Tetrahedron. Vol. 34, pp. 453 to 456. Pergamon Press 1978. Printed in Great Britain

REACTIONS OF N,N′-THIOCARBONYL DIIMIDAZOLE WITH 1,3-DIPOLAR AGENTS

THE SYNTHESIS OF 5-SUBSTITUTED-2-(1-IMIDAZOLYL)-1,3,4-THIADIAZOLES AND 5-(1-IMIDAZOLYL)-1,2,3,4-THIATRIAZOLE

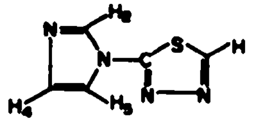
A. Martvoň,* L. Floch and S. Sekretár
Institute of Organic Chemistry, Slovak Technical University, 880 37 Bratislava, Czechoslovakia

(*Received in the UK 4 July 1977; Accepted for publication 16 August 1977*)

Abstract—By the reaction of N,N′-thiocarbonyl diimidazole with diazomethane, diazoacetic ethylester, phenyl diazoketone and 4-nitrophenyl diazomethyl ketone catalysed by tertiary amines, 5-substituted 2-(1-imidazolyl)-1,3,4-thiadiazoles were prepared. by the action of N,N′-thiocarbonyl diimidazole with azoimide, trimethylsilyl azide and thiophosgene 5-(1-imidazolyl)-1,2,3,4-thiatriazole was synthesised. The structure of compounds prepared was proved by ^{1}H NMR and mass spectrometry.

It is known that in view of the possibility of thione-thiol tautomerism and the existence of several resonance structures of diazomethane the reaction of thioketones with diazomethane can proceed in several ways.[1] Since N,N′-thiocarbonyl diimidazole does not contain an enolic hydrogen only the addition of diazomethane to its thiocarbonyl group takes place. According to Schönberg *et al.*[2] the formation of 1,3-dithiocyclopentanones could be anticipated. Also, it is known that sterically hindered phenyl thioketones react with diazomethane to give compounds containing an unstable thioirene ring decomposing into disubstituted ethylene derivatives and sulphur.[2,3] However, our experiments showed that the product of the reaction of thiocarbonyldiimidazole with diazomethane was found to be 2 - (1 - imidazolyl) - 1,3,4 - thiadiazole, which explains that diazomethane reacts in the resonance structure, $\overset{+}{C}H_2{-}N{=}\overset{\ominus}{N}$. If diazomethane reacted in the structure, $\overset{\ominus}{C}H_2{-}N{=}\overset{\oplus}{N}$, then the product should be 2-(imidazolyl)-1,2,3-thiadiazole (Scheme 1), its presence, however, was not observed. Proof of the 1,3,4-thiadiazole skeleton was based on ^{1}H NMR and mass spectrometry.

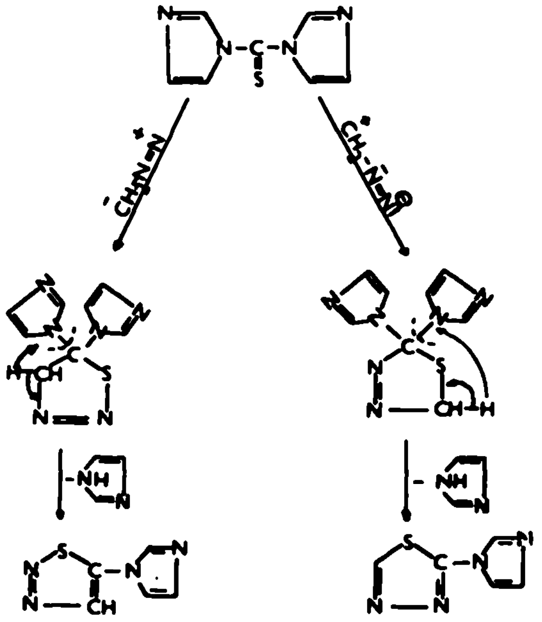
The ^{1}H NMR spectrum of unsubstituted 2 - (1 - imidazolyl) - 1,3,4 - thiadiazole shows the following signals (δ, ppm)



H −8.96 s
H_2 −8.15
H_4 −7.18
H_5 −7.50 d
$J_{2,4}$ − 0.7 Hz, $J_{2,5}$ − 1.5 Hz
$J_{4,5}$ − 1.6 Hz

Chemical shifts and coupling constants of protons of the thiadiazole and imidazole ring was similar to other derivatives studied. The high chemical shift of the thiadiazole proton is characteristic of 1,3,4-thiadiazoles.

Mass spectra provided further evidence that the compounds prepared have a 1,3,4-thiadiazole skeleton. Thus, the mass spectrum of 1 (Fig. 1) does not contain a peak corresponding to the loss of nitrogen (M–N$_2$) which is characteristic of all 1,2,3-thiadiazoles.[3,4] However, a peak of M–HCN is observed which can be formed by fragmentation either of 1,3,4-thiadiazole or imidazole ring. by a comparison of mass spectra of 1 and 7 (Figs. 1 and 2) one can conclude that HCN is a fragment of the thiadiazole ring. The course of the reaction as well as mass spectra of other compounds studied (2–6) supported this conclusion. The reaction of thiocarbonyl diimidazole with diazomethane proceeds rapidly, but if other diazo compounds were used, the reaction needed to be catalysed with triethylamine. Solvents such as ether and tetrahydrofuran solvate the additional product and therefore inhibit the cleavage of imidazole whereby the course of the reaction is influenced. In our experiments benzene and toluene appeared to be the most suitable solvents.



Scheme 1.

If thiocarbonyl diimidazole was treated with azoimide or trimethylsilyl azide, 5 - (1 - imidazolyl) - 1,2,3,4 - thiatriazole was formed (Scheme 2). The course of the reaction differs from that of the reaction of thioketones with azoimide by which azomethines, nitrogen and sulphur were produced.[5] In our case the formation of

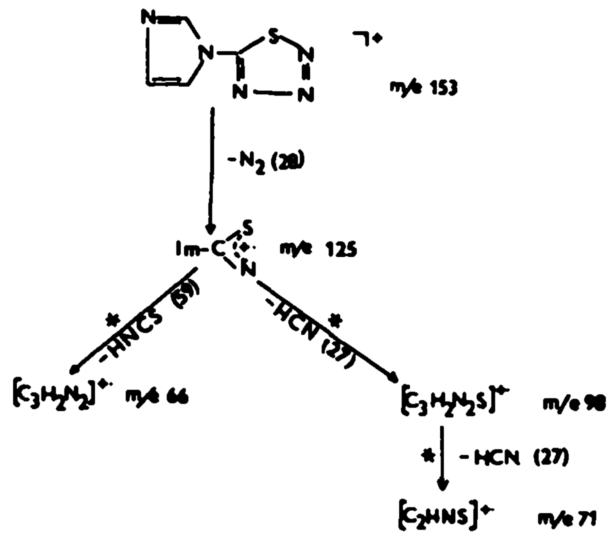


Fig. 1.

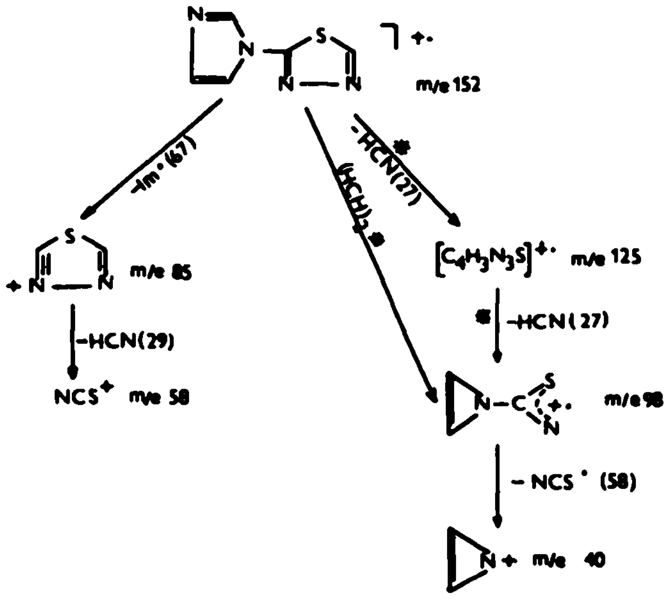
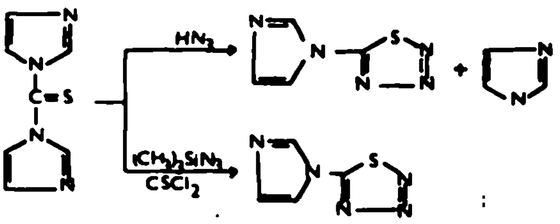


Fig. 2.

Table 1. A survey of compounds prepared

Compound No.	Formula (M.v.)	M.p. °C (Yield)	Calc./Found C	H	N
1	$C_5H_4N_4S$	118–119	42.85	3.95	24.98
	(152.18)	(51)	42.90	3.62	25.24
2	$C_8H_8N_4O_2S$	124–125	39.46	2.65	36.82
	(224.24)	(74)	39.80	2.66	36.52
3	$C_{12}H_8N_4OS$	156–157	56.38	3.46	21.62
	(256.28)	(45)	56.55	3.08	21.77
4	$C_{12}H_7N_5O_3S$	241–242	47.86	2.41	23.24
	(301.3)	(30)	48.61	2.42	23.29
5	$C_{10}H_6N_4O_2S$	171–172	48.77	2.45	22.75
	(246.25)	(45)	48.99	2.55	22.75
6	$C_{10}H_6N_4OS_2$	170–171	45.79	2.31	21.36
	(262.31)	(51.1)	45.54	2.44	21.05
7	$C_4H_3N_5S$	126–127	31.37	1.97	45.75
	(153)	(99)	31.64	1.94	45.35

azomethines was not observed, the reaction product being exclusively thiatriazole (7). According to our procedures we obtained 5 - (1 - imidazolyl) - 1,2,3 - thiatriazole in good yield: by using azoimide (method A, 42%) and trimethylsilyl azide (method B, 55%), respectively. In the case of the thiocarbonyl diimidazole with trimethylsilyl azide and thiophosgene (method C) the yield of 7 was quantitative.



Scheme 2.

Table 2. UV, IR and mass spectra data of compound prepared

	UV	IR [cm^{-1}]			Mass
Compound No.	λ_{max}[nm] (log)	ν(skeleton)	ν(C=O)	ν(CH)	*m/e* [%]
1	257 (3.96)	1514 1310 1055	—	3135 3040 3010	152(100), 125(59), 98(13), 85(13), 71(97), 58(11), 52(23), 40(24)
2	278 (4.06)	1503 1312 1099	1754 1720	3138 3050 3010	224(100), 197(9), 179(10), 169(13), 152(52), 111(11), 94(13), 93(67), 84(10), 71(21), 68(18), 59(14), 12(18), 45(11), 40(20)
3	300 (4.32)	1501 1312 1100	1656	3130 3040 3010	256(38), 163(25), 136(45), 135(13), 105(100), 77(80), 51(26)
4	278 (4.24) 307 (4.22)	1498 1320 1040	1665	3135 3040 3010	301(100), 208(20), 181(71), 151(11), 150(98), 120(20), 104(55), 98(14), 92(22), 76(40), 75(22), 52(11), 50(20)
5	325 (3.59)	1504 1361 1099	1647	3130 3040 3010	262(46), 169(3), 142(9), 141(9), 111(100), 83(11), 39(27)
6	329 (3.51)	1499 1312 1100	1640	3132 3040 3010	246(60), 125(26), 95(100), 67(4), 39(26)
7	245 (3.92) 271 (3.83)	1505 1310 1100	—	3135 3050	153(95), 98(83), 93(36), 86(26), 79(52), 73(13), 71(76), 68(11), 67(15), 66(50), 58(29), 53(19), 52(62), 51(13), 49(19), 45(31), 44(10), 41(24), 40(100), 39(33), 38(13), 33(12), 31(14), 26(25)

EXPERIMENTAL

IR spectra were recorded with a Zeiss UR 20 instrument for chloroform solns. The wavenumber calibration was checked against the spectrum of polystyrene. Wavenumber measurements were believed to be accurate to ±1 cm^{-1}. UV spectra were recorded in MeOH with a Zeiss Specord UV VIS spectrophotometer. Mass spectra were run on a AEI MS 902 S spectrometer at 70 eV, ion chamber temp. 60–150°.

^{1}H NMR spectra were recorded in $CDCl_3$ on a Tesla BS 487 C with hexamethyl disiloxane as an internal standard.

Preparation of 2 - (*imidazolyl*) - 1,3,4 - *thiadiazole* (**1**). N,N'-thiocarbonyldiimidazole (1.78 g, 0.01 mole) was dissolved by heating in absolute toluene (15 ml) and after cooling an equimolar amount of an ethereal soln of diazomethane and several drops of triethylamine were added. After 1 hr stirring at 40° a white ppt had separated. The crude product was chromatographed on silica gel eluted with $CHCl_3$:acetone (10:1) affording white crystals, 0.77 g (51%) of **1**.

Preparation of 5 - *carboethoxy* - 2 - (1 - *imidazolyl*) - 1,3,4 - *thiadiazole* (**2**). N,N'-thiocarbonyldiimidazole (1.78 g, 0.01 mole) was dissolved by heating in absolute toluene (15 ml) and diazoacetic ethyl ester was added. After adding several drops of triethylamine the mixture was stirred for 3 hr at 50°. After standing several hrs, a solid compound (needles) were filtered off and chromatographed on silica gel and eluted with $CHCl_3$:acetone (10:1) affording 1.65 g (74%) of **2**. Compounds **5** and **6** were prepared in a similar way.

Preparation of 5 - *benzoyl* - 2 - (1-*imidazolyl*) - 1,3,4 - *thiadiazole*. N,N'-thiocarbonyl diimidazole (1.78 g, 0.01 mole) was dissolved by heating in absolute toluene (15 ml) and a soln of phenyl diazomethyl ketone (1.47 g, 0.01 mole) in absolute benzene (10 ml) and triethylamine (0.5 ml) was added. The mixture was stirred for 6 hr at 80°. After removal of the solvents, the crude product was chromatographed on silica gel eluted with $CHCl_3$:acetone (10:1) affording 1.14 g (45%) of a white crystalline compound (3).

Preparation of 5 - (4 - *nitrobenzoyl*) - 2 - (*1 - imidazolyl*) - 1,3,4 *thiadiazole* (4). N,N'-thiocarbonyl diimidazole (1.78 g, 0.01 mole) was dissolved in absolute *p*-xylene by heating (15 ml) and a soln of 4-nitrophenyl diazomethyl ketone (1.91 g, 0.01 mole) in absolute toluene (10 ml) and 1 ml of triethylamine was added. The mixture was stirred for 10 hr at 70–80°. After cooling the mixture was allowed to stand overnight. The product (brown needles) were filtered off and crystallized from nitromethane (yield 0.9 g, 30%).

Preparation of 5 - (1 - *imidazolyl*) - 1,2,3,4 - *thiatriazole* (7). *Method* A. N,N'-thiocarbonyl diimidazole (1.78 g, 0.01 mole) was dissolved in absolute toluene (10 ml) by heating and a soln of azoimide (0.04 mole) in toluene (10 ml) was added. The reaction proceeded immediately. After 1 hr, a white solid was filtered off and purified by the SiO_2 column chromatography with $CHCl_3$ as eluent.

Method B. N,N'-thiocarbonyl diimidazole (0.53 g, 0.003 mole) was dissolved in absolute toluene (5 ml) by heating and trimethylsilyl azide (0.4 ml, 0.003 mole) was added with stirring. The reaction started immediately and the yellow soln was decolourized. After 10 min, white crystals were filtered off. After cooling, absolute petroleum ether (5 ml) was added and the crystal line product filtered and recrystallized from abs. EtOH (yield 55%).

Method C. N,N'-thiocarbonyl diimidazole (1.78 g, 0.01 mole) was dissolved in absolute toluene (20 ml) by heating and under intense stirring a soln of trimethylsilyl azide (2.63 ml, 0.02 mole) in toluene (5 ml) was added. After decolourisation, a solution of thiophosgene (0.77 ml, 0.01 mole) in toluene (5 ml) was added at such a rate that the temp. was maintained at 40–50°. The mixture became yellow due to N,N'-thiocarbonyl diimidazole which was formed from the thiophosgene and imidazole liberated by the reaction (Scheme 3). After 1 hr the mixture was decolourised and white crystals filtered off. Petroleum ether (10 ml) was added, the crystals filtered off and recrystallized from a mixture of EtOH and THF (2:1) affording 3 g (99%) of 7. In the mother liquor only the presence of trimethylsilyl chloride was detected by GLC.

REFERENCES

[1] A. Padiva, *Angew. Chem.* 88, 131 (1976).
[2] A. Schönberg, B. König and E. Signer, *Chem. Ber.* 100, 767 (1967).
[3] J. M. Beiner, D. Lecadet, D. Paquer, A. Thuillier and J. Wialle, *Bull. Soc. Chim. Fr.* 1979 (1973).
[4] S. Holm and A. Sennig, *Tetrahedron Letters* 2389 (1973).
[5] K. P. Zeller, H. Meier and E. Müller, *Tetrahedron* 28, 1353 (1972).
[6] B. S. Millard and D. L. Pain, *J. Chem. Soc.* C, 2042 (1970).
[7] J. H. Bowie, R. G. Cooks, J. O. Lawesson and P. S. Schroll, *Austral. J. Chem.* 20, 1613 (1967).
[8] A. Schönberg and W. Urban, *J. Chem. Soc.* 530 (1937).