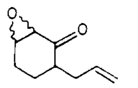
the related epoxyketones **15**[18] and **16**.[19] The lack of cyclization here is presumably due to the geometric difficulty of achieving the proper superposition of the necessary centers (cf. **17**), so that only the normal Wharton product is formed. More surprising is the lack of cyclization observed with the unsaturated epoxy ketone **18**, in which the carbonyl function is in a 1,5 relationship to the double bond, as it is in **4**: it has been reported to give the normal Wharton product in 70% yield.[20] No cyclization was observed.



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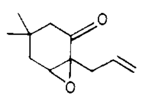

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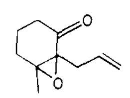

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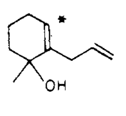

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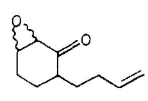
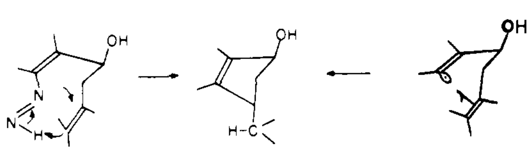


18

We now offer a few comments on possible mechanisms. The suggestion originally made that the cyclizations might involve addition of a vinyl carbanion[1] must be rejected because such a species could not survive in the methanolic medium, and would not be expected to add to an unactivated trisubstituted olefin (**8** → **9**; **12** → **13**). We have observed that formation of the cyclized products is not markedly affected by changing the medium from trifluoroethanol to *tert*-butyl alcohol, except that the overall rate of the reaction is faster, as a reflection of the faster rate of hydrazone formation in the more polar media. An intense yellow color is observed several minutes after the reactants are first mixed and fades progressively until the end of the reaction. This color is observed whether or not the reaction results in cyclization and strongly suggests a common intermediate, the vinyldiazene **19.** Indeed, the reaction mixtures exhibited a strong absorption maximum at 232 nm and a very weak one at 409 nm, as reported for simple vinyldiazenes.[21]

We believe that two possibilities may be considered seriously. One is that there is a concerted collapse of the vinyldiazene, as illustrated in **19**.[22] The other is that decomposition of the diazene gives a radical[21] which then adds to the double bond, as shown in **20.** The concerted diazene decomposition may be deceptively attractive because of the difficulty of achieving the proper arrangement of the relevant centers. With either mechanism, the difference between **18** and **4** is difficult to explain and may have to be ascribed to conformational problems in the transition state which are too subtle to interpret at this stage.



19 20

We finally point out that there is an operational difference between the two mechanisms: the new carbon-carbon and carbon-hydrogen bonds resulting from cyclization would be cis via the "concerted" diazene, but not via the radical path. We are attempting to elucidate this point.

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(14) In intriguing contrast to the successful cyclization of **12**, the epoxide of the corresponding aldehyde (citral) gives a low yield of the Wharton product, linalool, as had been reported (G. V. Nair and G. D. Pandit, *Tetrahedron Lett.*, 5097 (1966)).
(15) The reactions with hydrazine were conducted with ca. sixfold excess of hydrazine hydrate in methanol under nitrogen, and kept at 0 °C until VPC showed disappearance of starting material. The reactions which led to **5**, **9**, **11**, and **13** were thus kept for 80, 68, 12, and 24 h, respectively.
(16) Prepared from 6-allyl-2-cyclohexenone which was made by reaction of the kinetic lithium enolate of 2-cyclohexenone with allyl bromide (25–35% yield). Cf. (a) R. A. Lee, C. McAndrews, K. M. Patel, and W. Reusch, *Tetrahedron Lett.*, 965 (1973); (b) G. Stork and R. L. Danheiser, *J. Org. Chem.*, **38**, 1775 (1973).
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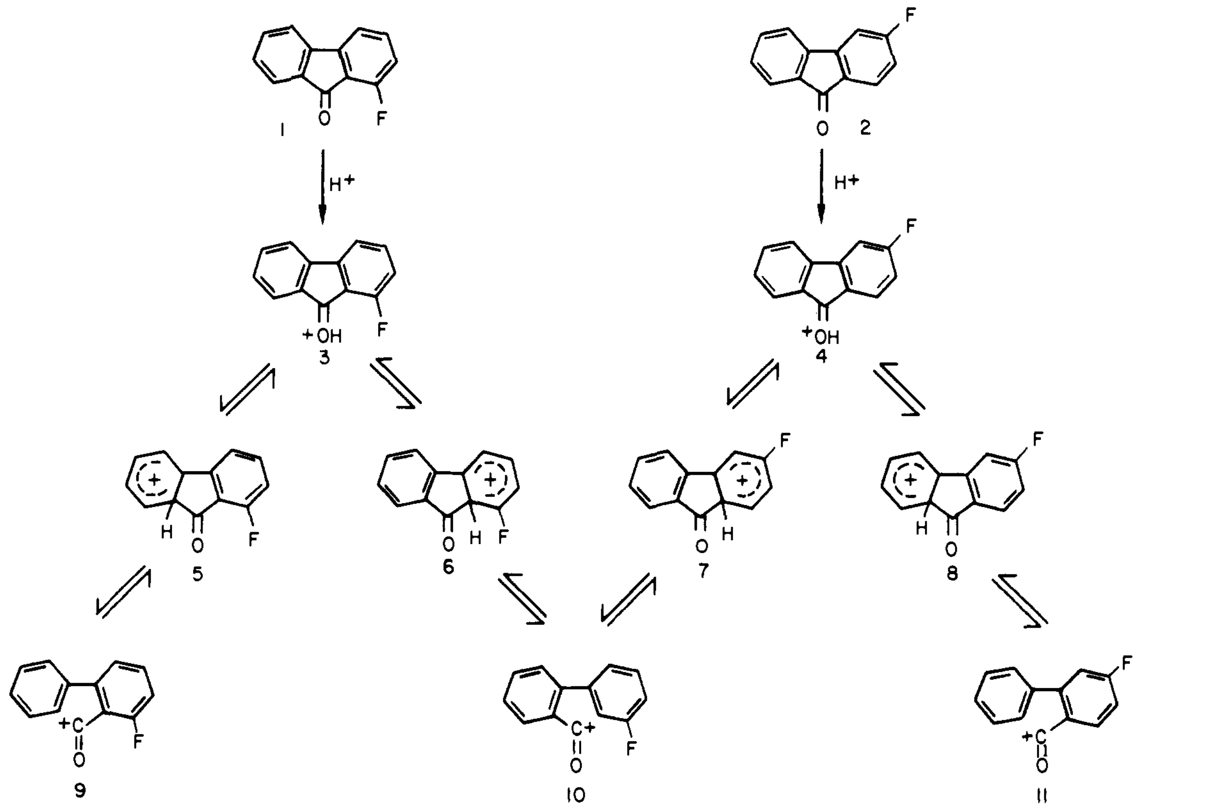
Remarkable Reversibility in Aromatic Friedel–Crafts Acylations. Para ⇌ Ortho Acyl Rearrangements of Fluorofluorenones in Polyphosphoric Acid

Sir:

"Acylation differs from alkylation in being virtually irreversible",[1] free of rearrangements and isomerizations.[2-5] This authoritative exposition of the state of the art of Friedel-Crafts chemistry[1] has been long recognized and not without reason. The difference in behavior between Friedel-Crafts acylation and Friedel-Crafts alkylation was attributed to the resonance stabilization existing between the acyl group and the aromatic nucleus.[2] It may serve as a barrier against rearrangements and reversible processes. However, if the acyl group is tilted out of the plane of the aromatic nucleus by neighboring bulky substituents, the resonance stabilization is reduced and the pattern of irreversibility of Friedel-Crafts acylation may be challenged.[2,6] The phenomenon of *reversibility* of Friedel-Crafts

Scheme I



acylation[7] has never been firmly established.[8] Its studies have been focused mainly on unusual aspects of selectivity, including deacylations, one-way rearrangements, and thermodynamic vs. kinetic control.[9,10] In the recent investigation of $\alpha \rightarrow \beta$ rearrangements of naphthyl ketones, the reverse ($\beta \rightarrow \alpha$) rearrangements could not be effected.[11,12] We report the first direct evidence of complete reversibility in aromatic Friedel-Crafts acylations, as revealed in the para $\rightleftharpoons$ ortho acyl rearrangements of fluorofluorenones in polyphosphoric acid (PPA). We note that a true reversibility, including thermodynamic equilibrium, may be realized even in the absence of the tilted carbonyl effect.[2]

Fluorofluorenones seemed to be an attractive testing ground for evaluating the notion of reversibility in Friedel-Crafts acylations, for the following reasons. (a) There is the striking directivity preference for para over ortho electrophilic substitution of *fluorine*-substituted aromatic compounds (compared, e.g., with the corresponding chloro aromatics).[13] This para orientation effect is especially pronounced in Friedel-Crafts acylations.[14] (b) There is the planarity of the 9*H*-fluorenone molecule;[15-16] its carbonyl group is not tilted out of the plane of the aromatic nucleus (in contrast, e.g., to α-naphthyl ketones[11]). (c) There is the steric resemblance between the fluorine atom and the hydrogen atom. Fluorine is the second smallest "atom" as measured at atomic radius and internuclear distance to carbon (van der Waals radii:[17] F, 1.35 Å; H, 1.2 Å, (F-H)/H, 12.5%; C-F, 1.305 Å (in fluorobenzene); C-H, 1.08 Å (in benzene); C(1)-H(1), 1.02 Å (in 9-fluorenone).[15] Thus, the introduction of a fluorine atom ortho to the carbonyl does not constitute a significant steric perturbation.[18] (d) There is the driving force of intramolecular reactions. Under such favorable circumstances, the para $\rightleftharpoons$ ortho rearrangements may perhaps be realized under thermodynamically controlled conditions, at "reasonable" temperatures. 1-Fluoro-9*H*-fluoren-9-one (**1**) was synthesized by diazotization of 1-amino-9*H*-fluoren-9-one in hydrofluoric acid (48%).[19] Purification by sublimation (95-110° (1 mm)) afforded **1** in 80% yield as yellow needles: mp 110 °C (from EtOH or cyclohexane) (lit.[20] 110-111 °C); TLC (silica gel, ether-hexane, 1:9) R_f (**1**) 0.34; VPC[21] retention time 7.5 min; ^{19}F NMR δ (CH_2Cl_2)[22] 51.4 ppm ("quartet", J_1 = 8,5 Hz, J_2 = 4.5 Hz). Treatment of **1** with PPA at 140 °C for 3.5 h followed by aqueous workup gave a crude mixture of **1** and 3-fluoro-9*H*-fluoren-9-one (**2**) in the ratio of 14:86. Preparative layer chromatography (silica gel, ether-hexane, 1:9), followed by recrystallization (EtOH or cyclohexane), afforded **2** 55% yield as yellow needles: mp 128 °C (lit.[23] mp 128 °C); TLC (silica gel, ether-hexane, 1:9) R_f (**2**) 0.52; VPC[21] retention time 5.0 min; ^{19}F NMR δ (CH_2Cl_2) 62.6 ppm ("double triplet", J_1 = 8,5 Hz, J_2 = 5.0 Hz). The structure of **2** was verified by comparison with an authentic sample of **2**[23] obtained by a rational multistep synthesis (melting point, mixture melting point, ^{19}F NMR, IR, TLC, VPC).

The rearrangement of **1** to **2** in PPA was carefully studied at 140 °C (±1°). The progress of the reaction was monitored by determining the ratio of the two isomers (VPC arnd ^{19}F NMR) as a function of time. After ~10 h, equilibrium was attained, the **1**:**2** ratio being 8:92. Prolonging the time of reaction (e.g., to 15 h) did not alter the isomeric distribution. The reverse rearrangement (**2** $\rightarrow$ **1**) would also be effected in PPA at 140 °C (±1°). After 4 h, the **1**:**2** ratio was 5:95. Equilibrium was reached after 4.5 h, with the ratio of **1**:**2** being 7:93. This ratio remained constant when the reaction was prolonged (e.g., to 8 h). The experimental evidence thus indicates that the **1** $\rightleftharpoons$ **2** rearrangement in PPA (at 140 °C) is a true reversible process, capable of reaching equilibrium from both directions. The conversion of **2** into **1** clearly establishes that the presence of a fluorine ortho to the carbonyl and a deviation from planarity of the carbonyl are not necessary conditions for the acyl rearrangements.

The **1** $\rightleftharpoons$ **2** rearrangement presumably involves protonation, deacylation, and intramolecular reacylation. A possible mechanism of the reversible rearrangement is described in Scheme I. The leading role is played by the intermediate acylium ion **10** (or the corresponding mixed anhydride with PPA) which acts as a *pivot*. It may be formed either from **1** by rearrangement of the conjugate acid **3** to the σ complex **6** followed by fission of the latter (**1** → **3** → **6** → **10**), or from **2** by the analogous sequence **2** → **4** → **7** → **10**). The **2** → **1** and **1** → **2** isomerizations are completed by the reverse sequences, respectively. The rearrangements may be degenerate not only through the reversibility of the above sequences, but also through the intermediacy of the acylium ions **9** and **11**, formed by the corresponding sequences **1** → **3** → **5** → **9** and **2** → **4** → **8** → **11**. In addition to the driving force of intramolecularity and the para-directivity preference, the following factors may participate in the various stages of the rearrangements. The deacylation of either **1** or **2** may be assisted by the antiaromatic destabilization of their conjugate acids (**3** and **4**, respectively). However, **3** may be stabilized by the intramolecular (six-membered ring) hydrogen bond formed by the *o*-fluoro substituent. The deacylation of **2** may further be assisted (relative to **1**) owing to the directivity preference for para over ortho in electrophilic substitutions of fluoro aromatics, including protonation.[13] In contrast to the $\alpha \rightarrow \beta$ rearrangements of naphthyl ketones,[11] the para ⇌ ortho acyl rearrangements of fluorofluorenones are not mutually exclusive.

As a corollary, the synthetic merits of the rearrangement are noted. The preparation of 3-substituted fluorenes (in contrast to the 1 and 2 isomers) is problematical, involving lengthy, multistep routes. The controlled rearrangement of **1** to **2** in PPA illustrates a direct rational entry into this unconventional substitution pattern in the fluorenone series.

It remains to be seen whether all three components—intramolecularity, polycyclic aromatic substrates, and fluorine substituents—are essential ingredients of complete reversibility in Friedel-Crafts acyl rearrangements.

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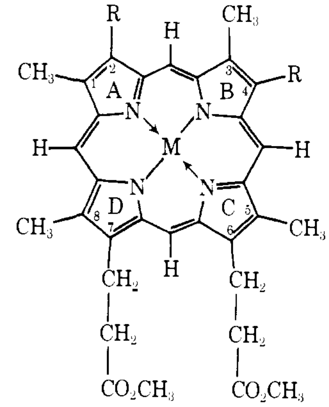
Regioselective Base-Catalyzed Exchange of Ring Methyl Protons in Protoporphyrin IX. A New Facet of Porphyrin Chemistry

Sir:

The literature documents several studies[1] of electrophilic deuteration at the methine (meso) positions of porphyrins, chlorins, and their metal complexes. However, with the exception of exchange reactions[2] which can be directly attributed to enolization, no example of a base-catalyzed exchange reaction of protons in porphyrin systems has been described. Such a phenomenon would be a further addition to the rapidly expanding literature[3] on the chemistry of porphyrin systems. In particular, susceptibility toward base-catalyzed exchange might be expected to be variable with respect to the nature of any chelated central metal ion in the inverse way to that noted for acid-catalyzed electrophilic substitution; i.e., it would be retarded by metals such as magnesium, yet be enhanced by metals such as iron.[4] In this communication we report a method for exchanging the methyl protons in protoporphyrin IX (**1**) and comment upon the nature of this novel process which provides both a convenient method for synthesis of regioselectively deuterated samples of protoporphyrin IX[5] and an insight into the mechanisms of electron delocalization in this porphyrin which is an indispensable feature of the prosthetic group in most heme proteins.



1, R = vinyl; M = 2 H
2, R = ethyl; M = 2 H
3, R = vinyl; M = $Mgpy_2$
4, R = vinyl; M = $Fe(CN)_2^-$
5, R = vinyl; M = FeX

Treatment of protoporphyrin IX (**1**) dimethyl ester[6] with CH_3ONa/CH_3OD in dimethylformamide over 5 days afforded a 50% recovery of the porphyrin. Mass spectrometric analysis indicated an extent of deuteration well in excess of that expected for exchange only of hydrogens adjacent to the two carbomethoxy functions. ^1H NMR of the exchanged **1** confirmed incorporation of deuterium in the methylenes α to the carbonyls; the integral also suggested deuteration in the largely unresolved ring methyl groups.