Tetrahedron Letters,Vol.29,No.10,pp 1127-1130,1988 0040-4039/88 $3.00 + .00
Printed in Great Britain Pergamon Press plc

PHOTOSENSITIZED OXYGENATION OF 2,3-DIHYDROPYRAZINES: UNEXPECTED SYNTHESES OF ISONITRILES

Klaus Gollnick* and Sigrid Koegler

Institut für Organische Chemie der Universität,
Karlstrasse 23, D-8000 München 2, Germany

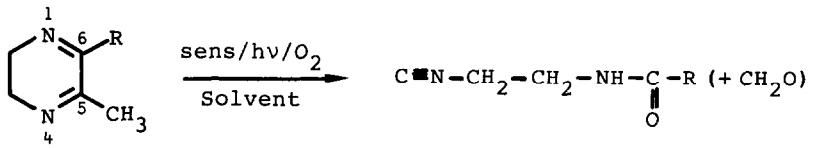
Rose bengal and tetraphenylporphin sensitized photooxygenations of 5,6-dimethyl- (1a) and 5-methyl-6-phenyl-2,3-dihydropyrazine (1b) yield 1-isocyano-2-(N-acetylamino)-ethane (2a) and 1-isocyano-2-(N-benzoylamino)-ethane (2b), respectively. 5,6-Diphenyl-2,3-dihydropyrazine (1c) is inert under the reaction conditions.

Some years ago, Bhat and George [1] reported on the attempted photooxygenation of 5,6-diphenyl-2,3-dihydropyrazine (1c), which is, to the best of our knowledge, the only report on this class of dihydro-heteroaromatic compounds as substrates for photosensitized oxygenation reactions. According to the reaction conditions applied by these authors [2], 1c underwent the well-known photorearrangement into 1-methyl-4,5-diphenylimidazole [3,4], and it was this latter compound which was subsequently photooxidized to afford finally 1,3-dibenzoylurea. Precautions were, therefore, taken in the present study in order to avoid such photorearrangements prior to photooxygenation.

Thus, when 5,6-dimethyl- (1a), 5-methyl-6-phenyl- (1b) and 5,6-diphenyl-2,3-dihydropyrazine (1c) were irradiated for several hours at $\lambda_{exc} > 300$ nm, (1) in the absence of sensitizers in either oxygen-free or oxygen-saturated acetonitrile (MeCN), and (2) in the presence of sensitizers such as rose bengal (RB) or tetraphenylporphin (TPP) in oxygen-free solvents, 1a-c were found to be inert under the reaction conditions (^{1}H NMR). In each case, 1a-c were recovered quantitatively.

When 1a and 1b were irradiated (λ_{exc} = 480-570 nm) in O_2-saturated solvents in the presence of RB (in MeCN or acetone) or TPP (in $CHCl_3$ or benzene), 1a as well as 1b consumed one mole of oxygen, whereas 1c did not absorb any O_2 and was thus recovered quantitatively [8].

After removal of the solvents from the photooxygenated solutions of 1a and 1b, vacuum distillation of the residues and sublimation of the resulting crystals, we obtained colorless compounds of m.p. 73-75°C (2a) and 79-81°C (2b), respectively, in yields up to about 55% [10]. The elemental analyses of 2a and 2b and their molecular weights indicated the loss of a methylene group during the photooxygenation, probably as formaldehyde [11]. On the basis of their spectral properties, products 2a and 2b turned out to be isonitriles:



1

a: R = CH_3

b: R = C_6H_5

2

a: m.p. 73-75°C

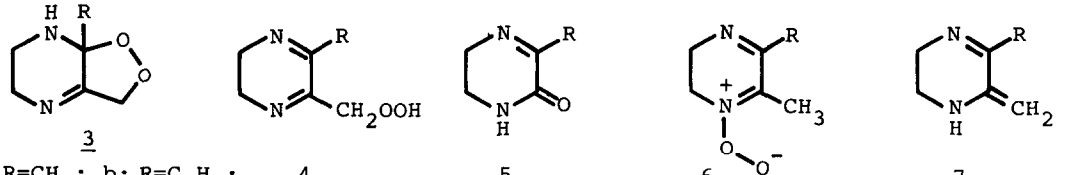
b: m.p. 79-81°C

Thus, 2a, 1-isocyano-2-(N-acetylamino)-ethane, shows ^{1}H NMR signals (in $CDCl_3$, TMS) at δ = 1.98 (s, 3H); 3.47 (m, 4H); 6.3 ppm (broad, 1H); and ^{13}C NMR signals (in $CDCl_3$, TMS) at δ = 23.0 (q, CH_3); 38.8 (t, CH_2); 41.7 (tt, J_{NC} = 6.7 Hz, CH_2); 157.3 (t, J_{NC} = 5.2 Hz, -NC); 170.9 ppm (s, CO). The isonitrile-^{13}C resonance is expected to appear at about 157 ppm as a triplet due to $^{13}C/^{14}N$ coupling. Similarly, $^{13}C/^{14}N$ coupling gives rise to a triplet of a triplet for the CH_2 group located next to the isonitrile group. In agreement with literature values [12], the isonitrile-N signal of the ^{14}N NMR spectrum was found at -209 ppm (in $CDCl_3$, nitrate as internal standard). The IR spectrum (KBr) confirms the proposed structure: strong absorption bands at 2150 and 2158 cm^{-1} are distinctive of isonitriles, whereas the acyclic N-monosubstituted amide displays strong absorption bands at 1675 and 1653 cm^{-1} (amide I, C=O streching) and at 1558 cm^{-1} (amide II, N-H bending) as well as medium-strong bands at 3260 and 3077 cm^{-1} (-NH-CO-).

Similarly, 2b, 1-isocyano-2-(N-benzoylamino)-ethane, shows ^{1}H NMR signals at δ = 3.61 (m, 4H); 6.9 (broad, 1H); 7.17-7.85 ppm (m, 5H); ^{13}C NMR signals at δ = 39.2 (t, CH_2); 41.7 (tt, J_{NC} = 6.7 Hz, CH_2); 127.1 (d), 128.6 (d), 131.9 (d), and 133.6 (s) (phenyl group); 157.4 (t, J_{NC} = 4.9 Hz, -NC); 168.0 ppm (s, CO); ^{14}N NMR signal at -209.4 ppm; IR (KBr): strong absorption bands at 2153 (-NC); 1653 and 1642 (amide I); 1558 (amide II); 3261 and 3084 cm^{-1} (-NH-CO-).

When the residues obtained from photooxygenation of 1a and 1b were dissolved in $CDCl_3$ immediately after removal of solvents, the ^{1}H NMR spectra revealed that, besides 2a, there was one more product formed with signals at 2.18 (s), 3.62 (m), and 4.86 (m) in a ratio of 3:4:2. Besides 2b, there was also one more product formed with signals at 3.70 (m), 4.80 (m), and 7.5-7.9 (m) in a ratio of 4:2:5. At +50°C, these compounds slowly transform into isonitriles 2a and 2b, respectively, as well as into some polymeric material.

The ^{1}H NMR spectra together with the thermal behavior of these not yet isolated new compounds appear to be in accord with dioxolane structures 3a,b rather than with the hydroperoxide structures 4a,b, the anticipated precursors of the isonitriles 2a,b as well as of the dioxolanes 3a,b [13]. The spectra are, however, incompatible with those obtained for the dihydropyrazinone derivatives 5a,b [14].



3

a: R=CH_3; b: R=C_6H_5;

4

5

6

7

Thus, the singlet at 2.18 ppm is undoubtedly due to the methyl group, the multiplet at 7.5-7.9 ppm to the phenyl group of the presumed compounds 3a and 3b, respectively. Whereas the multiplets at 3.62 and 3.70 ppm belong to the CH_2CH_2 groups of the still intact dihydropyrazine moieties, the signals at 4.86 and 4.80 ppm, representing two hydrogens in each case, should be due to the CH_2 groups of the dioxolane moieties of 3a and 3b, respectively.

Photooxygenation of 1a and 1b apparently involves singlet oxygen since DABCO quenches the reaction whereas 2,4,6-tri-t-butylphenol, a radical quencher, does not. Oxygenation of 1a,b induced by H-atom abstraction is thus excluded as is an electron transfer induced photooxygenation because of unfavorable energetics for the electron transfer between 1a,b and the excited sensitizers. In addition, non-polar solvents such as benzene, inappropriate for electron transfer induced photooxygenations [16], are well suited for a fast photooxygenation of 1a,b in the presence of TPP.

How the primary hydroperoxides 4a,b, the presumed but so far not yet even spectroscopically observed precursors of 2a,b and 3a,b, are formed from 1a,b and $^1O_2$, is another intriguing question. Of the various mechanisms that may be envisaged such as (1) addition of $^1O_2$ to N-4 of 1a,b to form a zwitterion 6a,b followed by a proton transfer and rearrangement to 4a,b, (2) photochemical isomerization of 1a,b to the corresponding enamines 7a,b which subsequently react with $^1O_2$ to 4a,b in an ene-type reaction, or (3) electron transfer from 1a,b to $^1O_2$ to yield the corresponding radical cations $1a^{\cdot+}$, $1b^{\cdot+}$ and $O_2^{\cdot-}$ followed by a proton transfer and radical combination to 4a,b, mechanism (1) appears to be the most likely. Mechanism (2) is rather unlikely to occur since enamine 7 should not only rearrange back to 1 very efficiently (see the RB and TPP sensitized experiments in O_2-free solvents), but would also be expected to yield at least some dihydropyrazinone 5 by interaction with $^1O_2$ (for a review on reactions of N,N-dialkyl substituted enamines with singlet oxygen, see ref. 17). Mechanism (3), however, can be eliminated from further consideration since the oxidation potentials of 1a (E_{ox} = + 1.84V vs. SCE) and 1b (E_{ox} = + 1.86V vs. SCE) and the reduction potential of $^1O_2$ ($E_{red} = E_{red}(^3O_2) + E(^1\Delta_g O_2)$ = -0.78 + 0.98 = 0.2V) in MeCN renders this process highly endothermic (by about 36 kcal/mol).

Work is presently in progress to isolate the spectroscopically observed, thermally unstable intermediates, to elucidate the mechanism as well as to check the possibilities of extending the rather unexpected isonitrile synthesis to other 2-alkyl substituted 1,4 - diaza-1,3-diene systems.

REFERENCES AND FOOTNOTES

1. V.Bhat, M.V.George, J. Org. Chem. 44 (1979), 3288.

2. 1c was irradiated in quartz vessels in benzene as solvent. Unfortunately, it is not clear whether the photooxygenation was carried out in the absence (ref.1, experimental part) or in the presence of RB as a sensitizer (ref.1, theoretical part).

3. P.Beak, J.L.Miesel, J. Am. Chem. Soc. 89 (1967), 2375.

4. T.Matsuura, Y.Ito, Bull. Chem. Soc. Jpn. 47 (1974), 1724.

5. 1a (b.p. 67°C/13 Torr; ^1H NMR ($CDCl_3$, TMS): δ = 2.10 (s, 6H); 3.26 (s, 4H)) was prepared

according to ref. 6. - 1c (m.p. 163-164°C; ^{1}H NMR: δ = 3.72 (s, 4H); 7.20 (m, 10H)) was prepared according to ref. 7. - 1b, prepared by condensation of 1-phenyl-1,2-propanedione with 1,2-diaminoethane according to the procedure used to synthesize 1a, shows the elemental analysis: C 76.83, H 7.09, N 16.36; $C_{11}H_{12}N_2$ (172.22) requires C 76.71, H 7.02, N 16.27; m.p. 38-39°C (after sublimation); ^{1}H NMR: δ = 2.08 (s, 3H); 3.50 (s, 4H); 7.35 (s, 5H).

6. I.Flament, M.Stoll, Helv. Chim. Acta 50 (1967), 1754.

7. A.T.Mason, Ber. Dtsch. Chem. Ges. 20 (1887), 267.

8. A 25 ml irradiation unit (Jena glass, transparent λ > 300 nm) with automatic oxygen consumption system[9] was used. A 150 W Halogen-Bellaphot lamp (Osram) and a band filter transparent between 480 and 570 nm (Hoya) was applied for electronic excitation of RB and TPP. The solvents containing 1 at varying initial concentrations between 0.04 and 0.144 M and the sensitizers at concentrations of $5 \cdot 10^{-4}$ M were saturated with oxygen before irradiation. The irradiation unit, the oxygen burette and the connecting tubings were kept at 13°C by cooling with water; thermostat JULABO-P.

9. H.Paur, Dissertation, University of München, (1982).

10. The best yields of 2a were obtained from photooxygenations of 1a in MeCN with RB as a sensitizer. After the oxygen uptake ceased (1 mol of O_2 per mol of 1a), the solvent was removed at 20°C/12 Torr. The residue was distilled at 90°C/10^{-4} Torr yielding colorless crystals. Sublimation at 100°C/10^{-4} Torr afforded a colorless compound, m.p. 73-75°C, in yield of 55%.

11. 2a: elemental analysis: C 53.58, H 7.33, N 24.77; $C_5H_8N_2O$ (112.13) requires C 53.55, H 7.19, N 24.98. Molecular weight (osmometric in $CHCl_3$): 121; MS (70 eV): 112 (M^+).
2b: elemental analysis: C 68.66, H 5.75, N 16.22; $C_{10}H_{10}N_2O$ (174.19) requires C 68.95, H 5.79, N 16.08.

12. R.W.Stephany, M.J.A.deBie, W.Dreuth, Org. Magn. Res. 6 (1974), 45.

13. Presently, we rationalize the results as follows: at the reaction temperature of 13°C, the primary hydroperoxide 4 may cyclize to 3 as well as to eliminate formaldehyde under concomitant ring cleavage to yield 2. At higher temperatures, dioxolane 3 starts to undergo homolysis of the O-O bond followed by elimination of CH_2O and formation of 2.

14. 5a was prepared according to ref. 15; m.p. 99-100°C; ^{1}H NMR: δ = 2.18 (t, 3H, J = 1 Hz); 3.37 (m, 2H); 3.67 (m, 2H); 7.35 (s, broad, 1H); ^{13}C NMR: δ = 21.0 (q, CH_3); 38.9 (t, CH_2); 47.4 (t, CH_2); 158.5 (s, C=N); 163.5 (s, C=O).

15. H.Masuda, M.Yoshida, T.Shibamoto, J. Agric. Food Chem. 29 (1981), 944.

16. K.Gollnick, A.Schnatterer, Photochem. Photobiol. 43 (1986), 365, and lit. cited therein.

17. A.P.Schaap, K.A.Zaklika, in "Singlet Oxygen", H.H.Wasserman, R.W.Murray, Eds., Vol. 40, Organic Chemistry, Academic Press, New York, 1979, p.173.

(Received in Germany 2 November 1987)