ALCOHOLYSIS OF 1,2-BIS(1-ISOCYANATO-1-METHYLETHYL)DIAZENE: UNEXPECTED FORMATION OF 5,5-DIMETHYL-1,2,4-TRIAZOLIN-3-ONE[1]

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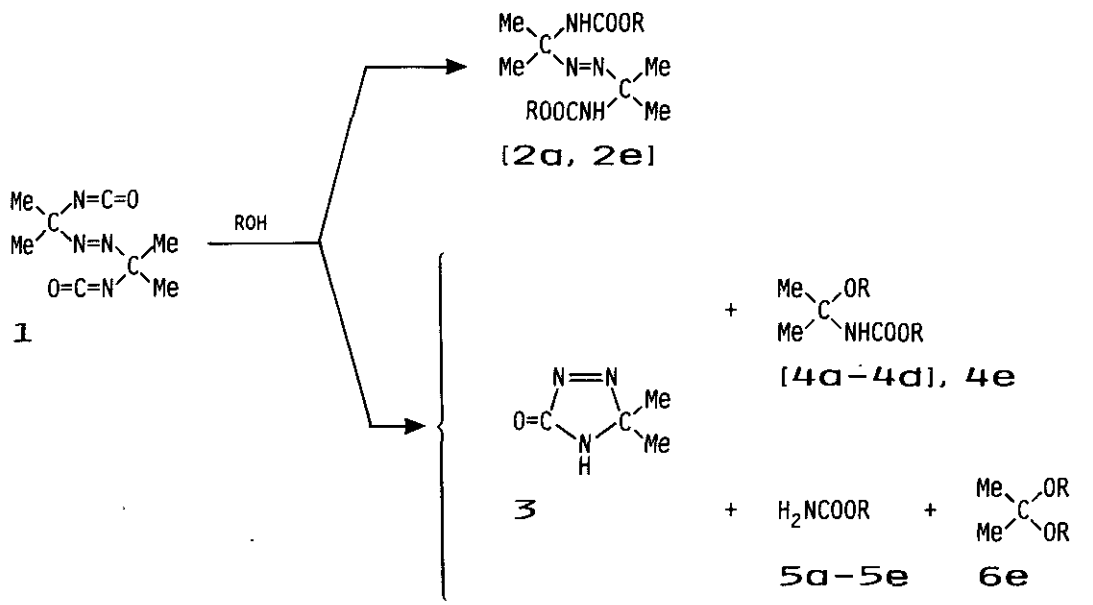
Abstract - From the reaction of the bis(isocyanatoalkyl)diazene **1** with alcohols the expected adducts **2** could not be isolated (though there is spectroscopic evidence of their formation). The main product obtained was the triazolin-3-one **3**, and in addition, several complementing products **4** - **6** were formed.

Like many azo alkane derivatives 1,2-bis(1-isocyanato-1-methylethyl)diazene **1**[2] has aroused some interest as a free radical source[3-5]. Apart from the investigation of the thermal stability[4,5] an attempt has been reported[4] to functionalize the isocyanate groups of **1**: Alcohols were anticipated to add to the isocyanate functions, but notably, from the reaction of **1** with alcohols the expected adducts, the 1,2-bis[2-[2-(alkoxycarbonylamino)]propyl]diazenes **2** could not be isolated, though spectroscopic evidence (without details) has been claimed[4]. Instead, merely the carbamates **4** have been isolated (no yields given)[4], and these compounds have been regarded to be the fragmentation products of the presumed intermediate diazenes **2**. However, no complementing fragment containing the propane moieties or the azo nitrogen atoms of the educt **1** has been found. This lack of stoichiometry led to the reinvestigation of this reaction.

As against the notoriously high reactivity of organic isocyanates toward protic nucleophiles[6] the low reactivity of the bis(isocyanatoalkyl)diazene **1** is striking. Compound **1** has been noted for its inertness toward water, thus permitting the synthesis of **1** (and its homologues) in aqueous solution[2]. The reaction of **1** with alcohols is sluggish too, and prolonged heating at elevated temperature is required to convert **1** into several products (Scheme 1).

The solution of **1** (1.96 g, 10 mmol) in methanol (20 ml) was boiled under reflux (2 h). After evaporation of the solvent the reaction mixture was worked up by Kugelrohr distillation (60°C, 1 Pa): The solid residue upon addition of ether furnished colorless crystals of 5,5-dimethyl-

Scheme 1



R : **a** Me; **b** Et; **c** i-Pr; **d** t-Bu; **e** $PhCH_2$

1,2,4-triazolin-3-one **3**[7] (0.86 g, 76%). The distillate (0.84 g) turned out to be a mixture of two products as was revealed by ^1H NMR ($CDCl_3$): Beside a broad NH signal at δ 5.1 three singlets are displayed at δ 1.52, 3.18, and 3.61, which are attributed, in turn, to the geminal dimethyl, the methoxy and the carbomethoxy protons of 2-methoxy-2-methoxycarbonylaminopropane **4a**. The integration of the methyl singlets (33.5 : 17.0 : 20.3) clearly deviates from the ratio 2 : 1 : 1 expected for compound **4a**, and indicates that the singlet at δ 3.61 arises from the isochronous carbomethoxy groups of **4a** and of an additional compound, the methyl carbamate **5a**, as was confirmed by an authentic sample[8]. *From the signal integration a 91 : 9 ratio of* **4a** *(52%) and* **5a** (10%) was evaluated. There was no indication of the adduct **2a**.

The reaction of **1** with methanol was repeated and worked up differently: After evaporation of the solvent, the product mixture was dissolved in ether (30 ml) and subjected to low pressure liquid chromatography on silica gel (250 g, 0.040-0.063 mm [Merck]; glass column 3.3 cm i.d., 50 cm length; 1.7 bar). The fractions collected upon elution with diethyl ether/petroleum ether (PE, boiling range 40-60°C) 3:1 afforded mixtures of products; subsequent exhaustive elution with diethyl ether furnished pure **3** (1.02 g, 90%). The combined mixture fractions (0.95 g) were analysed spectroscopically: The ^1H NMR spectrum ($CDCl_3$) exhibits the same chemical shift pattern as the mixture of **4a** and **5a** obtained before, with methyl singlets at δ 1.52, 3.18 and 3.61. However,

the integration of these signals (76.0 : 26.5 : 44.5) discloses the presence of a third product having in common with **4a** both the geminal dimethyl and the carbomethoxy groups (singlets at δ 1.52 and 3.61). This gives evidence of the formation of the adduct **2a**, and from the signal integration a ratio of 25 : 66 : 8 for **2a** (9%), **4a** (43%), and **5a** (11%) is revealed. The CI-MS (isobutane) of this mixture also is indicative of **2a**: The highest mass peak observed at m/z 231 is attributed to the ion resulting from the extrusion of diazene (N_2H_2) from the pseudomolecular ion of **2a** (MH^+-30)[9]. Under the conditions applied the mixture of **2a**, **4a**, and **5a** could not be separated; it was treated with 1 N HCl (2 ml, ambient temperature, 1 h) and converted into the single product **5a** (0.46 g, 86%, based on the yields of the mixture).

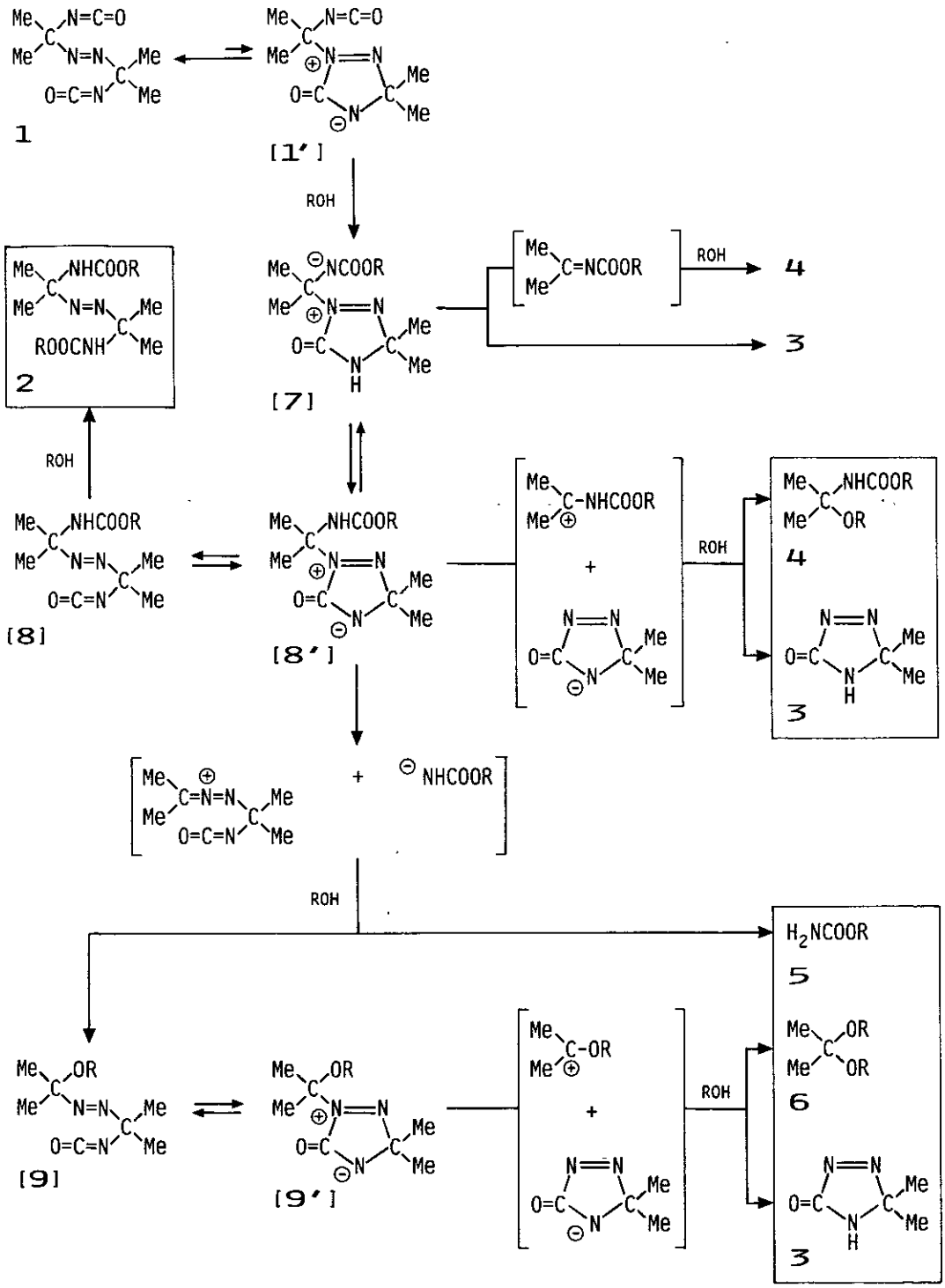
The reactions with ethanol and with 2-propanol were carried out accordingly. Again, the triazolin-3-one **3** was isolated in good yields either as the residue of a Kugelrohr distillation (70%), or as the final eluate (88%) from column chromatography. The forerunning fractions as well as the distillate were mixtures mainly of **4** and **5**[10,11], which upon acid hydrolysis were converted into ethyl carbamate **5b**[12] (81%) and isopropyl carbamate **5c**[13] (79%), respectively[14].

The reaction of **1** in t-butyl alcohol required prolonged refluxing (22 h). After evaporation of the solvent and upon addition of ether to the residue some crystals of urea were precipitated. The filtrate was subjected to liquid chromatography and furnished t-butyl carbamate **5d**[15] (29%) and the triazolin-3-one **3** (74%).

The solution of **1** (1.96 g, 10 mmol) in benzyl alcohol (20 ml) was kept at 90°C for 2 h. Subsequently, the major portion of the solvent was distilled off (80°C, 1 Pa), the residual oil (5 g) was dissolved in ether (20 ml) and subjected to liquid chromatography (1.6 bar). Upon elution with ether/PE 2:1 the following products were isolated: 2,2-Dibenzyloxypropane **6e**[16] (1.01 g, 39%); 2-benzyloxy-2-benzyloxycarbonylaminopropane **4e**[17] (1.15g, 38%). In the crude eluate containing **4e** the presence of some **2e** was indicated by CI-MS: The ion of highest mass at m/z 383 (beyond MH^+ of **4e**, m/z 299) is taken as evidence for compound **2e**. The fragment at m/z 383 is derived from the unobserved MH^+ (m/z 413) of **2e** by extrusion of diazene[9]. From the following fractions benzyl alcohol and benzyl carbamate **5e**[18] (0.50 g, 33%) were isolated. Upon final elution with ether the triazolin-3-one **3** (0.99, 88%) was collected. - Benzyl carbamate **5e** and acetone dibenzylketal **6e** have been ruled out to be successive products formed in the course of a conceivable solvolysis of the N,O-ketal **4e**: Under the condition of its formation, **4e** was treated with benzyl alcohol, and was recovered quantitatively.

The reactivity of the bisisocyanate **1** toward alcohols is exceptional. The tentative rationalization of this reaction as outlined in Scheme 2 takes into account both the unexpected failure of **1** to form appreciable amounts of the adducts **2**, and the surprising formation of the heterocycle **3** in company with the complementing products **4**, **5**, and **6**[19].

Scheme 2



The uncommonly reduced electrophilicity of the isocyanate functions of **1** is attributed to an intramolecular shielding exerted by the diazene nitrogen atoms. The X-ray analysis[4] of crystalline **1** in fact discloses a certain spatial proximity of the functional groups; since this folded conformation of **1** is not enforced by crystal packing (no close contacts between the molecules have been observed[4]) it may prevail also in solution. Moreover, to some extend an equilibrium may be considered between **1** and the cyclic valence isomer **1'**, and the reaction is supposed to be initiated by protonation at the negatively charged ring nitrogen atom of **1'** (this is closely related to the recent report[20] on the stabilization of a zwitterionic cyclic valence isomer through its protonation). Thereby, the remaining isocyanate function is rendered back its typical reactivity: Addition of alcohol provides the monoadduct **7**, which in turn is conceived to exist in an equilibrium with **8'** (both nitrogen atoms involved in this proton transfer are of the carbamic acid type). The intermediate species **8'** may undergo several competing reactions: (1) Solvolysis of **8'** (or likewise of **7**) furnishes the products **3** and **4**. (2) Heterolytic fragmentation[21] of **8'** into an ion pair[22] followed by the reaction of the fragments with the alcoholic solvent generates the carbamate **5** and another intermediate **9**. Again, the cyclic valence isomer **9'** is supposed to be the more reactive species (by analogous reasoning as used for **1'**), and subsequent solvolysis of **9'** gives rise to the formation of **6** along with **3**. (3) Valence isomerism of **8'** may be anticipated too: The monoisocyanate **8** (in much the same way as the bisisocyanate **1**) is expected to be a rather poor electrophile, but eventually the addition of the alcohol to the isocyanate function of **8** provides some **2**, as was actually found.

Thus the triazolin-3-one **3**, the main product of the alcoholysis of **1**, is presumed to be generated in the course of two competing reaction sequences, both accounting for the formation of the complementing products **4** as well as **5** and **6**.

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10 Mixture of **4b/5b**: IR ($CHCl_3$): 1720 (C=O, **4b**, **5b**). ^1H NMR ($CDCl_3$): δ 1.15 (t, CH_3CH_2O, **4b**); 1.22 (t, CH_3CH_2OCO, **4b**, **5b**); 1.53 (s, $(CH_3)_2C$, **4b**); 3.45 (q, CH_2O, **4b**); 4.05 (q, CH_2OCO, **4b**, **5b**); 5.05 (s broad, NH, **4b**, NH_2, **5b**).

11 Mixture of **4c/5c**: IR ($CHCl_3$): 1710 (C=O, **4c**, **5c**). ^1H NMR ($CDCl_3$): δ 1.11 (d, $(CH_3)_2CHO$, **4c**); 1.21 (d, $(CH_3)_2CHOCO$, **4c**, **5c**); 1.52 (s, $(CH_3)_2C$, **4c**); 3.93 (h, CHO, **4c**); 4.82 (h, CHOCO, **5c**); 4.85 (h, CHOCO, **4c**); 4.8-5.2 (broad, NH, **4c**, NH_2, **5c**).

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