Table III. Internal *vs.* External Bond Fission

Reactant	Multiplicity	Sigmatropic rearr, %	Internal bond stereoisom, %[a]	Ratio ext/int fission[b]
1a	Singlet	81	0.05	0.20
1a	Triplet	30	2	2.1
1b	Singlet	21	16	1.7
1b	Triplet	0	2	49.0

[a] Product of the per cent stereoisomerization in total reaction and the fraction occurring by internal bond fission. [b] In product formation.

tion[4] of the lack of applicability of ordinary microscopic reversibility to photochemical reactions and shows the absence of a common potential energy surface utilized in the singlet interconversion. This derives from the product excited state not being reached in such reactions.

Table III gives the relative amount of internal *vs.* external bond fission as a function of multiplicity and reveals a greater tendency for triplets to react with fission of external bonds than the corresponding singlets. This can be understood as a triplet tendency to lead to maximum odd electron separation, with an approach to a double doublet (*i.e.*, biradical) where spin change and intersystem crossing to product is facile.[6] External bond fission gives such maximum separation. Conversely, the cyclic delocalized half-reacted species involved in the internal bond sigmatropic rearrangements has the HOMO and LUMO degenerate, or nearly so, at half-reaction, and ground and excited singlet states can approach one another in energy. The delocalized array allows maximum vibronic mixing of S_0 and S_1 and facile collapse to product. It does appear that these two types of orbital situations—separated and cyclic delocalized—are involved in singlet *vs.* triplet differences more generally.

Acknowledgment. Support by the National Science Foundation and by NIH Grant No. GM-07487 is gratefully acknowledged.

(6) The preference of singlets for concerted reactions has been noted by us[7] in the case of the barrelene derivative reactions where singlets tend to cycloadd and the triplets react *via* biradicals. This general tendency has also been noted by Fukui.[8] However, there are really three factors controlling excited state reaction rates in such cases: (a) a potential rate inhibition if excited state reactant needs to change multiplicity to get to product, (b) energy gain by having maximum electron delocalization as in cyclic concerted mechanisms, and (c) energy changes due to separation of two electrons in the reacting excited state. The last factor is complex and will be considered in our full paper. Which of these three factors is controlling depends on the molecular system involved.

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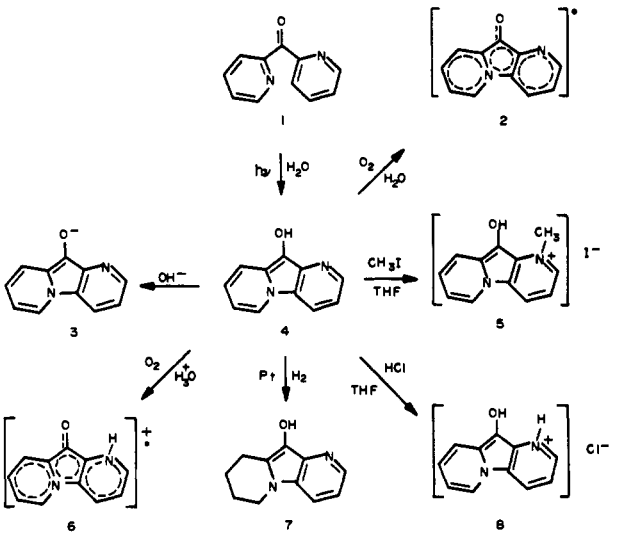
Photocyclization of Di(2-pyridyl) Ketone and 2-Benzoylpyridine in Aqueous Solution

Sir:

The mechanism of photoreduction of aromatic ketones is quite complex and still controversial.[1-20] Unlike benzophenone, which undergoes photopinacolization in a variety of solvents,[1,8,21-26] di(2-pyridyl) and di(4-pyridyl) ketones irradiated in isopropyl alcohol yield the corresponding hydrols.[20] There is general agreement by most investigators that an excited state (n-π^* triplet) of the ketone abstracts a hydrogen atom from the donor or solvent.

Here we report the unusual behavior of di(2-pyridyl) ketone (**1**) (Scheme I) and 2-benzoylpyridine (**9**) (Scheme II) when photolyzed in aqueous solution. Although

Scheme I



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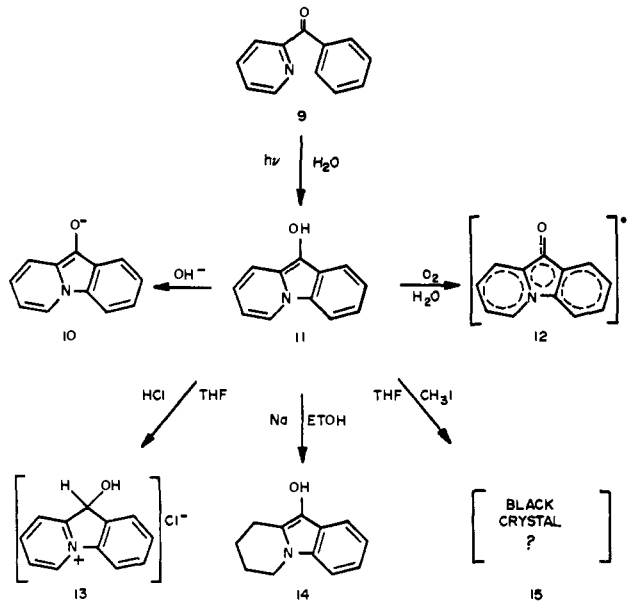
Scheme II



in isopropyl alcohol **1** yields the corresponding hydrol, the photoreduction took a completely different course in water and produced 9-hydroxydipyrido[1,2-*a*,2′,3′-*d*]-pyrrole (**4**) with a quantum yield of ~0.2. Analogously, 2-benzoylpyridine yields 3-hydroxypyrido[1,2-*a*]-indole (**11**). Apparently the tricyclo heteroaromatic ring system **4** has not been synthesized previously and cyclization involving a ring nitrogen through photolysis in a fused **5**–**6** system has not been effected before.

Irradiation of **1** or **9** in degassed aqueous solution with light from a mercury arc (254, 313, or 366 nm) precipitated brick-red **4** and orange **11**. For analytical work the products were sublimed *in vacuo*. **4** and especially **11** are air-sensitive in solution (see Schemes I and II) and somewhat less in the dry state.

Elemental analysis and molecular weight showed **4** to be an isomer of **1**. The ir spectrum shows two broad weak bands in the region 2000–4000 cm^{-1} and absence of the carbonyl band. Actually, the ir spectrum in the region above 2000 cm^{-1} resembles closely that of 8-hydroxyquinoline which has the aromatic hydroxyl and heterocyclic nitrogen in the same similar structural relationships as **4**. Furthermore, except for the fingerprint region, the ir spectrum of **5**, the *N*-methiodide of **4** (3425 and 3040 cm^{-1}), was very much like that of *N*-methyl-8-hydroxyquinolinium iodide.[27] This not only tends to confirm structure **4** but indicates that N-methylation in **4** occurs as expected at the pyridine and not at the pyrrole nitrogen. With dry HCl in degassed tetrahydrofuran, **4** gave a deep-red monohydrochloride **8**. The mass spectrum of **4** obtained by direct inlet at 195° gave M^+ at 184 and fragmentation peaks at *m/e* 183, 155, and 128 attributable to successive losses of H, CO, and C_2H_4. Other prominent peaks were found at *m/e* 167 (M^+ − OH), 92 (azepinium), 78 (pyridyl), and 51 (cyclobutadienyl). Catalytic hydrogenation of **4** at room temperature and atmospheric pressure yielded 9-hydroxy-5,6,7,8-tetrahydrodipyrido[1,2-*a*,2′,3′-*d*]pyrrole (**7**), whose nmr spectrum in D_2O–D_2SO_4 showed characteristic 2,3-disubstituted pyridine δ 7.7–8 ppm (overlapping doublet of quarters, 2 H, $H_{2,4}$), 7 (q, 1 H, H_3; $J_{2,3}$ = 5, $J_{3,4}$ = 8, and $J_{2,4}$ = 1 Hz), 3.82 (t, 2 H, H_8, J = 5 Hz), 2.77 (t, 2 H, H_5, J = 6 Hz), 1.4–2.2 (complex multiplet, 4 H, H_6 and H_7). The mass spectrum of **7** showed M^+ at *m/e* 188 and fragmentation peaks at mass units 187, 171, 160, 147, 131, and 82, presumably corresponding to losses of H, OH, CO, $CH_3CH_2CH_2$, (H, CO, and HCN), and (CO and pyridine), respectively.

When briefly exposed to air, photolyzed solutions of **1** developed a green color (λ_{max} 351, 368, 390, and 425 nm) and became intensely paramagnetic. If the diffusion of oxygen into the sample were arrested, free radical **2** appeared to be stable indefinitely (months). Also, an aqueous solution of the hydrochloride **8** is paramagnetic and yields a deep-red solution (λ_{max} 498 nm); the red radical cation **6** was very long-lived in the absence of excess oxygen. However, photolysis of **1** in aqueous hydroxide solutions or addition of base to irradiated samples generated the purple anion **3** (λ_{max} 535 nm). As expected **3** is oxygen sensitive but diamagnetic. Traces of free radical precluded recording of high-resolution nmr spectrum in NaOD–D_2O.

Compound **11** appears to have the same chemistry as that of **4** with the exception of those reactions resulting from the pyridine nitrogen in **4**. One would not expect **11** to form the hydrochloride or the methiodide with ease in the conventional way. The methiodide of **11** has not been prepared as yet. However, with dry HCl in degassed tetrahydrofuran an air-sensitive hydrochloride **13** is formed whose ir spectrum showed two broad bands above 2000 cm^{-1} (ν_{KBr} 3400 and 3000 cm^{-1}). The nmr spectrum in DMSO-d_6 of **13** showed a singlet at δ 10.04 ppm (1 H), a 2,3-disubstituted benzene and pyridinium complex multiplet at 7.45 (4 H, benzene), an overlapping complex multiplet at 8.45 and 8.27 (4 H, pyridinium), and a singlet at 2.43 (1 H). This suggested that **11** forms salts similar to the 2,3-benzopyrrocoline system.[28,29a] Also, sodium reduction of **11** in EtOH yields a yellow-orange solid, **14**. Elemental analysis, mass spectrum, and the integration of a poorly resolved nmr spectrum seem to suggest that reduction took place in the pyridine ring which reacts in a manner like the 2,3-benzopyrrocoline reduction.

The near-zero quantum yield found in solvents such as benzene and H_2O for photochemical reduction reactions of benzophenone has been attributed to high activation energy for hydrogen abstraction. We suspect that the lowest triplet state of **1**[29b] is unable to abstract hydrogen from water (HO–H bond energy is 117.5 kcal). However, the reaction is believed to proceed by way of the lowest N–π* triplet excited state of the reactants **1** and **9**. Partial rearrangements of **1** and **9** may occur through one of two resonance struc-

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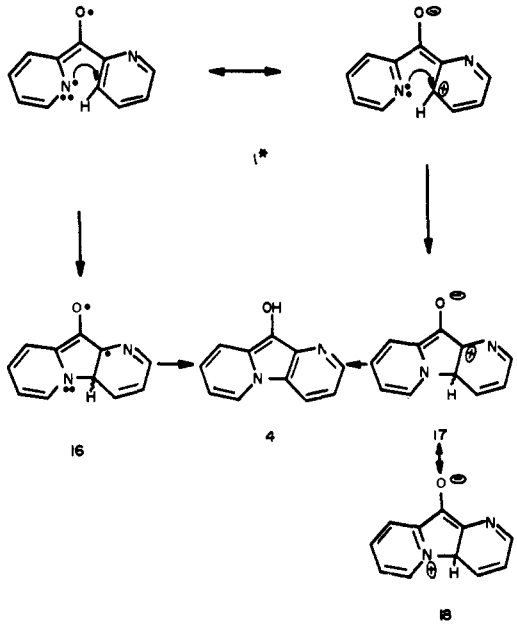
Scheme III



tures of the n–π^* excited state, namely the radical or dipolar form. The electronic distribution of the resonance forms of the excited state could conceivably produce species **16** from the radical or **17** from the dipolar structure of **1**[29b] on the reaction path to final product **4** (Scheme III). The same is proposed for **9–11**. Similar intermediates, as the zwitterion **17**, along reaction paths have been suggested and reported by Clark, *et al.*,[30] for the photocyclization of anilinopyridines to carbolines and by Linschitz and his coworkers,[31] who discussed the mechanism of oxidative photocyclization of diphenylamine to carbazole.

A considerable body of information concerning the photochemical reactions of conjugated unsaturated ketones can be rationalized on the basis of a positive charge being developed on the carbon atom β to the carbonyl group in the product-controlling state.[32] This would support the dipolar formulation for the excited state of **1**,[29b] presumably the lowest n–π^* triplet, which leads to the zwitterion **18**, a resonance form of **17**, and subsequent prototropism to **4**. Further details and related experiments will be published later.

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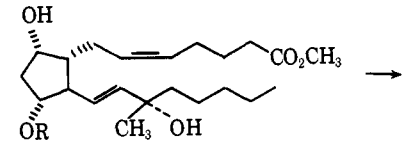
(15*S*)-15-Methylprostaglandins

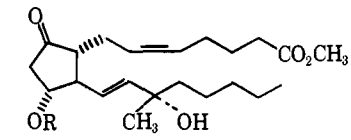
Sir:

Following studies designed to determine whether prostaglandins inert to the action of the enzyme 15-hydroxyprostaglandin dehydrogenase[1] might yet retain biological activity, we reported the preparation of several 15-methylprostaglandins and initial bioassay results.[2] We report now the preparation of (15*S*)-15-methylprostaglandin E_2, methyl ester (15-methyl PGE_2, methyl ester (**4**)). This substance and its precursor, (15*S*)-15-methylprostaglandin $F_2\alpha$, methyl ester (15-methyl $PGF_2\alpha$, methyl ester (**1**)), are the most potent prostaglandins reported to date.

Selective silylation of 15-methyl $PGF_2\alpha$, methyl ester (**1**),[2,3] mp 55–56° (ether–hexane), $[\alpha]D$ +26° (*c*



1, R = H
2, R = trimethylsilyl (TMS)



3, R = TMS
4, R = H

1.00, 95% ethanol) at C-11 was accomplished using an excess of trimethylsilyldiethylamine[4] in acetone at −45°. The resulting monotrimethylsilyl derivative **2**,[3] mp 33–35° (hexane), was oxidized with Collins reagent[5,6] to give ketone **3** which, without purification, was treated with aqueous methanol containing a trace of acetic acid. This process gave, after silica gel chromatography using mixtures of ethyl acetate and Skellysolve B, 15-methyl PGE_2, methyl ester (**4**)[3] as an oil, $[\alpha]D$ −72° (*c* 1.53, chloroform) in 45% yield from **1**.

The (*S*) configurational assignment of C-15 in **1**, originally based on relative tlc mobilities and biological activities in a wide assortment of prostaglandin C-15 epimeric pairs,[2] was confirmed by an X-ray crystallographic determination[7] of the iodophenacyl ester of 15-methyl $PGF_2\alpha$.

Neither 15-methyl $PGF_2\alpha$, methyl ester (**1**) nor 15-methyl PGE_2, methyl ester (**4**) (nor the corresponding free acids[2]) was a substrate for pig-lung 15-hydroxyprostaglandin dehydrogenase.[8] Methyl esters of $PGF_2\alpha$ and 15-methyl $PGF_2\alpha$ have similar potencies *in vitro* on the gerbil colon and *in vivo*, given intravenously, on

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