A New Class of Non-classical Azapentalenes. Synthesis and C-13/N-15 NMR Characterization of 2*H*-Imidazo[1,5-*d*]tetrazoles

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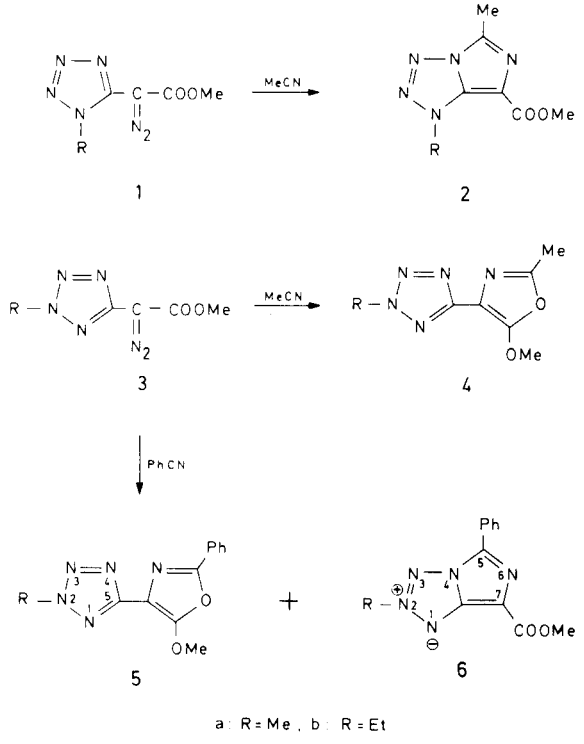
Received November 28, 1988

The title compounds **6** (as well as the oxazoles **5**) were obtained by thermolysis of 2-alkyl-5-(methoxycarbonyldiazomethyl)tetrazoles **3** in benzonitrile. They were fully characterized by ^1H, ^{13}C and ^{15}N nmr spectroscopy.

J. Heterocyclic Chem., **26**, 729 (1989).

Recently, we have reported on the different thermal behaviour of 1-alkyl and 2-alkyl-5-(methoxycarbonyldiazomethyl)tetrazoles **1** and **3** in acetonitrile [1]. Whereas the former yield 1-alkylimidazo[1,5-*d*]tetrazoles **2**, the latter furnish oxazole derivatives **4** (Scheme I). In continuation of this work, we have found that 2-alkyl-5-(methoxycarbonyldiazomethyl)tetrazoles **3a,b** thermolyze in benzonitrile to give the expected oxazoles **5a,b** in addition to the 2-alkylimidazo[1,5-*d*]tetrazoles **6a,b** which are the first representatives of this new class of heteropentalene mesomeric betaines [2].

Scheme I



1 2 3 4 5 6

a: R = Me, b: R = Et

Thus, when **3a** was refluxed in benzonitrile for 5 days, the ^1H nmr spectrum of the crude reaction mixture indicated the presence of two products with *N*-methyl absorptions at δ 4.42 and 4.62 in a ratio of 3.5:1; they were isolated in 25% (mp 128°) and 15% (mp 184°) yields respectively. Compound **3b** also decomposed in benzonitrile to give two products with melting points 96° (26%) and 165° (23%).

The structures of the lower melting compounds correspond to **5a,b** on the basis of the ^{13}C nmr data discussed previously [1] (see Experimental), and they are now confirmed by the ^{15}N nmr spectra (Table I). The assignment of the resonances was made by applying the following rules: (i) pyrrole-type nitrogen atoms absorb at higher field than pyridine-type nitrogen atoms; (ii) nitrogen atoms are more deshielded when adjacent to nitrogen than when adjacent to carbon; and (iii) for *N*-alkylazoles nitrogen atoms two or three bonds away from the alkyl protons can be detected selectively by the DEPT pulse sequence [3]. Thus, three nitrogen atoms of **5a,b** and four nitrogens of **4a** are detectable by this technique. The results, listed in Table I, agree with the published values for tetrazoles and oxazoles [4].

Table I

^{15}N NMR Data [a] for **4a** and **5a,b** in Deuteriochloroform

Compound	Tetrazole				Oxazole
	N-1	N-2	N-3	N-4	N-3
4a	295.2	272.5	378.7	323.1 [b]	247.4
5a	295.3	272.8	378.9	323.4 [b]	245.3 [b]
5b	293.3	286.2	377.1	– [b]	– [b]

[a] δ Values from liquid ammonia quoted, using nitromethane as external reference. [b] Not observed with the DEPT pulse sequence.

In order to elucidate the structures of the higher melting isomers, we have compared their ^{13}C nmr spectra with those of **7a,b**, obtained by heating **1a,b** in benzonitrile (see Table II). The downfield absorptions of the R-substituents at δ 43.1 and 52.4 indicate the mesomeric structures **6a,b**. Indeed, for the alternative structures **8a,b**, which would result from a different mode of cycloaddition, the *N*-methyl and *N*-methylene carbons would be expected to resonate at about δ 36 and δ 45 respectively, analogous to **7a,b** [5]. Furthermore, both series, **6a,b** and **7a,b**, exhibit two multiplet absorptions at δ 7.3-8.3 for the phenyl substituent in the ^1H nmr spectra, due to coplanarity with the heterocycle. For **8a,b**, steric hindrance between the phenyl and R substituents would force the phenyl ring to

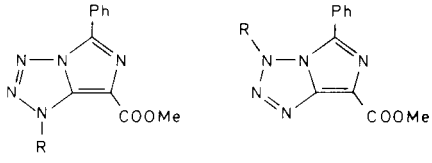
rotate out of the plane of the heterocycle, resulting in a singlet aromatic resonance.

Table II

^{13}C NMR Data for **6a,b** and **7a,b** in Deuteriochloroform [a]

Compound	R	C-5	C-7	C-7a
6a	43.1	127.0	105.4	150.4
6b	14.5, 52.4	126.8	105.2	150.4
7a	36.5	128.8	101.1	139.4
7b	15.4, 45.6	129.2	101.0	138.8

[a] For all the compounds the ester carbons absorb at δ 51.8 and 162, and the phenyl carbons resonate at δ 127.2-127.8 (C_i), 124.9-125.7 (C_o), 128.6-128.9 (C_m) and 128.4-129.3 (C_p).



7 8

a : R = Me , b : R = Et

We have also analyzed the ^{15}N nmr spectra of the imidazo[1,5-*d*]tetrazoles which fully support their structures (Table III). The signals were attributed by comparison with known values for imidazoles and tetrazoles [4], taking into account the following empirical increments in going from a monocyclic to a bicyclic azole [6]: (i) the ^{15}N atom is shifted downfield by 30-40 ppm when it is present at a ring junction; (ii) the ^{15}N atoms in the α-positions to a junction are shielded by 15-25 ppm; and (iii) the ^{15}N atoms in the β-positions to a junction are deshielded by 5-15 ppm. Furthermore, the non-detectable nitrogen atoms in the DEPT measurements are evidently N-3 for **2a**, N-3, N-4 and N-6 for **7a**, and N-4 and N-6 for **6a,b**. An inspection of Table III shows that only one nitrogen resonance of **6** is strongly deshielded when the methyl substituent is replaced by ethyl ($\Delta\delta$ = 14.8 ppm); this corresponds thus to N-2. The same phenomenon is observed for **5a,b** (Table I). The other two resonances of **6** in the DEPT pulse sequence are only slightly affected by the N-2 substituent (and in the same sense as **5a,b**) and the lowest field absorption (δ 311) is attributed to N-3 since this atom is surrounded by two nitrogen atoms instead of one for N-1. Finally, the N-4 and N-6 nitrogen resonances are assigned in concordance with the shift increments given above.

Table III

^{15}N NMR Data [a] of the Imidazo[1,5-*d*]tetrazoles in Deuteriochloroform

Compound	N-1	N-2	N-3	N-4	N-6
2a	186.0	375.6	322.8 [b]	259.5	271.8
7a	186.2	375.4	325.4 [b]	255.7 [b]	269.3 [b]
6a	280.8	276.4	311.3	242.5 [b]	277.3 [b]
6b	279.4	291.2	310.8	– [b]	– [b]

[a] δ Values from liquid ammonia quoted, using nitromethane as external reference. [b] Not observed with the DEPT pulse sequence.

EXPERIMENTAL

Spectra.

The ^{1}H and ^{13}C nmr spectra were recorded on a Bruker WM (FT) spectrometer at 250 and 62.9 MHz, respectively, using a 5 mm dual probe. The chemical shifts are reported in ppm relative to TMS as an internal reference.

Natural abundance ^{15}N nmr spectra were recorded on a Bruker WM-250 spectrometer, operating at 25.35 MHz, and equipped with a selective ^{15}N 10 mm probe. The chemical shifts were determined with respect to external nitromethane contained in a 4 mm capillary held centrally in the sample tube. This reference was given a δ value of 380.2 ppm, thus converting the N chemical shifts to the liquid ammonia shielding scale. The spectra of the products were recorded in deuteriochloroform using 0.1 to 0.5 molar solutions, depending on the solubility.

The DEPT pulse sequence [3], based on polarization transfer through long-range coupling ($^2J_{N\text{-}H}$ and $^3J_{N\text{-}H}$), was used to detect the nitrogens two or three bonds away from the methyl and ethyl protons. To allow the detection of all the nitrogens, chromium-(III) acetylacetonate was added as a relaxation reagent, and the spectra were recorded by the inverse gated heteronuclear decoupling technique.

Typical acquisition parameters for the DEPT pulse sequence are: spectral width 8 kHz, pulse angle 45°, delay time 0.15 s and number of scans 1000 (for 0.5 *M* solutions) to 10000 (for 0.1 *M* solutions), and for the inverse gated heteronuclear decoupling: spectral width 8 kHz, pulse angle 70°, relaxation delay 5 s and number of scans 3000 to 30000.

Thermolysis of 2-Alkyl-5-(methoxycarbonyldiazomethyl)tetrazoles **3a,b** in Benzonitrile.

General Procedure.

Compound **3** (1 g) was heated in benzonitrile (200 ml) at 70-80° (5 days for **3a** and 5 weeks for **3b**). After removal of the solvent, the residue was dissolved in chloroform and treated with ether to give a precipitate of **6**, which was filtered off and crystallized from acetone. From the filtrate, **5** was isolated by column chromatography on silica gel (eluent chloroform/hexane 70:30 for **5a** and ether/hexane 70:30 for **5b**) and crystallized from ether.

5-(5-Methoxy-2-phenyloxazol-4-yl)-2-methyl-2*H*-tetrazole (**5a**).

This compound was obtained in 25% yield, mp 128°; ir (potassium bromide): 1660 cm^{-1} (s); ^{1}H nmr (deuteriochloroform): δ 4.30 (s, 3H, OCH_3), 4.42 (s, 3H, NCH_3), 7.4-8.1 (two m, 5H, Ph); ^{13}C nmr (deuteriochloroform): δ 39.4 (NCH_3), 60.3 (OCH_3), 126.6, 125.7, 128.6 and 130.1 (Ph C_i, C_o, C_m and C_p), 152.5, 105.6 and 157.2 (oxazole C-2, C-4 and C-5), 158.9 (tetrazole C atom).

Anal. Calcd. for $C_{12}H_{11}N_5O_2$ (mol wt 257): C, 56.03; H, 4.31. Found: C, 55.94; H, 4.27.

7-Methoxycarbonyl-2-methyl-5-phenyl-2*H*-imidazo[1,5-*d*]tetrazole (**6a**).

This compound was obtained in 15% yield, mp 184°; ir (potassium bromide): 1720 cm^{-1} (s); ^1H nmr (deuteriochloroform): δ 4.01 (s, 3H, OCH_3), 4.62 (s, 3H, NCH_3), 7.3-8.3 (two m, 5H, Ph).

Anal. Calcd. for $C_{12}H_{11}N_5O_2$ (mol wt 257): C, 56.03; H, 4.31. Found: C, 55.88; H, 4.31.

2-Ethyl-5-(5-methoxy-2-phenyloxazol-4-yl)-2*H*-tetrazole (**5b**).

This compound was obtained in 26% yield, mp 96°; ir (potassium bromide): 1665 cm^{-1} (s); ^1H nmr (deuteriochloroform): δ 1.70 (t, 3H, CH_3), 4.30 (s, 3H, OCH_3), 4.75 (q, 2H, CH_2), 7.4-8.1 (two m, 5H, Ph); ^{13}C nmr (deuteriochloroform): δ 14.6 and 48.4 (Et), 60.4 (OCH_3), 126.7, 125.9, 128.6 and 130.1 (Ph C_1, C_o, C_m and C_p), 152.5, 105.9 and 157.3 (oxazole C-2, C-4 and C-5), 158.8 (tetrazole C atom).

Anal. Calcd. for $C_{13}H_{13}N_5O_2$ (mol wt 271): C, 57.56; H, 4.83. Found: C, 57.71; H, 4.80.

2-Ethyl-7-methoxycarbonyl-5-phenyl-2*H*-imidazo[1,5-*d*]tetrazole (**6b**).

This compound was obtained in 23% yield, mp 165°; ir (potassium bromide): 1710 cm^{-1} (s); ^1H nmr (deuteriochloroform): δ 1.88 (t, 3H, CH_3), 4.03 (s, 3H, OCH_3), 4.89 (q, 2H, CH_2), 7.3-8.3 (two m, 5H, Ph).

Anal. Calcd. for $C_{13}H_{13}N_5O_2$ (mol wt 271): C, 57.56; H, 4.83. Found: C, 57.70; H, 4.78.

Thermolysis of 1-Alkyl-5-(methoxycarbonyldiazomethyl)tetrazoles **1a,b** in Benzonitrile.

General Procedure.

A solution of **1** (1 g) in benzonitrile (200 ml) was heated at 70° for 2 weeks. After removal of the solvent, the residue was crystallized from acetone.

7-Methoxycarbonyl-1-methyl-5-phenyl-1*H*-imidazo[1,5-*d*]tetrazole (**7a**).

This compound was obtained in 75% yield, mp 185°; ir (potassium bromide): 1690 cm^{-1} (s); ^1H nmr (deuteriochloroform): δ 3.98 (s, 3H, OCH_3), 4.45 (s, 3H, NCH_3), 7.3-8.3 (two m, 5H, Ph).

Anal. Calcd. for $C_{12}H_{11}N_5O_2$ (mol wt 257): C, 56.03; H, 4.31. Found: C, 56.19; H, 4.30.

1-Ethyl-7-methoxycarbonyl-5-phenyl-1*H*-imidazo[1,5-*d*]tetrazole (**7b**).

This compound was obtained in 62% yield, mp 132°; ir (potassium bromide): 1685 cm^{-1} (s); ^1H nmr (deuteriochloroform): δ 1.65 (t, 3H, CH_3), 3.98 (s, 3H, OCH_3), 4.87 (q, 2H, CH_2), 7.3-8.3 (two m, 5H, Ph).

Anal. Calcd. for $C_{13}H_{13}N_5O_2$ (mol wt 271): C, 57.56; H, 4.83. Found: C, 57.53; H, 4.82.

Acknowledgement.

We thank P. Delbeke for his assistance in recording the nmr spectra. Financial support from the University, the N. F. W. O. and the "Ministerie voor Wetenschapsbeleid" is gratefully acknowledged.

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