Tetrahedron Letters, Vol.22, No.23, pp 2213 - 2216, 1981 0040-4039/81/232213-04$02.00/0
Printed in Great Britain

PHOTOCHEMICAL BENZYL MIGRATION IN 3-PYRAZOLIN-5-ONES

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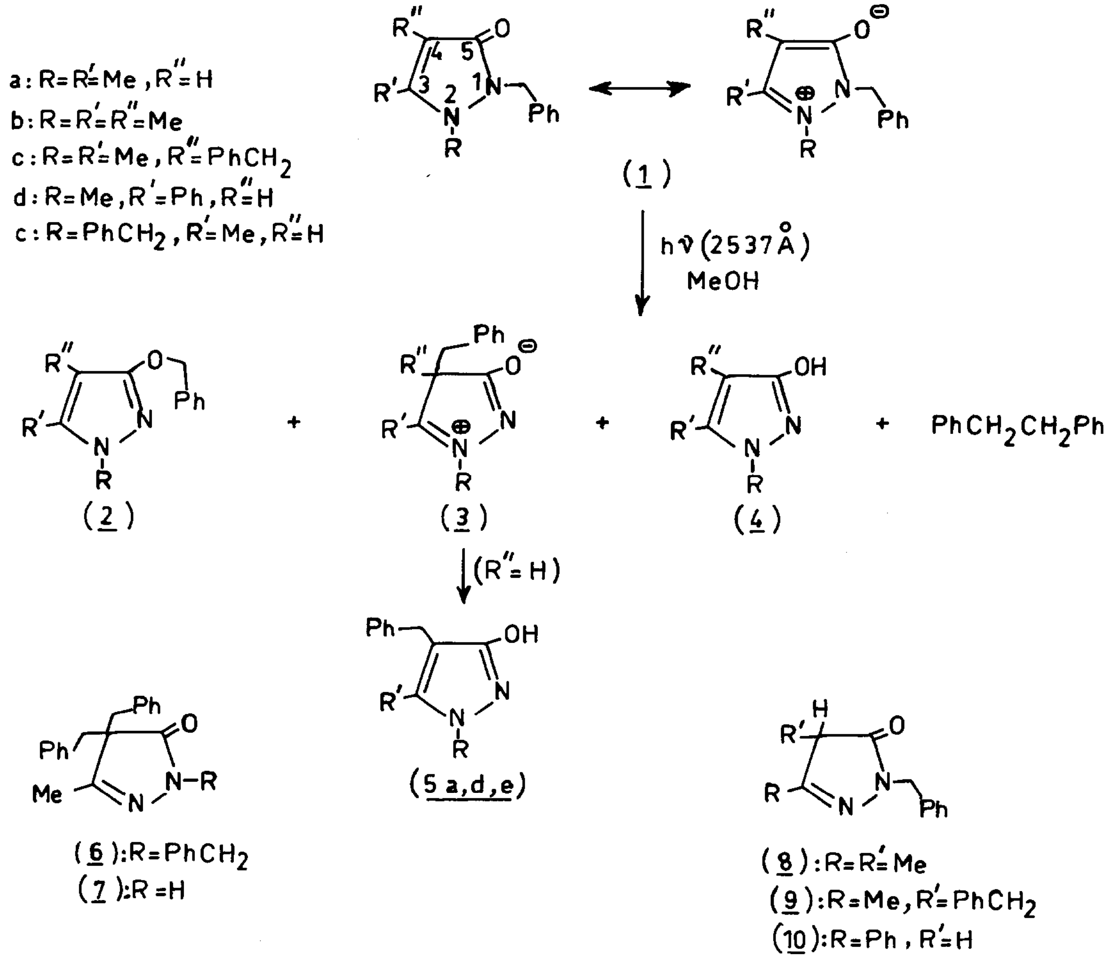
Abstract: The 3-pyrazolin-5-ones (1) undergo light induced rearrangement by N→O and N→C^4 benzyl migrations. A free radical mechanism is proposed.

The photochemical investigations on 3-pyrazolin-5-ones have, so far, been restricted to the examination of the photostability of a few important pharmaceuticals such as antipyrine, aminopyrine and Dipyrone in different media[1]. In this connection, a few related compounds have also been studied[2]. These phototransformations proceed through one or more of a variety of pathways involving rearrangement, ring cleavage, fragmentation, oxidation, and solvolysis, depending on the experimental conditions employed. A common feature of all these reactions is the fission of the ring N-N bond and destruction of the pyrazolinone ring. We now wish to report the photochemical N→O and N→C^4 benzyl migrations with retention of the integrity of the heterocyclic ring in the 3-pyrazolin-5-ones (1).

The pyrazolinones (1a)[3] and (1e)[4] were prepared by the literature methods. Compound (1b) (as monohydrate, bp[5] 160°/0.001 mm, 61%) and (1c) (as hemihydrate, mp 148°, 41%) were obtained by methylation with methyl iodide of the 2-pyrazolin-5-ones (8) (mp 145-146°) and (9) (mp 152-153°) respectively, which in turn were prepared by condensation of appropriately substituted ethyl acetoacetate with benzyl hydrazine in ethanol. Methylation of the pyrazolinone (10)[3] with dimethyl sulphate at 120° for 6 hr afforded (1d) (mp 86°, 23%). The resonance structures of these compounds are supported by their lower carbonyl IR absorption frequencies (1620-1650 cm^{-1}) than what would normally be expected for nontautomeric α,β-unsaturated-γ-lactams (1670-1730 cm^{1})[6].

Irradiation[7] of (1a-e) in methanol followed by thick-layer-chromatographic separation[8] of the photoproducts furnished the benzyloxypyrazoles (2a-e) (18-25%)[9] by N^1→O benzyl migration, the betaines (3b) [as monohydrate[10], $C_{13}H_{16}N_2O.H_2O$, mp 185-186° (dec.); 56%; IR(CHCl$_3$): 1650(s), 1620(m), 3350(m) cm^{-1}; PMR(CDCl$_3$): δ 1.37(s,3H), 2.20(d,J=1Hz,3H), 3.38(d,J=1Hz,3H)[11], 2.82, 3.32(AB q,J=13.5Hz,2H), 7.23(s,5H); UV(MeOH)[12]: λ_{max} 300nm(ϵ=4830) and (3c) [as monohydrate[10], $C_{19}H_{20}N_2O.H_2O$; mp 187° (dec.); 27%; IR(CHCl$_3$): 1650(s), 1620(m), 3350(m); PMR(CDCl$_3$): δ 2.10(s,3H), 3.05(s,3H), 2.95, 3.45(AB q,J=13.5Hz,4H), 7.22(s,10H); UV(MeOH)[12]: λ_{max} 307nm(ϵ=3940)] by N^1→C^4 benzyl migration or the hydroxypyrazoles


a: R=R'=Me, R''=H
b: R=R'=R''=Me
c: R=R'=Me, R''=PhCH$_2$
d: R=Me, R'=Ph, R''=H
c: R=PhCH$_2$, R'=Me, R''=H

(5a,d,e) (18–25%) by $N^1 \rightarrow C^4$ benzyl migration followed by prototropic shift, and the hydroxypyrazoles (4a–e) (16–32%) by fragmentation followed by hydrogen-abstraction, alongwith bibenzyl (7–17%) in every case except (1d) where the reaction was found to be very sluggish also and most of the starting material was recovered unchanged even after prolonged irradiation [120 hr as compared to 20–33 hr in the cases of (1a–c,e) for complete disappearance of the substrate]. The pyrazolinone (1e) yielded two additional compounds (6)[4] (14%) and (7) [mp 204°, 10%; IR(CHCl$_3$): 1715(s), 1610(m), 3440(m,sh,free NH), 3245(w,br, hydrogen bonded NH); PMR(CDCl$_3$): δ 2.08(s,3H), 3.02, 3.33(AB q,J=14Hz,4H), 7.37(s,10H), 8.50–9.00(bs,1H); UV(MeOH): λ_{max} 252nm(ϵ=3250)] also as a result of N^2-CH$_2$Ph bond cleavage. The monomeric nature of the betaines (3b,c) was established by molecular weight determinations (Mass spectra, differential vapour pressure method, Rast's camphor method). That the integrity of the heterocyclic ring was preserved during their photoformation was demonstrated as follows. Pyrolysis of (3b) at 200° gave the parent pyrazolinone (1b) (67%). On refluxing with 5N HCl for 5 hr, (3b) afforded the hydroxypyrazole (4b) (58%) probably by protonation at oxygen and subsequent elimination of benzyl cation[13]. Catalytic hydrogenation (10% Pd-C, r.t., 20 psi, 4 hr) of (3b) also yielded (4b) (96%)[14]. Attempted 1,3-dipolar cycloaddition of (3b) with dimethyl maleate was unsuccessful. With more reactive dipolarophiles such as dimethyl acetylenedicarboxylate and tetracyanoethylene only unidentifiable products were obtained[15].

A free radical mechanism involving the homolysis of the N^1-CH_2Ph bond and subsequent reactions of the radicals thus produced (recombination through different centres of high odd electron density followed by prototropic shift, if possible; hydrogen abstraction from the surroundings, and dimerisation) would rationalise the formation of the photoproducts (2-5) and bibenzyl. The pyrazolinone (6) arises, probably, by homolysis of the N^2-CH_2Ph bond of (1e) followed by recombination of the radicals through a different mode and substitution at the C^4 position of the intermediate 1,4-dibenzyl-3-methyl-2-pyrazolin-5-one, thus formed, with the benzyl radicals from the surroundings. The pyrazolinone (7) appears to be a secondary photoproduct formed, among other possibilities, from (6) by photocleavage of its N-CH_2Ph bond as was indicated by a separate irradiation of (6) under similar conditions.

Acknowledgement: We are grateful to the Council of Scientific and Industrial Research, New Delhi for the financial support to one of us (RNR).

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3. T. Curtius, *J. Prakt. Chem.*, **85**, 37 (1912).
4. M.A. Iorio, *Gazz. Chim. Ital.*, **94**, 1391 (1964).
5. Uncorrected and refers to the bath temperature.
6. D. Seebach, *Chem. Ber.*, **96**, 2723 (1963); A.R. Katritzky and A.P. Ambler, *Physical Methods in Heterocyclic Chemistry*, Vol. 2, Ed. A.R. Katritzky, Academic Press, New York, 1963, p. 194. See also G. deStevens, A.Halamandaris, P. Wenk, and L. Dorfman, *J. Am. Chem. Soc.*, **81**, 6292 (1959), and ref. 4.
7. In a quartz tube under nitrogen atmosphere with a Rayonet Photochemical Reactor, Model RPR 208 (The Southern New England Ultraviolet Company, Middletown, Connecticut) fitted with RUL 2537 Å lamps.

8. E. Merck silica gel plates (2 mm thick), Petroleum ether-ethyl acetate mixture as the mobile phase, R_f, bibenzyl >(**2a-e**) >(**5a,d,e**) >(**4a-e**) >(**3b,c**).
9. The yields of all the photoproducts are the isolated chemical yields based on the consumed substrate. The structures of all the new compounds were fully supported by analytical and spectral (Mass, IR, PMR, UV) data and, in most of the cases, by comparison with authentic samples prepared by unambiguous routes.
10. The existence of hydrated betaines is not unknown, e.g., see E.C. Kornfeld, E.J. Kornfeld, G.B. Kline, M.J. Mann, D.E. Morrison, R.G. Jones, and R.B. Woodward, *J. Am. Chem. Soc.*, **78**, 3087 (1956); J.S. Morley, *J. Chem. Soc.*, 2280 (1959). The water of crystallisation, however, did not show up in the PMR spectra of these betaines.
11. This long range homoallylic type coupling of $H_3C-N^2—C^3-CH_3$ protons indicates considerable amount of intervening π-electron density, thus supporting the betaine structure. However, such coupling in (**3c**) resulted only in slight broadening of the peaks.
12. The absorption maxima of these betaines suffered pronounced blue shift with increasing solvent polarity, a characteristic exhibited by structurally related mesoionic and zwitterionic compounds also, e.g., see P.B. Talukdar, S.K. Sengupta and A.K. Dutta, *Ind. J. Chem.*, **9**, 1018 (1971) and references cited therein; A.M. Kiwan and H.M.N.H. Irving, *J. Chem. Soc.*, **B**, 898 (1971); H.H. Jaffe' and M. Orchin, *Theory and Applications of Ultraviolet Spectroscopy*, John Wiley and Sons, New York, 1962, pp. 155, 381.
13. These transformations may be regarded as analogous to the aromatisation of isopyrazolium iodides on heating and of 1,3,4,4-tetrasubstituted-5-hydroxy-2-pyrazolines on acid treatment respectively, R. Fusco, "Pyrazoles, pyrazolines, pyrazolidines, indazoles and condensed rings" in the *The Chemistry of Heterocyclic Compounds*, Ed. R.H. Wiley, Interscience Publishers, New York, 1967, pp. 49-53.
14. This facile hydrogenolysis of the $C-CH_2Ph$ bond is probably due to the activation by the adjacent immonium group and the formation of aromatic product, B. Murin and W. Riedl, *Chem. Ber.*, **92**, 2029 (1959); T. Kappe and E. Ziegler, *Synthesis*, 74 (1969).
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(Received in UK 20 February 1981)