R.T.	24	83	17	17	-
10		distil. HMPA	H_2O	R.T.	24	65	35	35	-
11		distil. HMPA	H_2O	R.T.	2	30	70	70	-
12		distil. HMPA	H_2O-NEt_3	R.T.	2	30	70	70	-
13		distil. HMPA	H_2O-AcOH	R.T.	2	71	29	29	-
14		distil. HMPA	H_2O-AcOH	R.T.	12	100	-	-	-

a) All the reactions were carried out between equivalents of 1 and 2. b) distil. HMPA: Predried HMPA (on molecular sieves 5A) was distilled twice over CaH_2 under nitrogen. distil. THF: Sodium-dried THF was distilled over $LiAlH_4$ under nitrogen. c) Each an equivalent of H_2O, NEt_3, and AcOH was used except for entry 10 where five equivalents of water was employed. d) By ^{1}H-NMR spectra of crude reaction mixtures.

it was found that this reaction was extremely affected by reaction conditions (Scheme 1 and Table 1). The reaction in very dry hexamethylphosphoric triamide[4] (HMPA) resulted in a quantitative polymerization of maleimide 2a and the imine 1 was recovered unchanged both in the presence and absence of cesium fluoride as a silylophile. However in commercial grade of HMPA, a moderate yield of the cycloadducts 3a and 3a' was obtained. Surprisingly the presence of an equivalent of water inhibited the polymerization and gave the cycloadducts in a quantitative yield (entry 4 in Table 1). In distilled tetrahydrofuran (THF), both the starting materials were recovered, showing that HMPA was concerned with the desilylation.

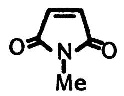
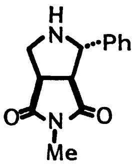
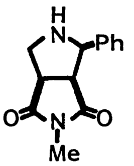
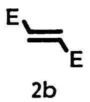
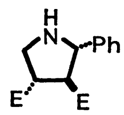
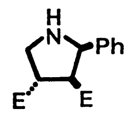
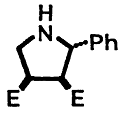
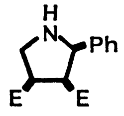
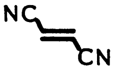
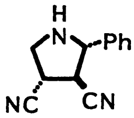
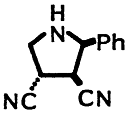
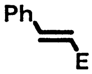
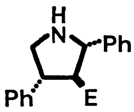
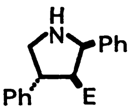
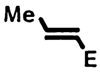
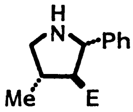
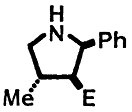
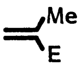
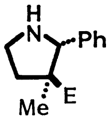
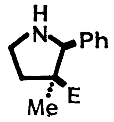
The structures of cycloadducts were confirmed on the basis of spectral data as well as elemental analysis.[5] The isomer 3a with a small J_{2-3} (2.0 Hz) is trans and the other 3a' with a large J_{2-3} (8.0 Hz) cis (Table 2).

Compared with the imide 2a, dimethyl fumarate 2b is rather sluggish in polymerization under similar conditions. Thus the reaction with 1 in dry HMPA afforded the cycloadduct mixture 3b and 3b'. In this case also, water was effective (entries 9 and 10). Although triethylamine did not affect the reaction at all, the use of water-acetic acid mixture gave satisfied results (entries 11 to 13).

As a result, the reactions of 1 with several other olefinic dipolarophiles 2 were carried out in dry HMPA in the presence of each equivalent of water and acetic acid, since at least water is essential to avoid the polymerization of 2. All the results obtained were shown in Table 2.

It is clear that this reaction is highly stereospecific but at the same time awfully nonstereoselective6) from the facts that each two stereoisomeric [3+2] cycloadducts 3b, 3b' and 3c, 3c' are formed in the reactions with 2b and dimethyl

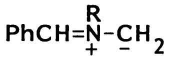
Table 2. Reactions of 1 with Olefinic dipolarophiles in the presence of water-acetic acid a)

Olefins	Products	Yield/% (3/3')b)	^{1}H-NMR spectra (δ ppm, Hz)					
				3-E	4-E	2-CH	J_{2-3}	others
 2a	 3a  3a'	100 (2/1)	3a 3a'	- -	- -	4.60^{d} 4.32^{d}	2.0 8.0	2.98^{s} (N-Me) 2.85^{s} (N-Me)
 2b	 3b  3b'	100 (1/1)	3b 3b'	3.63^{s} 3.15^{s}	3.70^{s} 3.70^{s}	4.50^{d} 4.27^{d}	8.0 7.0	
 2c	 3c  3c'	100 (7/3)	3c 3c'	3.62^{s} 3.20^{s}	3.63^{s} 3.63^{s}	4.59^{d} 4.39^{d}	6.0 6.0	
 2d	 3d  3d'	80 (5/7)	3d 3d'	- -	- -	4.46^{d} 4.25^{d}	7.0 9.0	
 2e	 3e  3e'	72 (1/3)	3e 3e'	3.55^{s} 3.11^{s}	- -	4.55^{d} 4.70^{d}	9.0 9.0	
 2f	 3f  3f'	65 (1/2)	3f 3f'	3.61^{s} 3.16^{s}	- -	4.44^{d} 4.46^{d}	8.0 8.0	1.10^{d} (4-Me) 1.13^{d} (4-Me)
 2g	 3g  3g'	75 (3/4)	3g 3g'	3.66^{s} 3.17^{s}	- -	4.55^{s} 3.84^{s}	- -	0.84^{s} (3-Me) 1.37^{s} (3-Me)

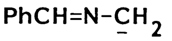
a) All the reactions were carried out by using each equivalent of 1, 2, water, and acetic acid in distilled HMPA at room temperature for 12 h. b) The ratios were based on the ^{1}H-NMR spectra of crude reaction mixtures.

maleate 2c, respectively, and that these four are different each other. The structural assignment was based on the downfield shift of 2-H cis to the 3-ester group as well as the upfield shift of 3-ester methyl cis to the 2-phenyl group.7) This cycloaddition reaction is also highly regioselective: the reactions of 1 with such unsymmetrically substituted olefins as methyl cinnamate 2e, crotonate 2f, and methacrylate 2g yielded the stereoisomeric mixtures of single regioisomers 3e+3e', 3f+3f', and 3g+3g', respectively.

Two types of 1,3-dipoles A and B might be possible for the active species involved in the above cycloadditions, while another species C is omitted on the basis of their different chemical properties.8) A is a new species that corresponds to a tautomer of imine 1.9) B has been proposed in the reaction of 1 with a silyl triflate.1b) So far no informations are available to know the actual species. We believe that the origin of high regioselectivity of the above reactions, especially of the orientation of products, may be an important clue for the determination of the involved intermediate.


$\mathrm{PhCH{=}\overset{R}{\underset{+}{N}}{-}\underset{-}{C}H_2}$

A: R=H; B: R=TMS


$\mathrm{PhCH{=}N{-}\underset{-}{C}H_2}$

C

References

1) a) K. Achiwa and M. Sekiya, Chem. Lett., 1981, 1213; b) K. Achiwa and M. Sekiya, Tetrahedron Lett., 23, 2589 (1982); c) T. Livinghouse and R. Smith, J. Chem. Soc., Chem. Commun., 1983, 210; d) R. Smith and T. Livinghouse, J. Org. Chem., 48, 1554 (1983); e) K. Achiwa, T. Motoyama, and M. Sekiya, Chem. Pharm. Bull., 31, 3939 (1983).

2) E. Vedejes and G. R. Martinez, J. Am. Chem. Soc., 101, 6452 (1979) and 102, 7993 (1980); Y. Terao, N. Imai, K. Achiwa, and M. Sekiya, Chem. Pharm. Bull., 30, 3167 (1982); A. Padwa and Y.-Y. Chen, Tetrahedron Lett., 24, 3447 (1983); A. Padwa, G. Hoffmann, and M. Tomas, ibid., 24, 4303 (1983); O. Tsuge, S. Kanemasa, S. Kuraoka, and S. Takenaka, Chem. Lett., 1984, 279 and 281; O. Tsuge, S. Kanemasa, and S. Kuraoka, submitted for publication.

3) O. Tsuge, S. Kanemasa, and K. Matsuda, J. Org. Chem., 49, xxx (1984).

4) Dry HMPA was obtained by repeated distillation of predried HMPA (on molecular sieves 5A) over calcium hydride under nitrogen.

5) It was unsuccessful to separate one isomer from the other, however the mixture gave satisfactory spectral data and elemental analysis. Other isomeric mixtures 3 and 3' were also treated in the same way.

6) This low stereoselectivity is in a surprising contrast to the high endo selectivity of stabilized azomethine ylides (O. Tsuge, S. Kanemasa, and S. Takenaka, Heterocycles, 20, 1907 (1983) and references cited therein).

7) The structures of 3b and 3b' were confirmed by the comparison of the ^{1}H-NMR spectrum with the reported one (Ref. 1b).

8) The anion C, generated by the desilylation of 1 in dry HMPA, readily cycloadds to stilbene and reacts with 2b, in the presence of water, to give a Michael adduct. The results will be soon published.

9) An imine-azomethine ylide tautomerism is known. As some recent reports: R. Grigg, L. D. Basanagoudar, D. A. Kennedy, J. F. Malone, and S. Thianpatanagul, Tetrahedron Lett., 27, 2803 (1982); O. Tsuge and K. Ueno, Heterocycles, 20, 2133 (1983); R. Grigg, H. Q. N. Gunaratne, and J. Kemp, Tetrahedron Lett., 25, 99 (1984).

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