Thermolysis and Photolysis of 6-Diazidomethyl-1,2,3,4-tetrahydro-2-oxopyrimidine-5-carboxylates

C. Oliver Kappe[*,a] **and Gerald Färber**[b]
[a] *Institute of Organic Chemistry,* [b] *Institute of Physical Chemistry, Karl Franzens University Graz, Heinrichstraße 28, A-8010 Graz, Austria*

The thermal decomposition of geminal diazides **1a, b** leading to pyrazolo[4,3-*d*]pyrimidines **4a, b** and the photochemical decomposition of **1a** yielding uracil-5-carboxylate **6** is described; the single crystal X-ray analysis of **4a** is also reported.

The interest in the chemistry of geminal diazido compounds[1] focuses mainly on thermal and photochemical decomposition reactions, which usually proceed with loss of molecular nitrogen and subsequent rearrangement of further decomposition of the so formed α-azidonitrenes to more stable compounds. The thermolysis and photolysis of different types of geminal diazides have been described,[1-3] however, only a few publications deal with diazides having an α-hydrogen atom such as benzyl diazides. Thermolysis of substituted benzyl diazides was reported to yield either the corresponding tetrazoles[3a] or nitriles,[3b] whereas sensitized photolysis at 77 K was shown to furnish carbenes.[3c] In a continuation of our studies on the reactions of biologically active dihydropyrimidines,[4] we have recently prepared 6-diazidomethyl-1,2,3,4-tetrahydro-2-oxopyrimidine-5-carboxylates **1a**, **b**.[4c] In this communication, we report on the thermal and photochemical decomposition of these compounds.

Results and Discussion

Compound **1a** was heated at reflux in dry DMF for 20 min, the solvent was removed by evaporation and the residue treated with cold ethanol to yield 86% of **4a**. The structure elucidation was initially based on microanalytical data, which showed that the thermolysis of **1a** had proceeded with loss of two molecules of nitrogen. Earlier studies showed that the elimination of 2 equiv. of nitrogen upon controlled thermolysis of geminal diazides leads to diazo compounds (probably *via* tetrazoles as intermediates).[2d] In the case of **1a**, the resulting α,β-unsaturated diazo compound **2a** would be expected to undergo spontaneous

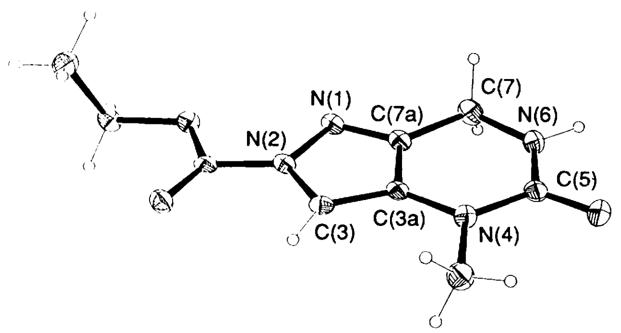
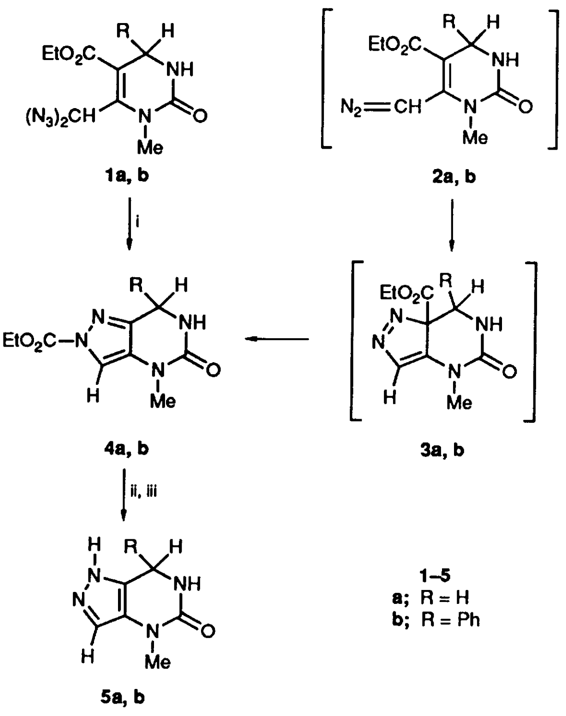


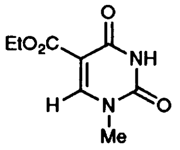
Fig. 1 ORTEP drawing of the X-ray structure of **4a**. Thermal ellipsoids are drawn at the 50% probability level

1,5-electrocyclization to pyrazolopyrimidine **3a**. Many examples of these vinyldiazomethane→3*H*-pyrazole interconversions are known in the literature[5a] and the reaction mechanism has been discussed.[5b] The ^{13}C NMR spectrum* showed, however, no signal which could be assigned to the sp^3 carbon (C-7a) in **3a**; instead it featured two signals in the aromatic region at δ 130.1 and 142.4 consistent with two sp^2 carbon atoms (C-3a and C-7a, respectively) in isomeric **4a**. We therefore concluded that the ester group at C-7a in **3a** had migrated to one of the nitrogen atoms in the pyrazole ring. In fact, at elevated temperatures 3,3-disubstituted 3*H*-pyrazoles (such as **3a**) are known to undergo rearrangement to 1*H*-pyrazoles with migration of a substituent from the tetrahedral carbon (C-3) to either the adjacent nitrogen (N-2) or, in some cases also to N-1 (thermal van Alphen–Hüttel rearrangement).[6] To establish unambiguously the structure of the thermolysis product, an X-ray analysis of **4a** was carried out (Fig. 1), confirming the pyrazolo[4,3-*d*]-pyrimidine structure and the position of the ester group at N-2. The phenyl analogue **1b** reacted in a similar way leading to **4b** in 46% yield (m.p. 190 °C). Removal of the ester group from **4a, b** was achieved in near quantitative yield by treatment with aq. NaOH and subsequent acidification with conc. HCl. Although there can be no doubt about the structure of the thermolysis products **4a, b**, the proposed reaction mechanism outlined above (Scheme 1) remains speculative and warrants further investigation.

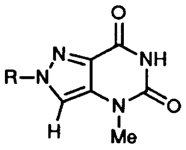


Scheme 1 *Reagents and conditions*: i, DMF, reflux; ii, NaOH; iii, HCl

In addition to the thermal decomposition, we also studied the photochemical decomposition of geminal diazide **1a**. Irradiation of an acetone solution of **1a** under an inert gas atmosphere for several hours afforded a complex mixture of products which could not be separated or identified. However, if the reaction was carried out in the presence of oxygen (see Experimental section), uracil derivative **6** was obtained in 48% yield. Surprisingly, in addition to the oxidation of the CH_2 group, the 6-diazidomethyl function was completely lost during the reaction, which was confirmed by microanalytical and mass spectroscopic data. In the ^1H NMR spectrum the C(6)H appears as a singlet at δ 8.14, whereas the ^{13}C NMR spectrum featured 3 carbonyl resonances (δ_C 152.5, 161.1 and 164.7) in excellent agreement with the previously reported values[7] for similar uracil-5-carboxylates. This novel type of photooxidation of dihydropyrimidines was successfully applied to pyrazolopyrimidine **4a** which, under similar conditions, was converted into **7** in 41% yield. Hydrolysis of the ester group led to xanthine analogue **8**.



6



7 R = CO2Et
8 R = H

The synthetic utility and mechanistic details of the thermal and photochemical decomposition of this type of geminal diazides are currently being explored.

Experimental

Ethyl 1,2,3,4-Tetrahydro-1-methyl-2,4-dioxopyrimidine-5-carboxylate **6**.—A solution of diazide **1a**[4c] (200 mg, 0.71 mmol) in acetone (100 cm^3) was irradiated with a Hanau high-pressure mercury lamp (TQ 150 at 365 nm) while a gentle stream of oxygen was passed through the solution. After 1.5 h, the solution was evaporated and the oily residue treated with cold ethanol to give **6** (67 mg, 48%). An analytical sample was obtained on crystallization from ethanol, m.p. 233 °C (lit.,[8] 237 °C) (Found: C, 48.52; H, 5.07; N, 14.02%. Calc. for

---

* All new compounds gave spectroscopic and analytical data in accordance with assigned structures. Data are quoted for compounds **4a**, **5a**, **7** and **8**. For **4a**: m.p. (ethanol) 192–194 °C; $\nu_{max}(KBr)/cm^{-1}$ 1735 (CO) and 1680 (urea CO); $\delta_H[(CD_3)_2SO]$ 1.34 (t, 3 H, CH_2Me), 3.06 (s, 3 H, NMe), 4.41 (q, 2 H, CH_2Me), 4.44 (s, 2 H, 7-H), 7.10 (b, 1 H, 6-H) and 7.90 (s, 1 H, 3-H); $\delta_C[(CD_3)_2SO]$ 15.6 (Me), 32.1 (4-Me), 40.9 (C-7), 65.6 (OCH_2), 114.2 (C-3), 130.1 (C-3a), 142.4 (C-7a), 150.8 (CO) and 154.7 (C-5).

For **5a**: m.p. (methanol) 248–251 °C; $\nu_{max}(KBr)/cm^{-1}$ 1670 (CO); $\delta_H[(CD_3)_2SO]$ 3.00 (s, 3 H, NMe), 4.34 (s, 2 H, 7-H), 6.71 (br, 1 H, 6-H), 7.32 (s, 1 H, 3-H) and 12.25 (br, 1 H, 1-H).

For **7**: m.p. (propan-1-ol) 227–228; $\nu_{max}(KBr)/cm^{-1}$ 1750 (ester CO), 1725–1700 (amide CO) and 1685 (urea CO); $\delta_H[(CD_3)_2SO]$ 1.37 (t, 3 H, CH_2Me), 3.20 (s, 3 H, NMe), 4.48 (q, 2 H, CH_2Me), 8.51 (s 1 H, 3-H) and 11.40 (br, 1 H, 6-H); $\delta_C[(CD_3)_2SO]$ 14.0 (Me), 31.6 (4-Me), 65.6 (OCH_2), 116.2 (C-3), 131.1 (C-3a), 136.3 (C-7a), 149.0 (CO), 150.8 (C-5) and 157.9 (C-7).

For **8**: 88% yield; m.p. (acetic acid) > 390 °C; $\nu_{max}(KBr)/cm^{-1}$ 1700 (amide CO) and 1665 (urea CO); $\delta_H[(CD_3)_2SO]$ 3.32 (s, 3 H, NMe), 7.86 (s, 1 H, 3-H), 11.16 (br, 1 H, 6-H) and 12.35 (br, 1 H, 1-H).

$C_8H_{10}N_2O_4$: C, 48.49; H, 5.09; N, 14.14%); ν_{max}(KBr)/cm^{-1} 1745 (ester CO), 1700 (amide CO) and 1655 (urea CO); δ_H[$(CD_3)_2SO$] 1.25 (t, 3 H, CH_2*Me*), 3.12 (s, 3 H, NMe), 4.19 (q, 2 H, C*H*$_2$Me), 8.14 (s, 1 H, 6-H) and 11.83 (br, 1 H, 3-H); δ_C[$(CD_3)_2SO$] 15.4 (Me), 28.5 (Me), 61.8 (CH_2), 104.3 (C-5), 149.3 (C-6), 152.5 (C-2), 161.1 (C-4) and 164.7 (ester CO); *m/z* (CI, CH_4) 199 (M + 1) and 227 (M + 29).

X-Ray Analysis of **4a**.—Crystals of $C_9H_{12}N_4O_3$ were obtained from dioxane, $M = 224.22$, triclinic, $a = 4.126(1)$, $b = 11.180(3)$, $c = 13.512(5)$ Å, $\alpha = 72.43(2)$, $\beta = 89.08(3)$, $\gamma = 81.28(3)°$, $V = 587.1(3)$ Å^3 (cell parameters obtained by a least-squares fit to the diffractometer setting angles of 43 reflections with $10° < 2\theta < 26°$), space group P-1, $Z = 2$, $D_{obs} = 1.42$ g cm^{-3} (flotation method, CCl_4/cyclohexane, $T = 295$ K), $D_{calc} = 1.44$ g cm^{-3} (disordered solvent included), $\mu = 1.0$ cm^{-1}. Investigated crystal specimen: colourless, prismatic, $0.18 \times 0.26 \times 0.36$ mm^3. Diffraction data were collected on a modified STOE diffractometer at 93(2) K, using Mo-Kα radiation ($\lambda = 0.710\,69$ Å, graphite monochromator, ω-scan with variable speed, width = 1.5°), leading to a total of 5523 reflections and 5178 unique reflections with $5.5° < 2\theta < 70°$ ($R_m = 0.0167$), 2085 of them with $F > 4\sigma(F)$. The structure was solved by direct methods; after several refinement cycles, an empirical absorption correction was applied, with all non-hydrogen-atoms of the molecule and four disordered solvent atoms included at this stage (Walker/Stuart, Program DIFABS). Three low-order reflections were excluded due to supposed extinction. Finally all non-hydrogen atoms of the molecule were refined anisotropically, the hydrogens isotropically, all of them at observed positions. Disordered solvent (dioxane) was found in the crystal and accounted for by 3 oxygen and 6 carbon atoms per asymmetric unit, with refined site occupation factors and a common refined U_{iso}. Final R and R_w are 0.061 and 0.056 for 2083 observations and 230 parameters [weighting scheme $1/\sigma^2(F)$]. The final difference electron density map shows features up to 0.38 and down to -0.33 e Å^{-3}. Atomic co-ordinates, bond lengths and angles, and thermal parameters have been desposited at the Cambridge Crystallographic Data Centre. See 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 1*, 1991, issue 1.

References

1 W. Lwowski, *Nitrenes*, Interscience, New York, 1970, p. 75.

2 (*a*) M. Ramezanian, A. B. Padias, F. D. Saeva and H. K. Hall, *J. Org. Chem.*, 1990, **55**, 1768; (*b*) W. Ogilvie and W. Rank, *Can. J. Chem.*, 1987, **65**, 166; (*c*) R. M. Moriarty, B. R. Bailey, I. Prakash and R. S. Miller, *J. Org. Chem.*, 1985, **50**, 3710; (*d*) T. Kappe, G. Lang and E. Pongratz, *J. Chem. Soc., Chem. Commun.*, 1984, 338; (*e*) H. W. Moore and D. S. Pearce, *Tetrahedron Lett.*, 1971, 1621; (*f*) G. Ege and G. Jooss, *Chem.-Ztg.*, 1970, **94**, 215.

3 (*a*) Sanwa Kagaku Kenkyusho Co., Jap P 59 98023/1984; (*b*) K. Nishiyama, M. Oba and A. Watanabe, *Tetrahedron*, 1987, **43**, 693; (*c*) L. Barash, E. Wasserman and W. A. Yager, *J. Am. Chem. Soc.*, 1967, **89**, 3931.

4 (*a*) C. O. Kappe and P. Roschger, *J. Heterocycl. Chem.*, 1989, **26**, 55; (*b*) C. O. Kappe and U. G. Wagner, *Heterocycles*, 1989, **29**, 761; (*c*) C. O. Kappe, *Liebigs Ann. Chem.*, 1990, 505.

5 (*a*) E. C. Taylor and I. Turchi, *Chem. Rev.*, 1979, **79**, 181; (*b*) R. Huisgen, *Angew. Chem.*, 1980, **92**, 979; also see ref. 6a.

6 For a detailed description of the van Alphen–Hüttel rearrangement in the 3*H*-pyrazole series see: (*a*) M. P. Sammes and A. R. Katritzky, *Adv. Heterocycl. Chem.*, 1983, **34**, 1; examples with ester groups: (*b*) P. Schiess and H. Stalder, *Tetrahedron Lett.*, 1980, **21**, 417; (*c*) R. Huisgen, H. U. Reissig and H. Huber, *J. Am. Chem. Soc.*, 1979, **101**, 3647.

7 P. D. Ellis, R. B. Dunlap, A. L. Pollard, K. Seidman and A. D. Cardin, *J. Am. Chem. Soc.*, 1973, **95**, 4398.

8 N. J. Cusack, B. J. Hildick, D. H. Robinson, P. W. Rugg and G. Shaw, *J. Chem. Soc., Perkin Trans. 1*, 1973, 1720.

Paper 1/00289I
Received 21*st January* 1991
Accepted 13*th February* 1991