

Figure 1. Proton nmr spectrum of a CDCl_3 solution, 0.070 M in TPPFeCl and 0.175 M in NMIm , at 35° . The peaks for $[\text{TPPFe}(\text{NMIm})_2]^+\text{Cl}^-$ are indicated by LS (low spin), and the peaks for TPPFeCl are designated by HS (high spin). The remaining phenyl resonance for the HS species is obscured by the LS spectrum as well as by the free NMIm peak in the region -4 to -7 ppm.

for this reaction are obtained by standard line width analysis.¹⁹ The preliminary conclusions from the analysis of the effect of temperature on the proton nmr spectra are as follows.

There are two dominant ferric porphyrin species present in solution whose relative amounts depend on the porphyrin concentration and the imidazole-porphyrin ratio. The major component is the 2:1 adduct described above (peaks labeled LS in Figure 1); the minor component is the high spin (HS) complex, TPPFeCl (peaks labeled HS in Figure 1), readily identified by the previously reported²⁰ spectrum for this complex. For a solution 0.070 M in TPPFeCl and 0.175 M in NMIm , integration of the pyrrole-H peak for the two species reveals that $\sim 20\%$ of the porphyrin is present in the high-spin form. The resulting $K_{\text{eq}} \sim 10^3$ at 35° is significantly smaller than that reported⁷ for the analogous imidazole complex with hemin ($K_{\text{eq}} \sim 10^6$). The preexchange lifetimes for the coordinated NMIm in the LS form are essentially independent of the TPPFeCl and NMIm concentrations, indicating that bond rupture is the rate-determining step, as also found for the ruthenium(II) system,^{2,3} and as suggested for the substitution reactions of the hemin complexes.⁶⁻⁸ Rate data for (1) are: $\tau_1^{-1} = k_0^{298} \sim 60 \text{ sec}^{-1}$, $E_a \sim 17 \text{ kcal/mol}$, $\log A \sim 14$, indicating a small (~ 7 eu) entropy of activation. These kinetic

(19) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill, New York, N. Y., 1959, Chapter 10.

(20) G. N. La Mar, G. R. Eaton, R. H. Holm, and F. A. Walker, *J. Amer. Chem. Soc.*, in press.

parameters are surprisingly similar to those reported for the ruthenium(II) system with pyrazoles² and imidazole.³

The lability of the coordinated NMIm depends on the porphyrin substituents, with the rate of exchange an order-of-magnitude faster in $\text{OEPFe}(\text{NMIm})_2^+$. This increase in axial lability may be expected due to the more basic porphyrin ligand.²¹ For $\text{PPDMEFe}(\text{NMIm})_2^+$, the porphyrin methyl signals⁹ overlap seriously with the coordinated N-CH_3 peak, making line width analysis difficult; however, a rate intermediate to that of TPP and OEP is suggested.

At high temperatures, $\gtrsim 50^\circ$, we have obtained indirect evidence for a third species in solution which is in dynamic equilibrium with both free NMIm and $\text{TPPFe}(\text{NMIm})_2^+$, as indicated in (2), which we tentatively



suggest to be a high-spin mono- NMIm complex. These preliminary conclusions are based on the observation that, in this temperature range, the pyrrole-H peak in $\text{TPPFe}(\text{NMIm})_2^+$ begins to broaden with increasing temperature (reversibly), with a simultaneous increase in the free NMIm line width in excess of that consistent with the kinetic data for reaction 1. This increasing pyrrole-H line width can be suppressed by increasing the NMIm concentration, which is consistent with driving the equilibrium in (2) to the left. The kinetic data reported for (1) were obtained at a NMIm-TPPFeCl ratio of 10:1, and only in the temperature region where the pyrrole-H resonance line width indicates only a single imidazole complex.

Preliminary results from investigations in progress indicate that the present and related systems are excellent candidates for the elucidation of the influence of a variety of factors, such as imidazole or porphyrin substituent, solvent, counterions, on the dynamics and thermodynamics of (1) and (2), and may therefore serve as useful models for understanding the dynamics and thermodynamics of the imidazole-metal bond in metalloporphyrins.

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(21) W. S. Caughey, H. Eberspraecher, W. H. Fuchsman, and S. McCoy, *Ann. N. Y. Acad. Sci.*, **153**, 722 (1969).

(22) Fellow of the Alfred P. Sloan Foundation, 1972-1974.

Gerd N. La Mar*²²

Department of Chemistry, University of California
Davis, California 95616

F. Ann Walker

Department of Chemistry, California State University
San Francisco, California 94132

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The Wittig Modification of the Hofmann Elimination Reaction. Evidence for an α',β Mechanism

Sir:

Wittig and Polster¹ reported that trimethylcyclooctylammonium bromide (1) reacted with phenyllithium to give trimethylamine and *cis*- and *trans*-cyclooctene in a ratio of 81:19. They suggested that the mechanism in-

(1) G. Wittig and R. Polster, *Justus Liebigs Ann. Chem.*, **612**, 102 (1957).

Table I. Mass Spectral Data



| | Base/solvent | % <i>cis</i> -cyclooctene | | % <i>trans</i> -cyclooctene | | Syn k_H/k_D | Dimethyl- <i>n</i> -butylamine |
|---|---|---------------------------|----------------------------------|-----------------------------|---------------------|-------------------------|--------------------------------|
| 3 | LiNH ₂ ^a /NH ₃ (1) | 32.6 | 58.4 D ₁ ^b | 67.4 | 97.9 D ₁ | (Cis) 1.40 ^c | 11.7% D ₁ |
| | | | 41.6 D ₀ | | 2.1 D ₀ | | 88.3% D ₀ |
| 4 | LiNH ₂ ^a /NH ₃ (1) | 38.4 | 91.9 D ₁ | 61.6 | 66.9 D ₁ | (Trans) 2.02 | 18.4% D ₁ |
| | | | 8.1 D ₀ | | 33.1 D ₀ | | 81.6% D ₀ |
| 3 | MeLi/Et ₂ O | 56.5 | 57.9 D ₁ | 43.5 | 100 D ₁ | (Cis) 1.38 | 22.6% D ₁ |
| | | | 42.1 D ₀ | | 0 D ₀ | | 77.4% D ₀ |
| 4 | MeLi/Et ₂ O | 53.6 | 100 D ₁ | 46.4 | 57.8 D ₁ | (Trans) 1.37 | 24.2% D ₁ |
| | | | 0 D ₀ | | 42.2 D ₀ | | 75.8% D ₀ |
| 3 | <i>t</i> -BuLi/Et ₂ O | 44.3 | 55.2 D ₁ ^d | 55.7 | 100 D ₁ | (Cis) 1.23 | 17.9% D ₁ |
| | | | 44.8 D ₀ | | 0 D ₀ | | 82.1% D ₀ |
| 4 | <i>t</i> -BuLi/Et ₂ O | 44.2 | 100 D ₁ ^d | 55.8 | 56.3 D ₁ | (Trans) 1.29 | 25.3% D ₁ |
| | | | 0 D ₀ | | 43.7 D ₀ | | 74.7% D ₀ |
| 3 | <i>n</i> -BuLi/pentane | 56.5 | 60.3 D ₁ ^d | 43.5 | 100 D ₁ | (Cis) 1.52 | 22.9% D ₁ |
| | | | 39.7 D ₀ | | 0 D ₀ | | 77.1% D ₀ |
| 4 | <i>n</i> -BuLi/pentane | 59.5 | 100 D ₁ ^d | 40.5 | 55.7 D ₁ | (Trans) 1.26 | 23.1% D ₁ |
| | | | 0 D ₀ | | 44.3 D ₀ | | 76.9% D ₀ |

^a Reaction time was 5 hr. ^b All values are corrected for the isotopic purity of the *N,N*-dimethylcyclooctylamines. Syntheses and deuterium analyses were carried out as previously reported.² ^c This isotope effect should be corrected for amount of anti E2 elimination. ^d The amount of *trans*-cyclooctene is corrected for addition of RLi to the strained double bond. The *trans* olefin is not isomerized under the reaction conditions.

involved initial formation of an ylide followed by intramolecular proton abstraction from the β -carbon atom with resultant olefin formation. The implication of an α',β elimination was based principally upon the *cis/trans* olefin ratio. Convincing evidence for this mode of elimination was provided by the observation¹ that treatment of bromomethyldimethylcyclooctylammonium bromide with methyllithium gave a 90/10 *cis/trans* olefin ratio. Substitution on nitrogen of an activating benzyl group² also affords a 95/5 *cis/trans* olefin ratio. In addition, the Cope elimination of the amine oxide,³ which proceeds by an intramolecular five-membered cyclic transition state, affords exclusively *cis*-cyclooctene. In contrast, the normal Hofmann elimination *via* pyrolysis of the hydroxide³ and the KNH₂ induced elimination¹ of **1** in liquid ammonia afforded the *trans* olefin as the dominant product. In the latter examples, an E2 elimination was invoked.¹ Coke⁴ has recently excluded an ylide mechanism in the Hofmann elimination on the basis of deuterium labeling experiments. However, we have recently established that elimination of dimethyl-*n*-butylcyclooctylammonium iodide (**2**) in liquid ammonia with KNH₂ proceeds exclusively by an α',β elimination to afford both *cis*- and *trans*-cyclooctene in a ratio of 32:68.² In principle, the *cis/trans* ratio should be independent of the base used if an α',β elimination is involved. The discrepancy in *cis/trans* ratios observed with phenyllithium and KNH₂ prompted us to investigate the Wittig modification of the Hofmann elimination to establish the mechanism on the basis of deuterium labeling experiments.

Recent reports⁵ on base ion-pairing in elimination

(2) R. D. Bach and D. Andrzejewski, *J. Amer. Chem. Soc.*, **93**, 7118 (1971).

(3) A. C. Cope, R. A. Pike, and C. F. Spencer, *ibid.*, **75**, 3212 (1953).

(4) J. L. Coke and M. C. Mourning, *ibid.*, **90**, 5561 (1968).

(5) R. A. Bartsch, G. M. Pruss, R. L. Buswell, and B. A. Bushaw, *Tetrahedron Lett.*, 2621 (1972); M. Pankova, M. Svoboda, and J. Zavada, *ibid.*, 2465 (1972).

reactions prompted us to examine the effect of the cation influence on the stereochemistry of elimination of **2** in liquid ammonia solvent. It is conceivable that a covalent carbon-lithium bond could stabilize the nitrogen ylide intermediate and influence the *cis/trans* ratio. However, treatment of **2** with LiNH₂, NaNH₂, and KNH₂ in liquid ammonia afforded *cis/trans* ratios of 36/64, 41/59, and 32/68, respectively. Thus, the effect of the cation on the ratio of *cis*- to *trans*-cyclooctene is minor in liquid ammonia solvent. Deuterium labeling experiments established that the treatment of **3** and **4** (Table I) with LiNH₂ in liquid ammonia affords both *cis*- and *trans*-cyclooctene by an α',β elimination. Formation of *cis*-cyclooctene from **4** with the loss of 8.1% deuterium suggests the intervention of an anti E2 elimination (*ca.* 10%). The *trans* olefin is formed by >96% α',β elimination with a syn $k_H/k_D = 2.02$.

Treatment of **2** with a series of RLi reagents (R = CH₃, C₆H₅, *n*-C₄H₉, *sec*-C₄H₉, *tert*-C₄H₉) in diethyl ether solvent for 24 hr at 25° afforded *cis*- and *trans*-cyclooctene in essentially a 1:1 ratio.⁶ The *cis/trans* ratio did not vary significantly upon a fourfold increase in solvent, a twofold increase in concentration of BuLi, or upon lowering the reaction temperature to 0°. Deuterium labeling experiments (Table I) using CH₃Li and (CH₃)₃CLi as the base established that both olefins are derived from a 100% syn α',β elimination within experimental error. Formation of *trans*-cyclooctene from **3** and *cis*-cyclooctene from **4** with essentially no loss of deuterium is compelling evidence for a syn elimination. The deuterium

(6) The eliminations were carried out using 5 mmol of **2** and 10 mmol of RLi in 50 ml of ether. The *cis/trans* ratios were 57/43, 48/52, 46/54, 48/52, and 46/54, respectively, as determined by gc analysis. Comparable results were obtained with trimethylcyclooctylammonium iodide and the *cis/trans* ratios were ~ 60/40. The difference in *cis/trans* ratio from that reported by Wittig¹ probably reflects the inadequacy of the infrared analysis.

content initially present in **3** and **4** was found either in the product olefins or in the dimethyl-*n*-butylamine. This result precludes all mechanisms other than an intramolecular elimination and also the exchange of hydrogen in the dimethyl-*n*-butylamine under the reaction conditions. The results of this study are thus analogous to those reported² when KNH₂ was used as the base. The observation of both olefins being derived completely by a syn α',β elimination allows the direct measure of the kinetic isotope effect for the formation of both olefins (Table I). The isotope effects are comparable with those observed in liquid ammonia with LiNH₂ as the base. Thus, the cis/trans ratio of olefins is not markedly affected by a difference in base strength of the RLi. However, a measurable difference in product composition exists from our results in liquid ammonia despite the fact that identical ylide mechanisms are operating in both cases.

The increase in the amount of cis olefin formed when the solvent polarity was decreased on going from liquid ammonia to diethyl ether suggested the possibility of a solvent effect. Treatment of **2** with *n*-butyllithium, *sec*-butyllithium, and *tert*-butyllithium for 24 hr at 25° in pentane solvent afforded cis/trans ratios of 66/34, 59/41, and 60/40, respectively. A fourfold increase in the amount of solvent did not alter the cis/trans ratio when *n*-butyllithium was the base. However, when the *n*-butyllithium concentration was increased by a factor of 4 and the *sec*-butyllithium concentration was increased by a factor of 2.5, the observed cis/trans ratios were 85/15 and 87/13, strongly suggesting the intervention of a surface phenomenon in this heterogeneous reaction medium. Deuterium labeling experiments with *n*-butyllithium clearly established that the $\alpha'\beta$ mechanism was also operating in pentane solvent.

Thus, the different ratios of *cis*- and *trans*-cyclooctene formed under different reaction conditions does not have the mechanistic significance that previous investigators have ascribed to it. One explanation for the change in product composition could be an aggregation phenomenon. This should be particularly true in non-polar solvents such as pentane where the nitrogen ylide will be destabilized and many form a heterogeneous aggregate with the alkyllithium reagents. The degree of association of the carbanion basic center of the ylide intermediate with the lithium alkyl could influence its effective basicity, thereby increasing the amount of the more stable cis stereoisomer. Finally, it should be emphasized that not all trimethylalkylammonium salts undergo $\alpha'\beta$ elimination reactions in liquid ammonia solvent. In the *exo*-norbornyl system elimination with LiNH₂ in liquid ammonia proceeds principally by an E2 pathway.⁷

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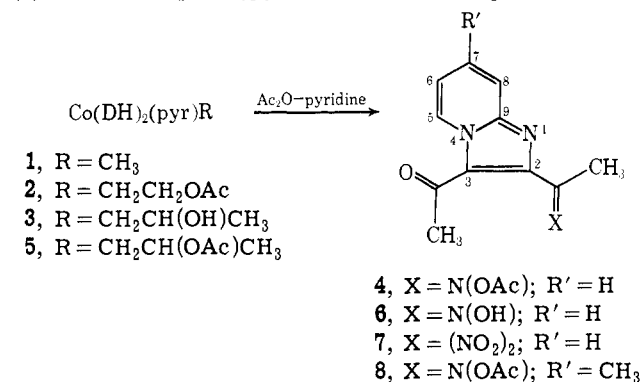
(7) Unpublished results.

Robert D. Bach,* Kenneth W. Bair, Denis Andrzejewski
Department of Chemistry, Wayne State University
Detroit, Michigan 48202
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Degradation of Alkyl(pyridine)cobaloximes to Derivatives of Imidazo[1,2-*a*]pyridine

Sir:

We have found that on prolonged exposure to acetic anhydride in pyridine the alkyl(pyridine)cobaloximes¹ (**1**–**3**) undergo a remarkable degradation to a derivative (**4**) of imidazo[1,2-*a*]pyridine. For example, treatment



DH₂ = dimethylglyoxime

of 2-hydroxypropyl(pyridine)cobaloxime (**3**) with acetic anhydride (10 mol equiv) in pyridine for 24 hr at room temperature gives 2-acetoxypropyl(pyridine)cobaloxime² (**5**) in excellent yield. However, if the reaction is run for a longer time then the **5** initially formed reacts further. After 9 days at room temperature (or 2 days at 60°), analysis of the reaction mixture shows the absence of **5** and the presence of the new compound **4**^{3–5} which has been isolated⁶ in yields up to 30%. Compound **4** was easily deacetylated (catalytic NaOCH₃-CH₃OH, 20°, overnight) giving **6**^{4,7} which on oxidation with concentrated nitric acid (5 min, 20°) gave a quantitative yield of a geminal dinitro compound **7**.^{4,8} Hence, **6** contains the structural unit C=NOH, which is O-acetylated in **4**. The presence of a 2-pyridoneimine system in **4**, **6**, and **7** was inferred from the characteristic⁹ splitting patterns in the nmr signals due to the protons of their pyridine ring.

(1) Alkyl(base)cobaloximes are bis(dimethylglyoximate)cobalt complexes with an alkyl group and a Lewis base as axial ligands. For a review of their chemistry, see G. N. Schrauzer, *Accounts Chem. Res.*, **1**, 97 (1968).

(2) B. T. Golding, H. L. Holland, U. Horn, and S. Sakrikar, *Angew. Chem., Int. Ed. Engl.*, **9**, 959 (1970).

(3) Mp 112°; C₁₃H₁₃N₃O₅⁴; nmr⁸ (CDCl₃) δ 2.27 (s, 3 H, OCOCH₃), 2.57 (s, 3 H, CH₃), 2.64 (s, 3 H, CH₃), 7.08 (d of d, 1 H, $J_{56} + J_{57} = 13.5$ Hz, 6-*H*), 7.49 (d of d, 1 H, $J_{57} = 6.5$, $J_{78} = 8.9$ Hz, 7-*H*), 7.73 (d, 1 H, $J_{78} = 8.9$ Hz, 8-*H*), 9.69 (d, 1 H, $J_{56} = 6.9$ Hz, 5-*H*); ir (CHCl₃) 1770, 1640 cm⁻¹.

(4) Satisfactory combustion analyses (C, H, and N) and high-resolution mass spectral data have been obtained for this compound.

(5) Spectral assignments are made on the basis of the structure rigorously established later.

(6) **4** was obtained by evaporating the reaction mixture and extracting the residue with dichloromethane, followed by chromatography on silica gel, evaporation, sublimation (ca. 100° (0.001 mm)), and recrystallization. In subsequent preparations, the crude sublimate of **4** was deacetylated to **6**, which was recrystallized (ethyl acetate). This procedure gives higher yields of pure material.

(7) Mp 191°; C₁₁H₁₁N₃O₅⁴; nmr similar to that of **4** excepting the loss of the signal at δ 2.27 and the gain of a signal at 9.30 (br, 1 H, OH); ir (CHCl₃) free and bonded O-H stretch at 3583 and 3320 (br) cm⁻¹, respectively; uv (CH₃OH) λ_{max} 219 (sh, ϵ 16,800), 227 (ϵ 17,350), 252 (ϵ 25,000), and 311 nm (ϵ 7,510).

(8) Mp 177°; C₁₁H₁₀N₃O₅⁴; nmr⁸ (CDCl₃) δ 2.65 (s, 3 H, CH₃), 2.70 (s, 3 H, CH₃), 7.31 (d of d, 1 H, $J_{78} = 11.3$, $J_{57} = 7.0$ Hz, 7-*H*), 7.71 (d, 1 H, $J_{78} = 11.3$ Hz, 8-*H*), 7.83 (t, 1 H, $J_{56} + J_{57} = 14.0$ Hz, 6-*H*), 8.91 (d, 1 H, $J_{56} = 6.7$ Hz, 5-*H*); ir (CH₂Cl₂) 1656, 1580 (C(NO₂)₂) cm⁻¹.

(9) See e.g., W. W. Paudler and H. L. Blewitt, *Tetrahedron*, **21**, 353 (1965).