Communications to the Editor

[3,3] Sigmatropic Rearrangements in Indoloazabicyclo[3.3.1]nonene Systems. Reversal of the Stereofacial Selectivity in the Claisen vs the Ortho Ester Claisen Rearrangement

Lin-Hua Zhang, Mark L. Trudell, Sean P. Hollinshead, and James M. Cook*

Department of Chemistry
University of Wisconsin—Milwaukee
Milwaukee, Wisconsin 53201

Received May 5, 1989

The synthetic utility of the Claisen rearrangement, including related [3,3] and [2,3] sigmatropic transformations, is widely accepted and has been employed with impressive success for carbon–carbon bond formation to provide highly functionalized acyclic systems.[1] In relation to studies[2] directed toward the synthesis of macroline-related alkaloids,[3] the inversion of the stereofacial selectivity of the [3,3] sigmatropic rearrangement in rigid indoloazabicyclo[3.3.1]nonenes has been observed and investigated. The following is an account of these studies, as well as an evaluation of this approach for the enantiospecific synthesis of indole alkaloids.

The acid-catalyzed ortho ester Claisen rearrangement[4] of allylic alcohol **1** (R = CH_2Ph)[5,6] with trimethyl orthobutyrate furnished the desired 15,16-functionalized system in 79% yield isolated as a mixture of diastereoisomers **3a–c** in a ratio of 63:30:7 (Scheme I). The [3,3] sigmatropic rearrangement occurred with a high degree of stereofacial selectivity from the β-face of the allylic alcohol (α:β > 13:1 for H_a).[7a] Confirmation of the stereochemical assignment[7a] of the major diastereoisomer **3a** was obtained from X-ray crystallography (see Figure 1).[7b] Rearrangement had been anticipated to occur from the less hindered α-face (see later), and it was postulated that the bulky N_b-benzyl group prevented this from occurring. However, rearrangement of the N_b-methyl allylic alcohol **2** (R = CH_3) gave a similar stereochemical product distribution (**4a**:**4b**:**4c**, 62:28:10), indicating that this was not the case. Confirmation of the stereochemistries of **4a–c** was achieved by chemical interconversion of the N_b-benzyl compounds **3a–c**

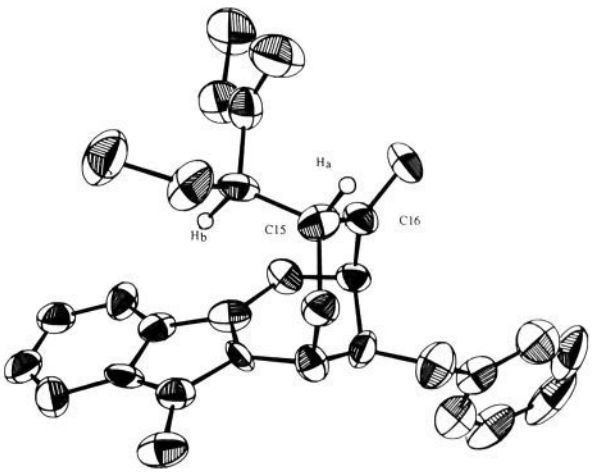


Figure 1. ORTEP plot of **3a**. Thermal ellipsoids are drawn at the 50% probability level. The hydrogen atoms have been omitted for clarity. **3a** crystallizes in the monoclinic space group $P2_1/n(14)$ with unit cell dimensions as follows: a = 15.805 (8) Å, b = 7.430 (3) Å, c = 20.567 (7) Å, β = 94.92 (4)°, V = 2406 (2) Å^3, and d_{calcd} = 1.183 g/cm^3 for Z = 4. Reflections within a 2θ range of $4° < 2\theta < 37°$ were collected with three check reflections every 120 min, yielding 2186 unique reflections, of which 1483 were coded observed, $I > 3\sigma(I)$. The structure was refined to R = 0.044, R_w = 0.045, $w = 0.8294(\sigma^2(|F| + 0.002\,057)F^2)^{-1}$.

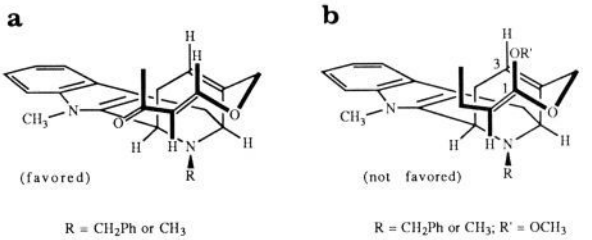
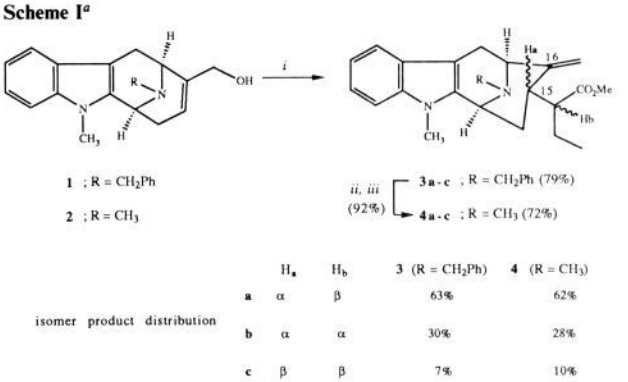


Figure 2.

Scheme I[a]



		H_a	H_b	3 (R = CH_2Ph)	4 (R = CH_3)
isomer product distribution	a	α	β	63%	62%
	b	α	α	30%	28%
	c	β	β	7%	10%

[a] Reagents: (i) $(MeO)_3C$–^{n}Pr/2,4,6-trimethylbenzoic acid (2%)/125 °C; (ii) $CH_3SO_3CF_3/CH_2Cl_2$/reflux; (iii) HCO_2NH_4/Pd–C/CH_3OH/25 °C.[8]

(1) Ziegler, F. E. *Acc. Chem. Res.* **1977**, *10*, 232. Bennett, G. B. *Synthesis* **1977**, 589. Ziegler, F. E. *Chem. Rev.* **1988**, *88*, 1423.

(2) (a) Cain, M.; Campos, O.; Guzman, F.; Cook, J. M. *J. Am. Chem. Soc.* **1983**, *105*, 907. (b) Hollinshead, S. P.; Grubisha, D. S.; Bennett, D. W.; Cook, J. M. *Heterocycles* **1989**, *29*, 529.

(3) Hesse, M.; Hurzeler, H.; Gemenden, C. W.; Joshi, B. S.; Taylor, W. I.; Schmid, H. *Helv. Chim. Acta* **1965**, *48*, 689. Hesse, M.; Bodmer, F.; Gemenden, C. W.; Joshi, B. S.; Taylor, W. I.; Schmid, H. *Helv. Chim. Acta* **1966**, *49*, 1173. Waldner, E. E.; Hesse, M.; Taylor, W. I.; Schmid, H. *Helv. Chim. Acta* **1967**, *50*, 1926. Kishi, T.; Hesse, M.; Vetter, W.; Gemenden, C. W.; Taylor, W. I.; Schmid, H. *Helv. Chim. Acta* **1966**, *49*, 946. Kishi, T.; Hesse, M.; Gemenden, C. W.; Taylor, W. I.; Schmid, H. *Helv. Chim. Acta* **1965**, *48*, 1349. Kahn, Z. M.; Hesse, M.; Schmid, H. *Helv. Chim. Acta* **1967**, *50*, 1002. Elderfield, R. C.; Nordman, C. E.; Kumra, S. K. *J. Am. Chem. Soc.* **1965**, *87*, 2059. Nordman, C. E.; Nakatso, K. *J. Am. Chem. Soc.* **1963**, *85*, 353. Burke, D. E.; Cook, J. M.; LeQuesne, P. W. *J. Am. Chem. Soc.* **1973**, *95*, 546. Cook, J. M.; LeQuesne, P. W.; Elderfield, R. C. *J. Chem. Soc. D* **1969**, 1306. Burke, D. E.; DeMarkey, C. A.; LeQuesne, P. W.; Cook, J. M. *J. Chem. Soc., Chem. Commun.* **1972**, 1346. Burke, D. E.; Cook, G. A.; Cook, J. M.; Haller, K. G.; Lazar, H. A.; LeQuesne, P. W. *Phytochemistry* **1973**, *12*, 1467.

(4) (a) Johnson, W. S.; Werthermann, L.; Bartlett, W. R.; Brockson, T. J.; Li, T.-t.; Faulkner, D. J.; Peterson, M. R. *J. Am. Chem. Soc.* **1970**, *92*, 741. (b) Raucher, S.; McDonald, J. E.; Lawrence, R. F. *Tetrahedron Lett.* **1980**, 4335. (c) Raucher, S.; Huang, K. J.; McDonald, J. E. *Tetrahedron Lett.* **1979**, 3057. (d) Raucher, S.; McDonald, J. E.; Lawrence, R. F. *Tetrahedron Lett.* **1980**, 4355. (e) Daub, G. W.; Teramura, D. H.; Bryant, K. E.; Burch, M. T. *J. Org. Chem.* **1981**, *46*, 1485.

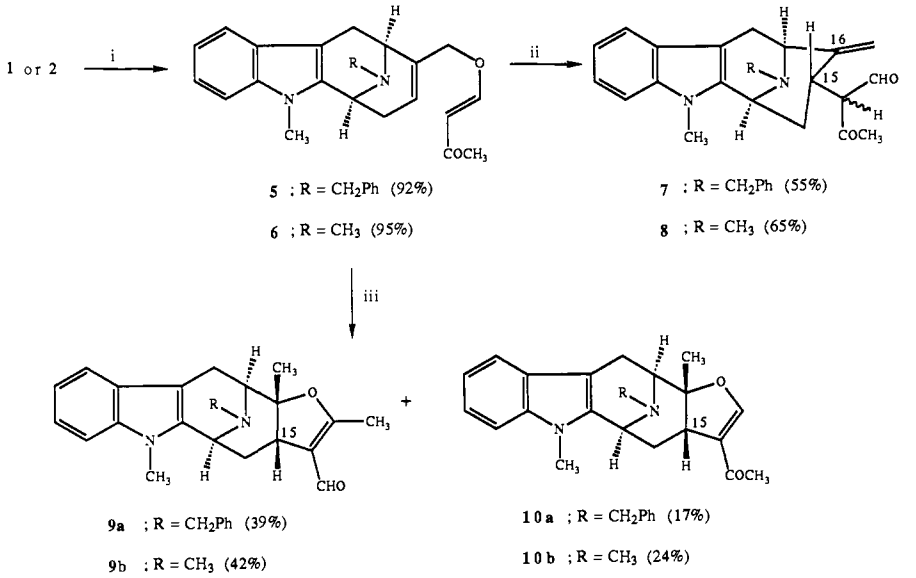
(5) Trudell, M. L.; Cook, J. M. Studies Directed Toward the Synthesis of the Indole Alkaloid Suaveoline. 20th Central Regional Meeting of the American Chemical Society, West Virginia University, Morgantown, WV, June 1–3, 1988; Abstract 139.

(6) Trudell, M. L.; Cook, J. M. *J. Am. Chem. Soc.* **1989**, *111*, 7504.

(7) (a) The stereochemical outcome of the reaction was determined by ^{1}H NMR spectroscopy; diastereoisomeric ratios were determined via integration of the ethyl (CH_2CH_3) protons (for **3a–c**) and the N_b-methyl (N_b-CH_3) protons (for **4a–c**) in the ^{1}H NMR spectra of the mixtures. (b) We thank Desirée S. Grubisha and Dennis W. Bennett for the X-ray crystallographic structure determination of **3a**.

0002-7863/89/1511-8263$01.50/0

Scheme II[a]



[a] Reagents: (i) $(MeO)_3CC^nPr$/2,4,6-trimethylbenzoic acid (2%)/125 °C; (ii) $CH_3SO_3CF_3/CH_2Cl_2$/reflux; (iii) HCO_2NH_4/Pd–C/CH_3OH/25 °C.[8]

into the N_b-methyl congeners **4a–c** (Scheme I). These bases were indistinguishable, spectroscopically, from **4a–c** prepared directly from **2** via the ortho ester Claisen rearrangement.

In contrast, when either of the enol ethers **5** (R = CH_2Ph) or **6** (R = CH_3)[9] (Scheme II) was heated at 135–140 °C (PhH, sealed tube), the desired β-dicarbonyl compounds **7** and **8** were obtained as single diastereoisomers at C-15 in 55% and 65% yields, respectively. Higher reaction temperatures (180 °C) afforded the enol ethers **9a/10a** and **9b/10b**.[9] In this case, the thermal Claisen rearrangement has occurred stereospecifically from the desired α-face of the azabicyclo[3.3.1]nonene to provide **7** and **8**, respectively, presumably via the α-face of **1** and **2** via a chair transition state (see Figure 2a).[10] As illustrated, the α-face is more accessible to attack, for approach from the β-face of the double bond would encounter steric interactions with the indolomethylene bridge. Execution of the Claisen rearrangement, stereospecifically, from the desired α-face has important implications for the enantiospecific synthesis of the macroline-related and sarpagine/ajmaline alkaloids since these intermediates **9/10** have been functionalized at C-15 with the natural stereochemistry common to all three alkaloid families.

The transition state of the ortho ester Claisen rearrangement is often partitioned between chair- and boat-like conformations,[11] and the effect of the *Z* and *E* isomers on the stability of these conformations in the present system has been analyzed.[5] Although it is well-known that *E* isomers are favored in the ortho ester rearrangement,[4a,d] the steric constraint imposed upon the system by the rigid indolomethylene bridge, however, has resulted in partitioning between transition states. The preferred conformations which lead to the transition states for formation of **3a/4a**, **3b/4b**, and **3c/4c** are outlined in Figure 3a–c. As illustrated, alkenic esters **3a/4a** and **3b/4b** arise, predominantly via boat transition states,[4a,e,11] while the minor isomer **3c/4c** presumably arises from the chair transition state related to Figure 3c. Depicted in Figure 4a–c are the corresponding conformations felt too high in energy for consideration as potential contributors to transition states in this series. The unfavorable interactions in these conformations are graphically illustrated, as shown. For example, there are severe steric interactions present in either transition state represented by Figure 4b or 4c, and there are additional interactions with the indolomethylene bridge for **4b**. The transition state represented by Figure 4a is thought to be disfavored for reasons outlined below.

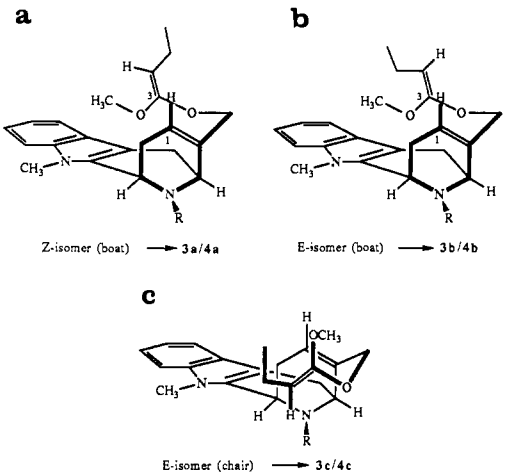


Figure 3. Proposed intermediates. R = CH_2Ph (**3a–c**) or CH_3 (**4a–c**).

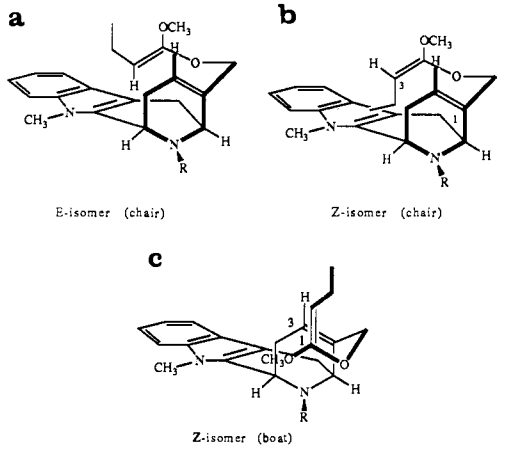


Figure 4. Not favored. R = CH_2Ph or CH_3.

(8) Anwer, M. K.; Spatola, A. F. *Synthesis* **1980**, 929.

(9) (a) Zhang, L.-H.; Cook, J. M. *Heterocycles* **1988**, *27*, 1357. (b) Zhang, L.-H.; Cook, J. M. *Heterocycles* **1988**, *27*, 2795. Zhang, L. H.; Cook, J. M. Manuscript in preparation.

(10) Ireland, R. E.; Vevert, J. R. *J. Org. Chem.* **1980**, *45*, 4259. Ireland, R. E.; Mueller, R. H.; Willard, A. K. *J. Am. Chem. Soc.* **1976**, *98*, 2868. Rhoads, S. J.; Raolins, N. R. *Org. React.* (*N.Y.*) **1977**, *22*, 1 and references cited therein.

(11) Cave, R. J.; Lythgoe, B.; Metcalfe, D.; Waterhouse, I. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1218.

In summary, the ortho ester Claisen rearrangement has occurred in this system predominantly (9–13:1) from the top face of the double bond, while the Claisen rearrangement has taken place exclusively from the bottom face of the olefinic system. Since the Claisen rearrangement has presumably occurred via a chair transition state[10] (Figure 2a), this work provides strong evidence that the ortho ester rearrangement must have occurred predominantly through boat transition states (see Figure 3a,b). Evidently attack from the α-face via the chair transition state (Figure 2a) is favored in the Claisen rearrangement, while the analogous transition state (Figure 2b) for the ortho ester Claisen rearrangement is not. Moreover, substitution of the smaller N_b-methyl group for the N_b-benzyl function had virtually no effect on the product ratios in either of the rearrangements. This suggests that the interaction between the enol ether group (OCH_3) and the proton located 1,3 to it in the ortho ester rearrangement may play a role in destabilizing this transition state (Figures 2b and 4a) relative to that of the Claisen rearrangement (Figure 2a) rather than the N_b-substituent.

These represent the first cases in a rigid system wherein the Claisen rearrangement has proceeded via a chair transition state while the corresponding ortho ester Claisen rearrangement, under similar stereochemical constraints, has proceeded principally by the boat transition state. Alkenic esters **3a–c** have recently been converted into suaveoline,[6] while work is currently in progress to convert the 1,3-dicarbonyl compound **8** into alstonerine.[3] Further work (computational and chemical) is currently under way to fully understand the reasons for the reversal in stereofacial selectivity in the Claisen and the ortho ester Claisen rearrangements.

Acknowledgment. We thank Dr. Suzanne Wehrli and Dr. David Nettesheim for the 500-MHz and 250-MHz NMR spectra. This work was supported by a grant from the NIH (NS-22287).

Supplementary Material Available: Details of the structure determination, crystal data, and lists of fractional coordinates and anisotropic temperature factors for **3a** (4 pages). Ordering information is given on any current masthead page.

Controlled One-Dimensional Energy Migration in the Crystals of Binuclear Platinum(II) Diphosphite Complexes[1]

Tatsuya Uchida, Haeng-Boo Kim,* Takashi Hiraga, and Shigeo Tazuke†

Research Laboratory of Resources Utilization
Tokyo Institute of Technology, 4259 Nagatsuta
Midori-ku, Yokohama 227, Japan

Received May 23, 1989

Energy migration among chromophores of identical nature is one of the simplest but most fundamental photophysical processes in particular in molecular aggregate systems. Nevertheless, its quantitative rate analysis has not been reported until very recently.[2] The energy transfer process involving either the singlet or triplet state is highly relevant to material science (e.g., photodegradation of polymers[3]), photoreactions (energy harvesting and sensitization[4]), and expected photonic devices.[5] In the last case, the controlled one-dimensional flow of energy and/or electrons is a key process, which has hardly been surveyed. To test the possibility, we chose $X_4[Pt_2(P_2O_5H_2)_4]$ (X = Na^+, K^+, Et_4N^+, and $(n\text{-}Bu)_4N^+$) crystals and measured the laser-induced phosphorescence.[6,7] Judging from its crystal structure[8b] and preceding discussion on the nature of orbital interactions,[8c] the possible path for the triplet energy migration is exclusively along the Pt–Pt direction (i.e., along the z axis). In the well-grown crystals, the phosphorescence decay profile is nonsingle exponential and dependent on the excitation density. The lower the excitation density, the better the decay profile analysis by a single exponential function. This indicates explicitly the participation of T–T annihilation even at room temperature under atmospheric pressure.[9] It should be noted that *the phenomenon is observed only for well-grown crystals but not for amorphous samples* which have random arrangement of the Pt_2 unit.[10] This supports the interpretation of anisotropic energy migration via overlapped $5d_{z^2}$ orbitals directing to the z axis in the crystals.

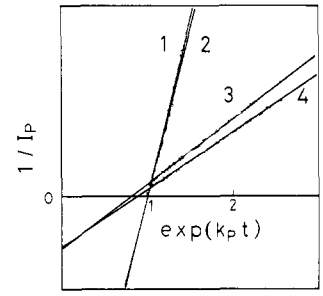


Figure 1. Plots expressing the participation of a bimolecular decay path according to eq 2 for $X_4[Pt_2(P_2O_5H_2)_4]$; X = Na^+ (1), K^+ (2), Et_4N^+ (3), and $(n\text{-}Bu)_4N^+$ (4). $1/k_P$ was taken as 4.6 μs.[18] Phosphorescence decays were measured by the combination of a pulsed Nd:YAG laser (Spectron, SL803, 355 nm, pulse width ~ 13 ns), a photomultiplier (R-928, Hamamatsu Photonics), and a storage oscilloscope (TS-8123). The data were averaged over 30 measurements.

When T–T annihilation is involved, the kinetic expression of triplet state decay is given by eq 1 and 2, where n_T, k_P, and k_{TT}

$$-dn_T/dt = k_P n_T + k_{TT} n_T^2 \quad (1)$$

$$1/n_T(t) = (1/n_T(0) + k_{TT}/k_P)\exp(k_P t) - k_{TT}/k_P \quad (2)$$

are the population of T_1, the reciprocal of the normal triplet lifetime, and the T–T annihilation rate constant, respectively. The data of phosphorescence decay is plotted in the form of eq 2 in Figure 1, the negative intercept giving the T–T annihilation rate constant.[9,11]

Aiming at control of the energy migration probability from one site to the nearest neighbor, we modulate the distance between the Pt_2 units by changing the countercation from K^+ to Na^+, Et_4N^+, and $(n\text{-}Bu)_4N^+$.[12] The phosphorescence decay curves are similarly analyzed by eq 2, and the results are presented in Figure 1 as well. As we expect, the larger the size of the countercations,

† Deceased on July 11, 1989.

(1) The major part of this paper was reported at the 58th Annual Meeting of Chemical Society of Japan, Kyoto, April 1989; preprints 2ID12.

(2) Ikeda, T.; Lee, B.; Kurihara, S.; Tazuke, S.; Ito, S.; Yamamoto, M. *J. Am. Chem. Soc.* **1988**, *110*, 8299.

(3) Guilett, J. *Polymer Photophysics and Photochemistry*; Cambridge Univ. Press: Cambridge, 1985.

(4) (a) Tazuke, S. *Contemporary Topics in Polymer Science*; Plenum Press: New York, 1984; Vol. 4, p 871. (b) Yamazaki, I.; Tamai, N.; Yamazaki, T. *J. Phys. Chem.* **1987**, *91*, 3572.

(5) Balzani, V.; Moggi, L.; Scandola, F. *Supramolecular Photochemistry*; NATO ASI, C-214; 1987; p 1.

(6) (a) Roundhill, M. A.; Gray, H. B.; Che, C.-M. *Acc. Chem. Res.* **1989**, *22*, 55. (b) Zipp, A. P. *Coord. Chem. Rev.* **1988**, *84*, 47.

(7) (a) Hiraga, T.; Uchida, T.; Kitamura, N.; Kim, H.-B.; Tazuke, S.; Yagi, T. *J. Am. Chem. Soc.* **1989**, *111*, 7466. (b) Che, C.-M.; Butler, L. G.; Grunthaner, P. J.; Gray, H. B. *Inorg. Chem.* **1985**, *24*, 4662. (c) The preparation of $K_4[Pt_2(P_2O_5H_2)_4]$ was already reported.[7a] The corresponding Na^+ or $(n\text{-}Bu)_4N^+$ salt was obtained according to ref 7b or 8a, respectively. The Et_4N^+ salt was obtained by exchanging the countercation of the $(n\text{-}Bu)_4N^+$ salt with Et_4NCl in dichloromethane. The well-grown crystals formed by a slow evaporation method were used as samples.[7a]

(8) (a) Stiegman, A. E.; Rice, S. F.; Gray, H. B.; Miskowski, V. M. *Inorg. Chem.* **1987**, *26*, 1112. (b) Fiiomena Dos Remendios Pint, M. A.; Sadler, P. J.; Neidle, S.; Sanderson, M. R.; Sunbbiah, A.; Kuroda, R. *J. Chem. Soc., Chem. Commun.* **1980**, 13. (c) Mann, K. R.; Gordon, J. G., II; Gray, H. B. *J. Am. Chem. Soc.* **1975**, *97*, 3553.

(9) (a) Tanaka, Y.; Azumi, T. *Inorg. Chem.* **1986**, *25*, 247. (b) *Chem. Phys. Lett.* **1986**, *132*, 357.

(10) Previously it was reported that the T–T annihilation in solid $K_4[Pt_2(P_2O_5H_2)_4]$ occurred only at liquid helium temperature.[9]

(11) Beddard, G. S.; Porter, G. *Biochim. Biophys. Acta* **1977**, *462*, 63.

(12) Although crystallographic data are not available except for $K_4[Pt_2(P_2O_5H_2)_4]$, a similar crystal structure with different lattice parameters has been suggested for the $(n\text{-}Bu)_4N^+$ salt.[8a]

0002-7863/89/1511-8265$01.50/0