Photochemical and Acid-Catalyzed Reactions in the 2,3-Dihydropyridazine System (1)

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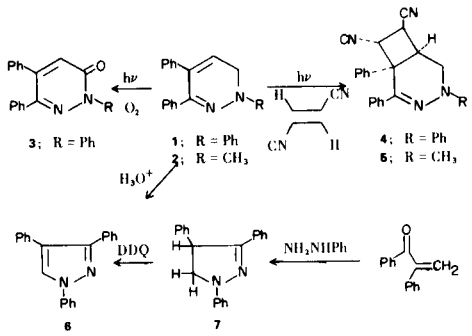
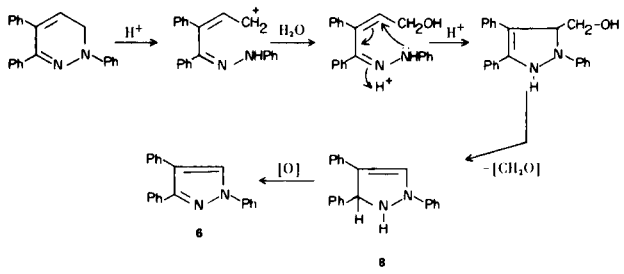
Despite the fact that photochemical isomerizations of cyclic dienes have been well documented (2,3), investigation of suitable heterocyclic analogs in light-induced reactions has been somewhat limited (4,5), even though the generality of the photochemical ring-opening reactions for systems isoelectronic with 1,3-cyclohexadienes was predicted by Barton 15 years ago (6). With a desire to discover new photochemical pathways of appropriate heterocycles, we have examined the irradiation of the 2,3-dihydropyridazine system with the expectation that this heterocyclic ring would undergo a photoinduced ring opening in a manner analogous to other azacyclohexadienes (5,7,8).

Irradiation of a solution of 2,5,6-triphenyl-2,3-dihydropyridazine (9) (**1**) in 95% ethanol in a Pyrex immersion apparatus with a 450-W Hanovia lamp led to the complete disappearance of starting material. The only product which could be isolated from the crude photolysate was 2,5,6-triphenyl-3(2*H*)pyridazinone (**3**). The formation of this compound corresponds to a photooxidation and presumably involves abstraction of one of the ring hydrogens followed by reaction of the radical produced with molecular oxygen to give a transient hydroperoxide which subsequently loses water to form pyridazinone **3** (10). When the irradiation of dihydropyridazine **1** was carried out in cyclohexane in the presence of fumaronitrile, a [2 + 2]-cycloadduct was obtained as the only identifiable photoproduct. The structure of this material was assigned as (1α,6α,7β,8α)-1,2,4-triphenyl-3,4-diazabicyclo[4.2.0]oct-2-ene,7,8-dicarbonitrile (**4**) on the basis of its spectroscopic properties (see Experimental Section). Irradiation of 2-methyl-5,6-diphenyl-2,3-dihydropyridazine (**2**) with fumaronitrile in cyclohexane afforded an analogous cycloadduct (**5**, m.p. 213-214°). From these results it can be seen that the excited state behavior of the 2,3-dihydropyridazine system differs from that of other diazacyclohexadienes. The reason for this is not obvious at this time and further work needs to be done before an adequate explanation can be offered.



During the course of our photochemical studies, we noted that the dihydropyridazine system underwent a deep-seated skeletal rearrangement when treated with aqueous acid. Thus, reaction of dihydropyridazine **1** with aqueous hydrochloric acid resulted in the formation of 1,3,4-triphenylpyrazole (**6**). The structure of **6** was assigned on the basis of its spectroscopic properties (see Experimental) as well as by comparison with an authentic sample which was prepared by treating α-phenylacrylophenone with phenylhydrazine and oxidizing the initially formed pyrazoline (**7**) with DDQ.

A mechanistic rationale which satisfactorily accounts for the formation of **6** involves initial protonation of the amino-nitrogen followed by ring opening to give an allylic carbonium ion which is captured by water. This step is followed by an acid-catalyzed internal Michael addition to give a compound which subsequently loses formaldehyde to produce a transient pyrazoline (**8**) which is oxidized under the reaction conditions.



EXPERIMENTAL

Irradiation of 2,5,6-Triphenyl-2,3-dihydropyridazine.

A solution containing 200 mg. of 2,5,6-triphenyl-2,3-dihydropyridazine (9) in 400 ml. of 95% ethanol was irradiated with a 450-W Hanovia lamp equipped with a Pyrex Filter for 2.5 hours. Removal of the solvent under reduced pressure gave a dark red oil which was taken up in methanol to yield 62 mg. of a green solid. Recrystallization of this material from ethyl acetate gave 2,5,6-triphenyl-3(2*H*)pyridazinone as a light yellow solid, m.p. 242-243°; ir (potassium bromide): 5.97 μ; uv (95% ethanol): 240 nm (ϵ, 11,000); nmr (deuteriochloroform): τ 2.81 (*s*, 1H), 2.0-2.7 (*m*, 15H); m/e 324 (M^+), 323, 296, 191, 105 and 77.

Anal. Calcd. for $C_{22}H_{16}NO$: C, 81.46; H, 4.97; N, 8.64. Found: C, 81.12; H, 5.05; N, 8.56.

The structure of 2,5,6-triphenyl-3(2*H*)pyridazinone was unambigously verified by comparison with an authentic sample synthesized by the procedure of Schmidt and Druey (11).

A solution containing 200 mg. of 2,5,6-triphenyl-2,3-dihydropyridazine and 200 mg. of fumaronitrile in 400 ml. of cyclohexane was also irradiated with a 450-W Hanovia lamp for 70 minutes. Removal of the solvent under reduced pressure gave a yellow solid which was recrystallized from ethyl acetate-hexane to give 125 mg. (51%) of (1α,6α,7β,8α)-1,2,4-triphenyl-3,4-diazabicyclo[4.2.0]-oct-2-ene-7,8-dicarbonitrile as a white powder, m.p. 233-234°; ir (potassium bromide): 4.45, 6.23, 6.68, 6.91, 7.50, 8.25, 8.41, 8.78, 9.01, 10.61, 13.08, 13.21, 13.70 and 14.35 μ; uv (95% ethanol): 338 (16,200) and 240 nm (ϵ, 16,600); nmr (pyridine-d_5): (12) τ 6.38 (dd, 1H, J = 9.0 and 7.0 Hz), 5.97 (*d*, 1H, J = 7.0 Hz), 5.1 (*m*, 3H) and 2.0-2.9 (*m*, 15H); m/e 382 (M^+), 310, 256, 255 (base), 105, 104 and 93.

Anal. Calcd. for $C_{26}H_{20}N_4$: C, 80.38; H, 5.19; N, 14.42. Found: C, 80.15; H, 5.03; N, 14.31.

Irradiation of 2-Methyl-5,6-diphenyl-2,3-dihydropyridazine with Fumaronitrile.

A solution containing 100 mg. of 2-methyl-5,6-diphenyl-2,3-dihydropyridazine (9) and 100 mg. of fumaronitrile in 200 ml. of cyclohexane was irradiated with a 450-W Hanovia lamp for 90 minutes. Removal of the solvent followed by recrystallization of the white powder gave 52 mg. of (1α,6α,7β,8α)-1,2-diphenyl-4-methyl-3,4-diazabicyclo[4.2.0]oct-2-ene-7,8-dicarbonitrile, m.p. 212-213°; ir (potassium bromide): 4.45, 6.23, 6.30, 6.46, 6.70, 6.91, 8.12, 8.48, 9.90, 10.08, 10.61, 12.09, 13.12 and 14.30 μ; uv (95% ethanol): 300 nm (ϵ, 9,100); nmr (deuteriochloroform): τ 6.92 (*s*, 3H), 6.25 (*t*, 1H, J = 9 Hz), 5.66 (*d*, J = 9.0 Hz), 6.72-7.06 (*m*, 3H) and 2.8-3.2 (*m*, 10H); m/e 326 (M^+), 255, 248, 247 (base), and 77.

Anal. Calcd. for $C_{21}H_{18}N_4$: C, 77.27; H, 5.56; N, 17.17. Found: C, 77.39; H, 5.68; N, 17.08.

Reaction of 2,5,6-Triphenyl-2,3-dihydropyridazine with Hydrochloric Acid.

A solution containing 400 mg. of 2,5,6-triphenyl-2,3-dihydropyridazine, 30 ml. of a 5.5 *N* aqueous hydrochloric acid solution and 250 ml. of dioxane was allowed to stand at room temperature for 24 hours. The reaction mixture was neutralized with a 1.0 *N* potassium hydroxide solution and was then concentrated under reduced pressure. The mixture was extracted with ether and the ethereal layer was dried over magnesium sulfate and evaporated under reduced pressure. The yellow oil obtained was recrystallized from 95% ethanol to give 1,3,4-triphenyl pyrazole (120 mg), m.p. 93-94°; ir (potassium bromide): 6.25, 6.45, 6.59, 7.13, 7.38, 8.18, 9.39, 9.44, 10.26, 10.42, 10.86, 12.25, 13.22 and 14.40 μ; uv (95% ethanol), 282 nm (ϵ, 21,000); nmr (deuteriochloroform): τ 1.96 (*s*, 1H) and 2.0-2.8 (*m*, 15H); m/e 296 (M^+, base), 193, 165, 89, 77.

Anal. Calcd. for $C_{21}H_{16}N_2$: C, 85.11; H, 5.44; N, 9.45. Found: C, 84.76; H, 5.53; N, 9.45.

The structure of 1,3,4-triphenylpyrazole was independently verified by comparison with an authentic sample which was synthesized by treating 600 mg. of 1,3,4-triphenylpyrazoline (13) with 500 mg. of 2,3-dichloro-5,6-dicyanobenzoquinone in 25 ml. of benzene for 4 hours at 80°.

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(1) This investigation was supported in part by research grant No. CA-12195-08 from the National Institutes of Health.

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(10) A singlet oxygen mechanism does not appear to be involved in the formation of **3** since the yield of **3** was substantially diminished when the irradiation of **1** was carried out in the presence of Rose Bengal.

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(12) The difference in chemical shift of the three proton multiplet in compounds **4** and **5** can be attributed to the marked difference in the conformation of these molecules as a result of nonbonded interactions.

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