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Cycloaddition of Diazomethane to Unsymmetrical Carbodiimides and Mass Spectroscopy Study of 1,5-Disubstituted 1,2,3-Triazoles

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By the reaction of unsymmetrically substituted carbodiimides with diazomethane the corresponding 1,2,3-triazoles have been obtained. The structure of the adducts was elucidated by IR, UV, ^{1}H-NMR and high resolution mass spectrometry.

(Keywords: Cycloaddition; Mechanism; Sigmatropic shift; 1,2,3-Triazoles)

Cycloaddition von Diazomethan an unsymmetrische Carbodiimide und massenspektroskopische Studien an 1,5-disubstituierten 1,2,3-Triazolen

Die Struktur der aus unsymmetrischen Carbodiimiden und Diazomethan gebildeten 1,2,3-Triazolen wurde durch IR-, UV-, ^{1}H-NMR- und Massenspektrometrie aufgeklärt.

Introduction

The utility of the carbodiimide moiety as a precursor to a series of heterocycles has been the subject of several investigations[1]. In general, this heterocumulene has been found to undergoe both 2,3- and 2,2-cycloadditions, and the heterocycles so produced are usually obtained in good yields. In a previous study[2] we have described a preparative method for interesting heterocyclic compounds of type **3** obtained by the reaction of carbodiimides with diazomethane (Scheme 1). At that time we suggested a mechanism for the addition of the diazomethane to the C=N bond and the formation of the triazole ring.

In the present work, we report some results obtained by studying the reaction of unsymmetrically substituted carbodiimides with diazomethane.

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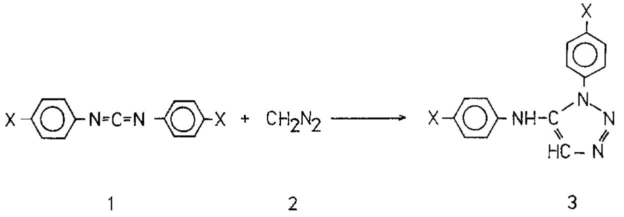
Scheme 1



X = H, $N(CH_3)_2$, CH_3, OCH_3, Cl, Br, $COCH_3$

Results and Discussion

Carbodiimides were prepared by desulphurisation of the disubstituted thioureas with yellow mercuric oxide[3]. Owing to their lability, these compounds were prepared directly before use. Carbodiimide allowed to stand at room temperature with ethereal solution of diazomethane give rise to colourless crystaline products in low yields (Table 1). As can be seen in Scheme 1, symmetrically substituted carbodiimides having two equivalent C=N bonds afford with diazomethane via a 1,3-dipolar cycloaddition reaction a product of unambiguous structure **3**. On the other hand, for mixed aryl and alkyl carbodiimides **4 a–d** and unsymmetric diaryl carbodiimides **4 e–f** two non-equivalent C=N bonds are characteristic. This renders possible a formation of the two alternative cyclic adducts **5** and **6** (Scheme 2).

Table 1. *Physical and analytical data of compounds* **5 a–d**

Product	Reaction time (days)	Yield (%)	Cryst.* solvent	M. p. (°C)	Molecular formula (Mol. Wt.)	Analysis (%) Calc/Found C	H	N
5 a	21	12	a	138-139	$C_{11}H_{14}N_4$ (202.26)	65.32 65.44	6.97 7.02	27.70 27.61
5 b	21	18	a	144-146	$C_{12}H_{16}N_4$ (216.28)	66.64 67.00	7.45 7.66	25.90 26.17
5 c	21	9	a	148-149	$C_{12}H_{16}N_4$ (216.28)	66.64 66.82	7.45 7.67	25.90 25.93
5 d	10	6	b, c	197-198	$C_{14}H_{18}N_4$ (242.32)	69.39 69.59	7.48 7.50	23.12 23.24

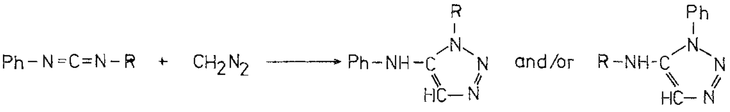
* a = Ether, b = methanol, c = acetone.

Table 2. IR ($CHCl_3$, cm^{-1}) *and UV* (*Et*OH) *data of compounds* **5a–d**

Product	Triazole ring breathing vibrations			Triazole vibrations	ν(C=C) arom.		ν(NH)	λ_{max}, nm (log ε)		
5a	976	1081	1111	1577	1507	1607	3417	213 (3.80)	239 (3.85)	265 (4.03)
5b	981	1083	1112	1576	1504	1603	3415	208 (4.07)	240 (3.81)	265 (4.08)
5c	975	1082	1111	1569	1507	1607	3410	207 (4.06)	238 (3.95)	263 (3.81)
5d	975	1080	1115	1574	1507	1604	3414	207 (4.13)	238 (3.89)	264 (4.09)

Adducts **5** and **6**, being very much alike, cannot be distinguished by means of IR, UV and elemental analysis data. However, mass and ^1H-NMR spectroscopy clearly suggest that carbodiimides **4a-d** afforded with diazomethane cyclic adducts of the structure **5** whilst carbodiimides **4e-f** afforded two products of the structure **5** and **6**.

Scheme 2



4 2 5 6

4a: *R* = *iso-Pr*
4b: *R* = *iso-Bu*
4c: *R* = *tert-Bu*
4d: *R* = C_6H_{11}
4e: *R* = 4-CH_3—C_6H_4
4f: *R* = 4-CH_3O—C_6H_4

The IR spectra of the prepared compounds are consistent with proposed structures **5** and **6** (Table 2). All the 1,5-disubstituted 1,2,3-triazoles exhibit characteristic absorptions in the region of 975-1 115 cm^{-1}, which are attributed to the ring breathing vibrations[4,5]. This observations is in conformity with the reported values for some 1,5-disubstituted 1,2,3-triazoles[6]. With the exception of intense bands in the range of 1,504-1,507 cm^{-1} and 1,603-1,607 cm^{-1} indicating the C=C aromatic stretching vibration, a strong third band at 1,569-1,577 cm^{-1} is regarded as a band due to triazole valence vibrations. The strong peak appearing at 3,410-3,417 cm^{-1} can be ascribed to vibrations of the secondary amino group. Aromatic and alkyl groups give rise to the expected well known absorption characteristics.

In the UV spectra of compounds three characteristic bands in the region of 207-265 nm are observed (Table 3) which are in agreement with reported values[2,5].

The ^1H-NMR spectral data (Table 3) give additional support that the compounds studied have a structure **5** and **6** which is also in accord with

Table 3. ^{1}H-NMR data of **5a**-**d** (δ, *ppm*)

Product	Triazole ring-protons	Phenyl protons	Alkyl and cycloalkyl protons
5a	7.48 (s, 1)	6.65-7.33 (m, 5)	1.54 (d, 3, CH_3) 4.43-4.78 (m, 1, CH)
5b	7.48 (s, 1)	6.73-7.35 (m, 5)	0.89 (d, 6, CH_3) 4.02 (d, 2, CH_2) 1.93-2.55 (sept, 1, CH)
5c	7.48 (s, 1)	6.63-7.30 (m, 5)	1.69 (s, 9, CH_3)
5d	7.48 (s, 1)	6.68-7.36 (m, 5)	0.80-2.18 (m, 10, C_6H_{10}) 4.00-4.48 (m, 1, CH of cyclohexyl)

Table 4. *Composition of some ions in the mass spectrum of compound* **5c**

m/e	Mass		Composition
	Measured	Calculated	
41	41.0398	41.0391	C_3H_5
93	93.0575	93.0578	C_6H_7N
104	104.0498	104.0500	C_7H_6N
117	117.0554	117.0578	C_8H_7N
124	124.0878	124.0875	$C_6H_{10}N_3$
160	160.0751	160.0749	$C_8H_8N_4$

literature data[5]. The triazole ring-proton signals appear as a sharp singlet at δ 7.48. Further, the ^{1}H-NMR spectra show a multiplet in the range δ 6.36-7.36 (phenyl protons) and broad singlet at δ 5.58-6.23 (NH proton) which rapidly disappeared upon addition of deuterium oxide. Other signals in the NMR revealed absorption due to alkyl groups. Spin-spin interactions of methyl-, methylene- and methine-protons with NH one in ^{1}H-NMR spectra of 1-phenyl-5-alkylaminotetrazoles prepared in our laboratory has been observed[7]. In comparison with 1-alkyl-5-anilinotetrazoles chemical shift values of protones of tetrazoles above mentioned are shifted upfield. It is concluded that in the analogous case the resonance of the methylene group of **6b** will be a quartet, while the low field CH_2 proton in **5b** should be a doublet. On the basis of these arguments and results from Table 4 the structure of the cycloadduct prepared from **4b** is consistent with structure **5b**. For the same reason, the structure of **5a** is also confirmed by the presence of the septet of the methine proton.

Mass spectra of synthesised triazoles are illustrated in Fig. 1 in which only peaks with a relative intensity $\geq 2\%$ are given. Primary products of a decomposition of molecular ions results from elimination of corresponding substituents attached to the heterocyclic ring. Only after loss of alkyl remainder a nitrogen molecule is eliminated as described previously[8-10]. Fragmentation of the parent ion of compound **5c** is illustrated in Scheme 3. The alkyl remainder is eliminated in the form of alkene with rearrangement of a hydrogen atom to the triazole ring. The composition of individual ions in

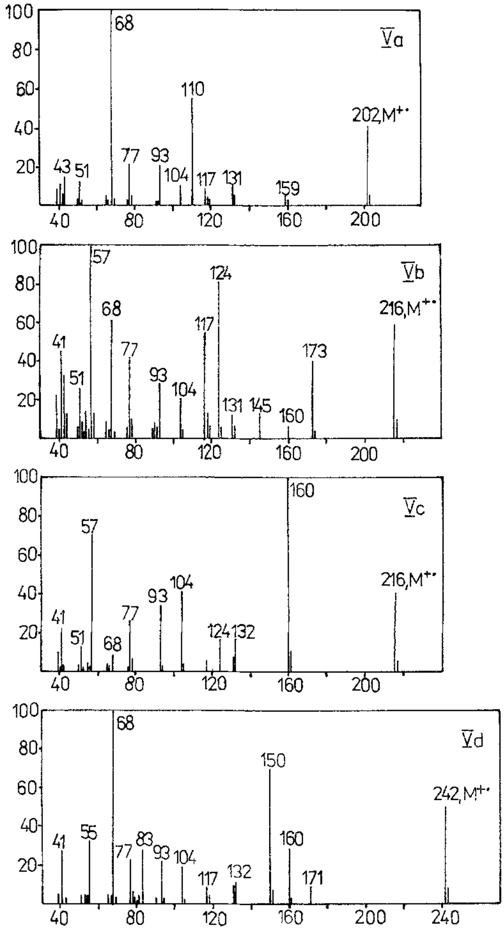


Fig. 1. Mass spectra of 1-isopropyl-5-anilino-1,2,3-triazole (**5 a**), 1-isobutyl-5-anilino-1,2,3-triazole (**5 b**), 1-*tert*-butyl-5-anilino-1,2,3-triazole (**5 c**), and 1-cyclohexyl-5-anilino-1,2,3-triazole (**5 d**)

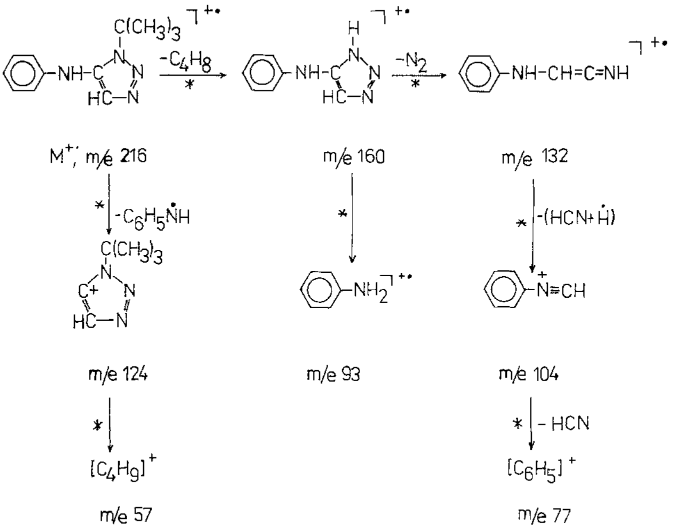
Scheme 3 was derived from the measurement of their exact masses (Table 4) and their formation was confirmed by the detection of metastable ions using a high voltage scan technique[11].

Fragmentation of the molecular ion of compound **5 b** is similar to that of **5 c**. The formation of relatively intense fragment ions at *m*/e 117 and *m*/e 68 is illustrated in Scheme 4.

In the case of compound **5 d** the most intense fragment ions are formed from molecular ion by loss of radical $C_6H_5\dot{N}H$ (*m*/e 150), followed by elimination of a neutral molecule C_6H_{10} (*m*/e 68).

"The aniline ion" with *m*/e 93 (relative intensity 21–35%) is observed in the spectra of all triazoles studied; it is formed by rearrangement of a hydrogen

Scheme 3



Scheme 4

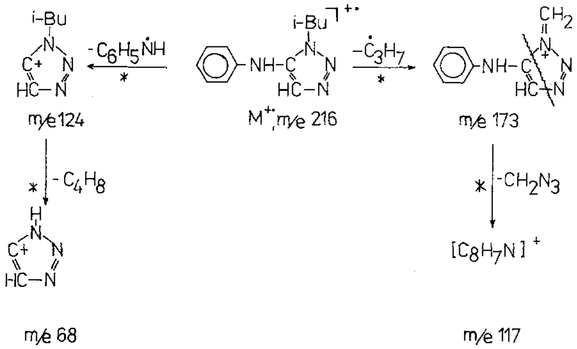


Table 5. *Composition of triazoles determined by* ^{1}H-NMR (*in acetone-d_6*)

Product	δ (ppm) CH$_3$-**5**	CH$_3$-**6**	Isomer ratio **5**:**6** (%)
5e + **6e**	2.41	2.27	72:28
5f + **6f**	3.87	3.73	76:24

atom from the triazole ring to the nitrogen atom of the NH group. This fact was confirmed by the presence of the ion [C_6H_5NHD] in the spectrum of 1-isopropyl-5-anilino-1,2,3-triazole-4-*d*.

In the case of unsymmetrical diaryl carbodiimides **4 e-f** the reaction proceeds substantially faster (10-12 h) as compared with that of above mentioned carbodiimide. By TLC two products were detected and we were unsuccesful in separating these product by usual laboratory methods. However, by ^{1}H-NMR spectroscopy both cycloadducts were determined using the signals of methyl groups (Table 5).

Conclusion

Unsymmetrical carbodiimides contain two concurrent reaction centers and therefore two product can be formed. It follows from the above that in mixed aliphatic-aromatic substituted carbodiimides one of the C=N bonds undergoes exclusively cycloaddition reaction. The attack of diazomethane upon the original carbodiimides takes place across the C=N bond with the more basic nitrogen atom, i.e., that adjacent to the alkyl group. Subsequent 1,3-hydrogen sigmatropic shift yields the final product 1-alkyl-5-anilino-1,2,3-triazole.

On the other hand a distribution of the electron density in the NCN group is not significantly influenced by the nature of the substituent attached to the benzene ring of unsymmetric diaryl-carbodiimides. Therefore, two reaction products are formed by the 1,3-cycloaddition reaction of compounds in question with diazomethane.

Experimental

Melting points were determined with a *Boetius* m.p. apparatus and are uncorrected. IR spectra were taken on a Zeiss UR-20 spectrophotometer. UV spectra were measured on a Zeiss Specord UV-VIS. ^{1}H-NMR were recorded with a Tesla BS 847 C (80 MHz) instrument in $CDCl_3$ using *HMDS* as internal standard. Chemical shifts are expressed in δ (ppm) relative to *TMS*. Mass spectra were measured with an AEI Manchester MS 902 S spectrometer equipped with a direct inlet system at a ionizing electron energy 70 eV, trap current 100 μA at temperature of the ionizing chamber varying between 80 and 130 °C with respect to the volatility of sample. The exact measurements of masses was done by usual technique of the peak matching using of heptacosafluorotributylamine as standard at resolving power 20,000 (10% valley definition).

Solvents and reagents were purified by conventional methods. Carbodiimides **4 a-f**[3] and diazomethane[12] were prepared according to know methods.

General method for the synthesis of 1,5-disubstituted 1,2,3-triazoles

A freshly prepared ethereal solution diazomethane (40 mmol) was added to a solution of freshly prepared carbodiimide (30 mmol) in 15 ml of dry ether and the mixture was allowed to stand at 0 °C. The solid material was removed by filtration and washed with cold ether. Unreacted carbodiimide was the only compound recovered from the filtrate. After two recrystallisations from a suitable solvent the pure product was obtained.

1-isopropyl-5-anilino-1,2,3-triazole-4-d

A 2*N*-CH_3ONa solution prepared by reaction of sodium metal with *Me*OD, was added to a solution of **5a** in *Me*OD and the resulting mixture was allowed to reflux for 6h. The solvent was removed under reduced pressure and the residue was thoroughly extracted with anhydrous diethyl ether. Evaporation to dryness and recrystallisation from absolute acetone left isotopically labelled **5a** containing 70% D in the 4-position of the triazole ring.

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