HETEROANALOGOUS DEAZAPURINES VIA NOVEL 4 + 2 CYCLOADDITION REACTIONS OF KETENIMINES

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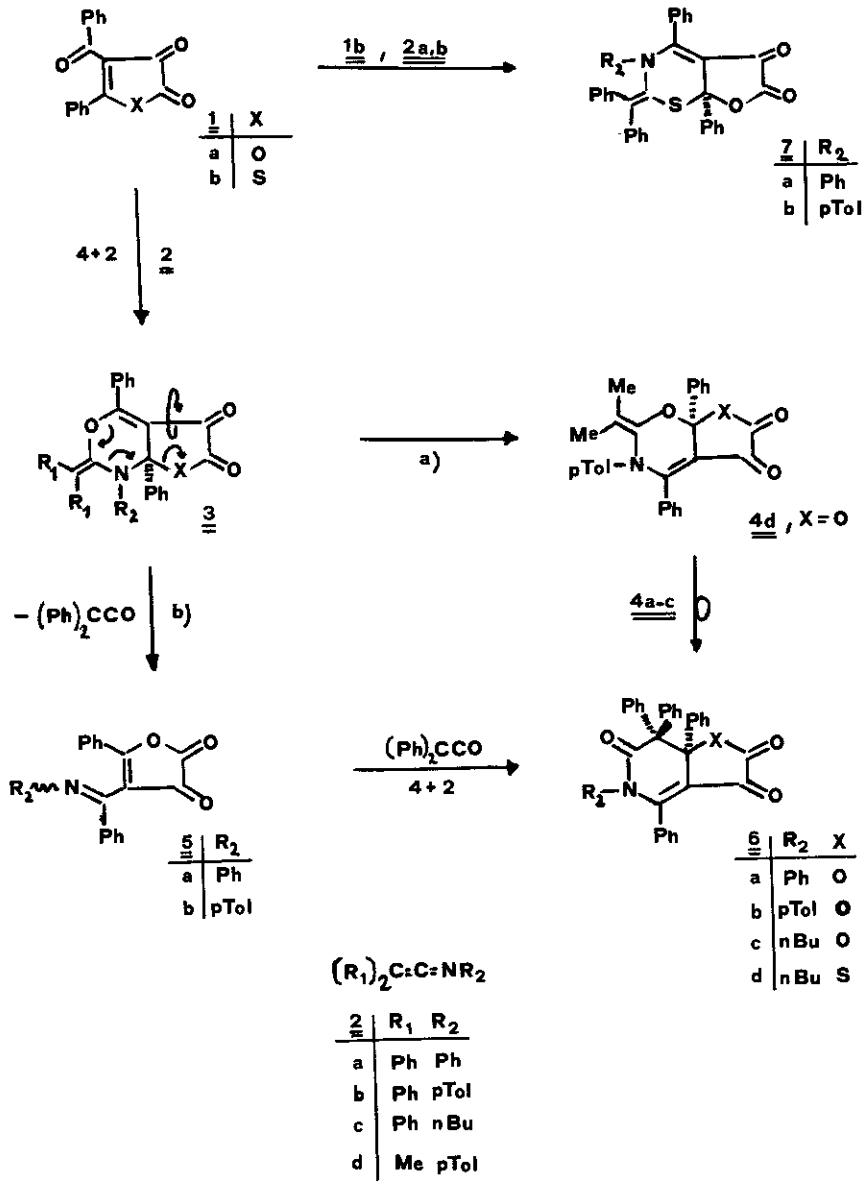
Abstract - The heterocyclic 2,3-diones 1 and the ketenimines 2 combine yielding heteroanalogous deazapurines 4, 6 and 7 partly having so far unknown molecular skeletons, which were made evident with aid of X-ray structure analyses (6b, 7a), IR- and ^{13}C NMR measurements. The reaction pathways include 4+2 cycloaddition processes across the C=N-bond of the ketenimine, accompanied by several surprising rearrangements. These are the first examples observed of 4+2 cycloaddition reactions with ketenimines of to oxa-1,3-dienes.

The oxa-1,3-diene system in 4-benzoyl substituted five-membered heterocyclic 2,3-diones (e.g. 1), formed from the benzoyl group and the endocyclic C=C-bond, is capable to add isocyanides [1,2], isocyanates [3] and carbodiimides [4] yielding various bicyclic heterocycles. Using now ketenimines 2 as dienophiles, a quite similar reaction behaviour is found: The heterocumulenes 2 again undergo 4+2 cycloaddition processes on to the oxa-1,3-diene moiety in 1 first, accompanied by special rearrangements, finally forming the heteroanalogous deazapurines 4, 6 and 7, some of them (4, 7) presenting so far unknown heterocyclic ring systems. 4+2 Cycloaddition reactions of ketenimines on to heterodienes of this type obviously are the first one to be observed.

The furandione 1a adds 2 to give the furo[3,2-c]pyridines 6a-c. The compounds 6a,b are obtained too from 4+2 cycloaddition reactions of diphenylketene on to 4-iminobenzyl-furandiones 5 [4]. This method for synthesizing 3,4-dihydropyridones and even condensed pyridines from ketenes and aza-1,3-dienes is well known. [6,7] The dimethyl-p-tolylketenimine 2d and 1a combine yielding the 1:1 adduct 4d representing a novel furo[3,2-e]1,3-oxazine skeleton. While the thiophenedione 1b adds 2c in a quite similar way leading to the thieno[3,2-c]pyridine 6d, it

surprisingly reacts with the ketenimines 2a,b to give the corresponding furo[3,2-e]1,3-thiazines 7, a so far unknown heteroanalogue deazapurine system too.



The structure determination of the condensed pyridones 6 is based on a X-ray structure analysis of 6b (Figure 1) [8]. The IR and ^{13}C NMR spectroscopic data [9]

confirm the structural analogy of all furopyridines 6a-c and the thienopyridine 6d : IR absorption bands at 1790 and 1700 cm^{-1} are characteristics of an untouched furan-2,3-dione moiety as seen in 6a-c. [2,4] From the ^{13}C NMR spectra of 6, the signals at 64.0 and 84.0 (6b,c) and 63.1, 60.2 (6d) respectively can easily be assigned to the sp^3-carbon atoms C-7 and C-7a, which are particularly informative concerning the structure elucidation of compounds 6. In the MS spectrum of 6b (80eV), taken as an example, there is no molecular ion M^+ detectable besides elimination of diphenylketene (m/z 367), which is found to be the base peak too (m/z 194).

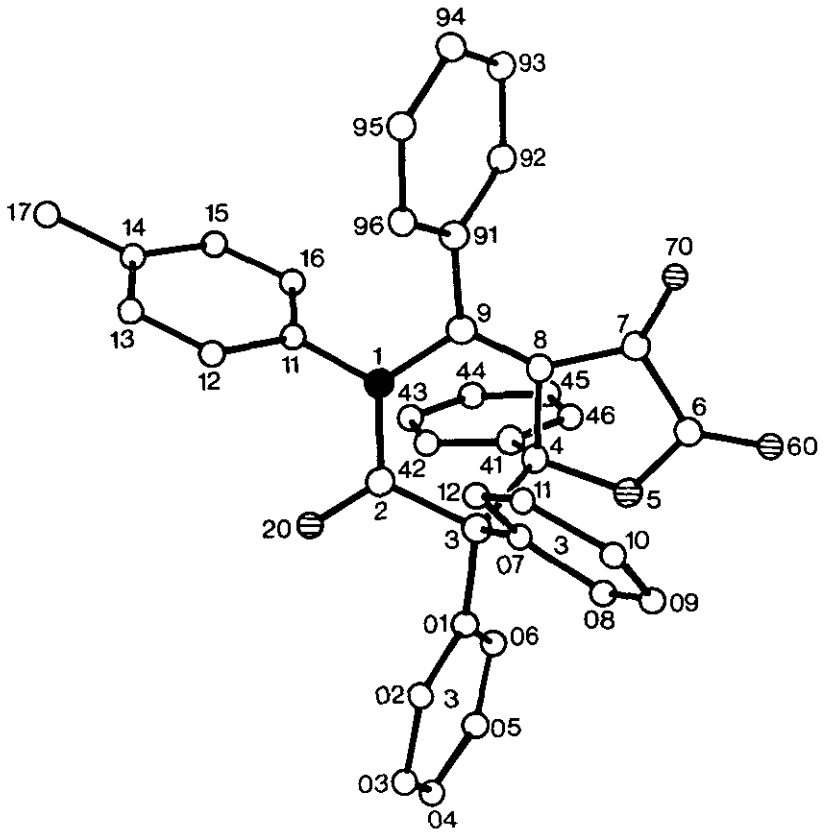


Figure 1. Stereographic drawings of 6b

The constitution of the furooxazine 4d could be clarified by means of IR and ^{13}C NMR spectroscopy [10]: The C=O absorption bands at 1790 and 1695 cm^{-1} again indicate the presence of a free furandione moiety. The chemical shifts of

all ring carbon atoms in the ^{13}C NMR show very good agreement with those of structural analogous compounds. [2,9,11-13] In particular this is found with the acetalic group at C-7a [2,11,12] and the oxazine ring with its exocyclic C=C-bond. [13] The bicyclic furothiazine ring of 7 again could be confirmed with aid of an X-ray study of 7a (Figure 2) [14]. It is remarkable that in this case the sulfur atom obviously has exchanged its position from the five-membered thiophene ring of the educt 1b into the six-membered thiazine ring of the product 7. The structural analogy of 7a and 7b is seen from comparison of IR and ^{13}C NMR spectroscopic data. [15]

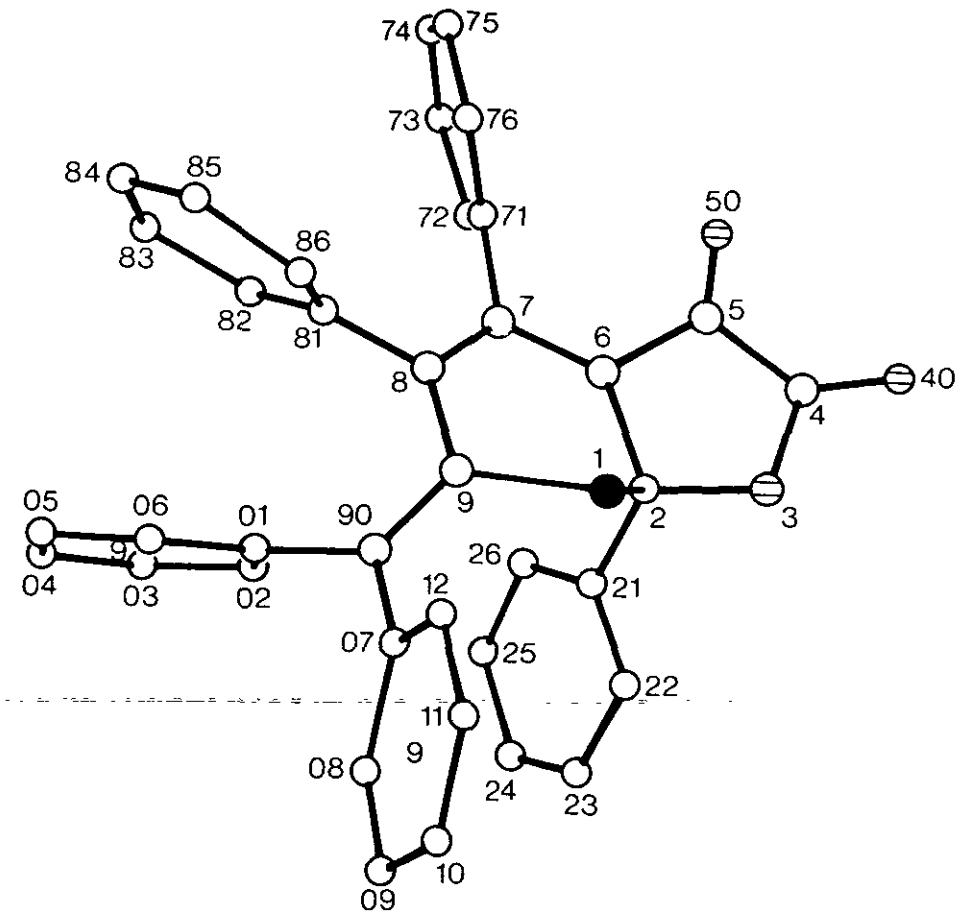


Figure 2. Stereographic drawings of 7a.

The reactions pathways leading to the products 4d and 6 as outlined in the formula scheme have found some experimental evidences: The primary adduct 3 should be an important key intermediate. Starting from 3 the subsequent reaction steps 3 → 4 or 3 → 5 respectively include a novel furandione-rearrangement, which was found first quite recently with similar reaction systems. [2-4] During this rearrangement the two oxygens of the lactone group must equalize, which could be made evident with aid of ^{17}O-labeling experiments. [16] Concerning reaction pathway a) by use of 2d the primary product of that rearrangement, namely 4d, is stable and therefore isolable out of the reaction mixture. In all other cases 4 must be seen as a further intermediate, which obviously easily isomerizes to the stable endproduct 6. Few examples of such isomerization reactions are known from the ketenimine [5] and ketene chemistry. [17] Regarding reaction pathway b) the elimination of diphenylketene from 3 should initiate the furandione rearrangement leading to 5, the azadiene moiety of which could add the diphenylketene again yielding 6. This could be verified from an independent synthesis of 6, starting with 5 and diphenylketene. The reaction pathway 1b → 7 seems to be more complex. ^{17}O-labeling experiments should be helpful again and are under investigation now. Finally it should be mentioned, that there are only few papers published so far, [5,13] reporting 4+2 cycloaddition reactions of ketenimines across their C=N-bond as discussed here. Furthermore the addition of ketenimines on to the oxa-1,3-diene system in 1 had not been observed before and offers a very simple way to some heteroanalogue deazapurine derivatives, often having surprising positions of the heteroatoms.

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8. Crystal data of 6b: monoclinic, $P2_1/a$ (Nr.14), a = 1863.3(7) pm, b = 975.1(3) pm, c = 1841.7(7) pm, $\beta = 118.57(3)^{\circ}$, $d_{calc} = 1.269\ g.cm^{-3}$, Z = 4; MoKα radiation, 2998 reflections ($F>3\sigma(F)$). The structure was solved by SHELXTL 83 and direct methods; $R_{aniso} = 0.043$. Further details of the structure determination are deposited at the Fachinformationszentrum Energie, Physik, Mathematik, D-7514 Eggenstein-Leopoldshafen 2 (West Germany). These data are available with quotation of the registry number CSD 51687, the authors, and the reference to this publication.

9. 6a: Yellow prisma, mp 243-244°C. IR (ν cm^{-1}, KBr): 1785(s), 1695(s). - 6b: Yellow crystals, mp 238-240°C. IR (ν cm^{-1}, KBr): 1795(s), 1705(s). ^{13}C NMR (δ, $CDCl_3$) ring carbons: 64.0 (C-7), 84.6 (C-7a), 116.6 (C-3a), 152.6 (C-4), 162.8 (C-2), 171.8 (C-6), 174.0 (C-3). MS (80eV, m/z): 367 (35), 339 (39), 310 (30), 194 (100). - 6c: Yellow needles, mp 225-227°C. IR (ν cm^{-1}, KBr): 1795(s), 1695(s). - ^{13}C NMR (δ, $CDCl_3$): 63.6 (m, C-7), 84.2 (t, C-7a), 116.4 (s, C-3a), 152.6 (t, C-4), 162.8 (s, C-2), 171.4 (dd, C-6), 173.3 (s, C-3). - 6d: Yellow disks, mp 222-224°C. IR (ν_2 cm^{-1}, KBr): 1700(s). - ^{13}C NMR (δ, $CDCl_3$): 60.2, 63.8 (C-7, C-7a, exchangeable), 115.6 (C-3a), 154.0 (C-4), 171.0 (C-6), 178.9 (C-3), 190.9 (C-2). All assignments are based on J_3-coupling constants of 6c. Satisfactory microanalytical results were obtained for all new compounds.

10. 4d: Yellow crystals, mp 124-126°C. - IR (ν cm^{-1}, KBr): 1790(s), 1695(s), ^{13}C NMR (δ, $CDCl_3$) ring carbons: 103.8 (C-7a), 106.8 (expo-sp^2C), 114.9 (C-4a), 138.0 (C-2), 162.5 (C-6), 170.8 (C-5).

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14. Crystal data of 7a: monoclinic, $P2_1/n$ (Nr. 14), a = 2444.9(20) pm, b = 1456.0(9) pm; c = 1899.7(12) pm, β = 108.91(5)°, d_{calc} = 1.251 g.cm^{-3}, Z = 8; MoKα radiation, 3420 reflections ($F>3\sigma(F)$). Further details of the structure determination are deposited at the Fachinformationszentrum Energie, Physik, Mathematik, D-7514 Eggenstein-Leopoldshafen 2 (West Germany). These data are available with quotation of the registry number CSD 51687, the authors, and the reference to this publication.

15. 7a: Yellow needles, mp 206-209°C. IR (ν cm^{-1}, KBr): 1780(s), 1690(s). ^{13}C NMR (δ, $CDCl_3$) ring carbons: 88.8 (C-7a), 111.6 (C-4a), 150.5 (C-2), 156.6 (C-4), 163.2 (C-6), 172.2 (C-5). - 7b: Yellow needles, mp 214-217°C. IR (ν cm^{-1}, KBr): 1780(s), 1690(s). - ^{13}C NMR (δ, $CDCl_3$): 88.2 (C-71), 111.0 (C-4a), 149.6 (C-2), 156.0 (C-4), 163.0 (C-6), 171.4 (C-5).

16. G.Kollenz and H.Sterk, unpublished results. The ^{17}O-label of the educt 1a is located in the furanring-oxygen, in the endproduct (f.e. 6b) it is distributed among the two lactone oxygens in a ratio of nearly 50 : 50.

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