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THE REARRANGEMENT OF 1-PHENYLIMINOPYRIDINIUM YLIDS TO 1,6-DIHYDROPYRIDAZINE DERIVATIVES

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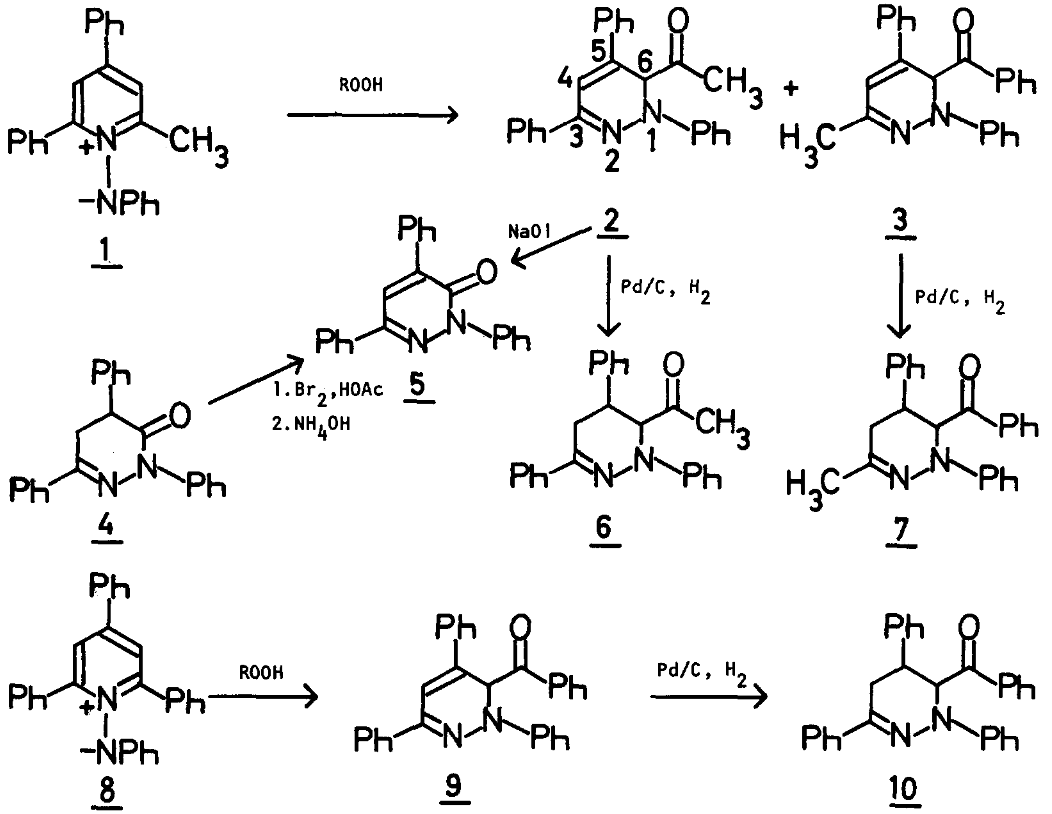
The reaction of peroxides with Nitrogen hetero-aromatic compounds is a well-travelled route for the preparation of a variety of synthetically useful N-oxides[1]. In contrast, the corresponding reaction with heterocyclic systems containing quaternary nitrogen has received little attention. Rieche and coworkers have obtained stable peroxides from the reaction of alkyl hydroperoxides and hydrogen peroxide with quinolinium and isoquinolinium salts, and with 2-(2,4-dinitroanilino)-3,4-dihydroisoquinolinium bromide[2,3]. Recently Bristol and Dittmer have briefly described the reaction of 1-methyl-3-carbamoylpyridinium chloride with alkaline hydrogen peroxide[4]. By way of enkindling renewed interest in this field we wish to report on a new peroxide induced rearrangement of 1-phenyliminopyridinium ylids to 1,6-dihydropyridazine derivatives (1 → 2 + 3 and 8 → 9). This reaction bears mechanistic resemblance to the rearrangement of pyrylium salts to furan derivatives with basic hydrogen peroxide[5] which is a method of some preparative utility for this class of compounds[6,7]. Thus, aside from mechanistic interest, our results may have directive value towards the development of a general synthetic entry for the hitherto unknown 1,6-dihydropyridazine heterocycles[8].

The addition of an equimolar amount of tert-butyl hydroperoxide to the blue-black methylene chloride solution of the ylid 1[9] at room temperature resulted in a gradual change of color (24 hr) to a bright orange solution[10]. Separation by preparative thick-layer chromatography gave the two isomeric compounds 2 (25%) and 3 (32%). The same two compounds were obtained from the reaction of 1 with cumyl hydroperoxide in methylene chloride (2: 27%; 3: 35%) and hydrogen peroxide in ethanol (2: 15%; 3: 32%). Structural assignments of 2 and 3 are based on the following spectroscopic and chemical evidence.

Compound 2, an orange-red crystalline solid, mp 146-148°, showed the following spectral data: mass spectrum (m/e, relative intensity) 352 (M^+, 6%), 309 (M^+ - $COCH_3$, 100%); ir($CHCl_3$) 1720 (C=O), 1620 (C=N) cm^{-1}; uv max (MeOH)[12] 425 (8,600), 282 (27,800), 252 (20,600), 230 (14,600) mμ; nmr ($CDCl_3$) τ 2.0-2.8 (m,15 H,aromatics), 3.0 (s,1 H,C_4-H), 4.25 (s,1 H,C_6-H), 7.96 (s,3 H,-CH_3). It gave a positive iodoform test, indicating the presence of a methyl ketone. Hydrogenation of 2 resulted in uptake of one mole of hydrogen and gave a pale yellow compound 6 [mp 194-195°; ir ($CHCl_3$) 1720 (C=O), 1600 (C=N) cm^{-1}; uv max (MeOH) 335 (15,100), 318 (18,350), 239 (18,000) mμ; nmr ($CDCl_3$) τ 2.2, 2.7 (m,15 H,aromatics), 5.1 (d,1 H,C_6-H, $J_{6,5}$= 5 Hz), 6.5 (m,1 H,C_5-H), 7.1 (m,2 H,C_4-H), 8.3 (s,3 H,-CH_3)]. In particular, the nmr spectrum[15] was in agreement with the proposed structure and the uv spectrum was very similar to that of a simple model, 1,3-diphenyl-1,4,5,6-tetrahydropyridazine[16].

Final chemical confirmation of structure 2 was secured by a preparative iodoform



reaction. Treatment of 2 with sodium hypoiodite solution for an extended period of time yielded 5 [mp 179-181°; ir ($CHCl_3$) 1650 (C=O), 1600 (C=N)cm^{-1}; uv max (MeOH) 340 (8,200), 265 (29,800), 238 (22,600), 228 (21,800)mμ; nmr ($CDCl_3$) τ 2.0-2.8 (m,aromatics)]. An authentic sample of 5, synthesized from the known[17] 1,4,5,6-tetrahydro-6-oxo-1,3,5-triphenylpyridazine (4) in two steps[18], was found to be identical with the degradation product as determined by mp, mixture mp and ir spectral criteria. The degradation of 2 to 5 may be seen as a further oxidation of the initially formed 6-carboxylic acid[19].

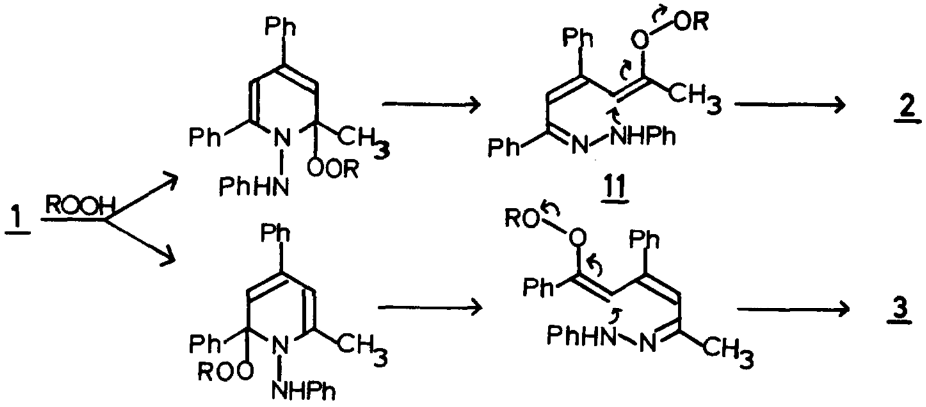
The second product (3), an orange crystalline solid, mp 158-160°, showed the following spectral properties: mass spectrum 352 (M^+,14%), 247 (M^+ - COPh,100%); ir ($CHCl_3$) 1685 (C=O), 1600 (C=N)cm^{-1}; uv max (MeOH)[12] 410 (2,650), 360 (7,500), 245 (23,800)mμ; nmr($CDCl_3$) τ 2.25-3.29 (m,15 H,aromatics), 3.60 (s,1 H,C_4-H), 3.82 (s,1 H,C_6-H), 7.12 (s,3 H,-CH_3). When compared to compound 2, the salient differences in certain spectral data for 3 (carbonyl absorption in the ir, base peak in the mass spectrum, and the C_6-H absorption in the nmr) pointed to the isomeric structural assignment as drawn.

Corroborative chemical evidence for 3 was obtained from its catalytic reduction to the dihydro derivative 7 [mp 159-160°; ir($CHCl_3$) 1685 (C=O), 1600 (C=N)cm^{-1}; uv max (MeOH) 277 (25,400), 262 (22,500)mμ; nmr ($CDCl_3$)[15] τ 2.6, 2.8 (m,15 H,aromatics), 4.3 (d,1 H,C_6-H,

$J_{6,5}$= 5 Hz), 6.5 (m,1 H,C_5-H), 7.3 (m, 2H, C_4-H), 7.85 (s,3 H,-CH_3)]. This data, in particular again the uv spectrum of 7 which may be compared with those of appropriate models[16], together with degradative definition of the ring structure presented above and mechanistic considerations discussed below, led us to assign structure 3 to the second product from the hydroperoxide reaction.

An analogous rearrangement was observed with the symmetrical ylid 8[20]; however, as expected, only a single product (9) was obtained (tert-BuOOH: 61%; PhC$(CH_3)_2$OOH: 64%; H_2O_2: 38%). Compound 9, a red crystalline solid, mp 146-148°, showed the following spectral data: mass spectrum 414 (M^+, 13%), 309 (M^+ - COPh, 100%); ir ($CHCl_3$) 1685 (C=O), 1601 (C=N)cm^{-1}; uv max (MeOH)[12] 430 (2,700), 370 (4,000), 278 (12,500), 252 (17,000) mμ; nmr (CCl_4) τ 2.09-3.18 (m,20 H, aromatics), 3.30 (s,1 H,C_4-H), 3.62 (s,1 H,C_6-H). Reduction of 9 yielded 10 [mp 224-225°; ir ($CHCl_3$) 1685 (C=O), 1601 (C=N)cm^{-1}; uv max (MeOH) 330 (22,800), 305 (14,200), 245 (25,800)mμ; nmr ($CDCl_3$)[15] 2.1, 2.8 (m,20 H, aromatics), 4.2 (d, 1 H,C_6-H,$J_{6,5}$=5Hz), 6.5 (m,1 H,C_5-H), 7.0 (m,2 H,C_4-H)]. As now may be foretold, the uv spectrum of 10 was very similar to that of 6 and that of a simple model system[16].

Reference to Rieche's work[2] and to the rearrangement of pyrylium salts[5,6a] leads to an understanding of our reaction in the mechanistic terms outlined for ylid 1[21]:



We are exploring the scope of this reaction with other 1-iminopyridinium ylids[22,23].

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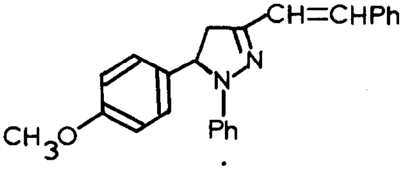

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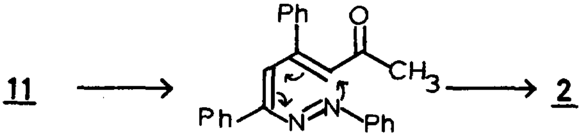

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