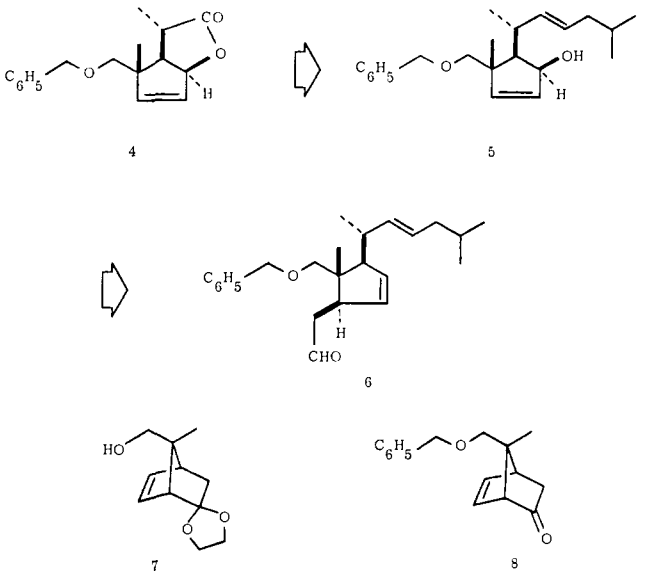
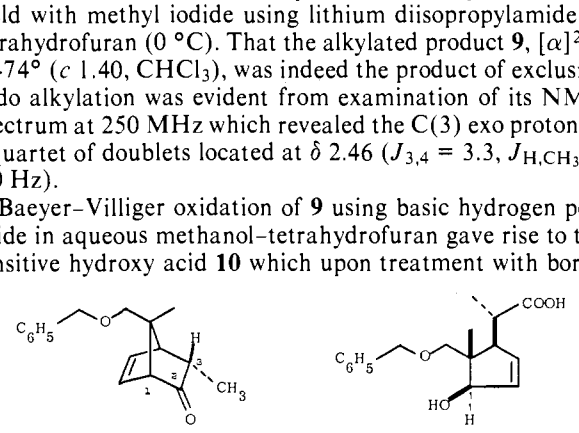


4 5 6 7 8

(c 1.35, $CHCl_3$), IR (CCl_4) 1749 cm^{-1}. Exclusive endo alkylation of ketone **8** was accomplished, as anticipated, in 90% yield with methyl iodide using lithium diisopropylamide in tetrahydrofuran (0 °C). That the alkylated product **9**, $[\alpha]^{25}_D$ −474° (c 1.40, $CHCl_3$), was indeed the product of exclusive endo alkylation was evident from examination of its NMR spectrum at 250 MHz which revealed the C(3) exo proton as a quartet of doublets located at δ 2.46 ($J_{3,4}$ = 3.3, J_{H,CH_3} = 7.0 Hz).

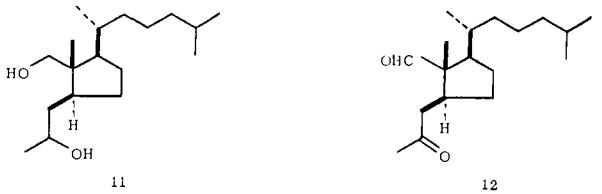
Baeyer-Villiger oxidation of **9** using basic hydrogen peroxide in aqueous methanol-tetrahydrofuran gave rise to the sensitive hydroxy acid **10** which upon treatment with boron



9 10

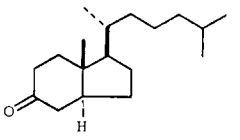
trifluoride etherate in methylene chloride at 0 °C rearranged (85% overall) solely to intermediate **4**, $[\alpha]^{25}_D$ +153° (c 1.50, $CHCl_3$), with the expected transfer of chirality from C(14) → C(16) (steroid numbering). Reduction (i-Bu_2AlH, toluene, −78 °C) of lactone **4**, followed by condensation with isopentylidenetriphenylphosphorane (generated with sodium *tert*-amylate in benzene), provided in 50% overall yield dienol **5** as a mixture of double-bond isomers about the C(22)–C(23) olefinic linkage. The required transfer of chirality from C(16) → C(14) was achieved classically by a two-step process. Allylic alcohol **5** was converted (ethyl vinyl ether, $Hg(OAc)_2$, reflux) into its corresponding vinyl ether (82% yield) which upon heating in decalin at 200 °C (5 h) under nitrogen generated aldehyde **6** in 90% yield.[7]

Addition of methyllithium to aldehyde **6**, followed by simultaneous catalytic hydrogenation (H_2, 10% Pd/C, EtOH) of the two olefins and hydrogenolysis of the benzyl ether, gave diol **11** in 90% overall yield as a mixture of diastereomers.



11 12

Oxidation (Jones reagent, −10 °C, 5 min) of diol **11** afforded a 74% yield of keto aldehyde **12** (IR (CCl_4) 2690, 1720 cm^{-1}; NMR (CCl_4) δ 2.01 (s, 3 H, CH_3CO), 9.24 (s, 1 H, -CHO)) which cyclized (10% KOH, CH_3OH) in 74% yield to the known enone **3**:[8] $[\alpha]^{25}_D$ +40.8° (c 3.45, $CHCl_3$); IR (CCl_4) 1678, 1601 cm^{-1}; NMR (CCl_4) δ 6.45 (AB q, 2 H, J = 10, $\Delta\nu_{AB}$ = 93.5 Hz). Enone **3** was analyzed as its 2,4-dinitrophenylhydrazone: mp 174–175 °C, $[\alpha]^{25}_D$ +21.8° ($CHCl_3$) (lit.[8] mp 176–177 °C, $[\alpha]^{25}_D$ +21.9° ($CHCl_3$)). Reduction (H_2, 5% Pd/C, EtOH) of de-*AB*-cholest-11-en-9-one (**3**) gave in near-quantitative yield the known de-*AB*-cholestan-9-one (**13**) which was characterized as its semicarbazone: mp



13

190–193 °C, mmp 190–193 °C, $[\alpha]^{25}_D$ +52.0° ($CHCl_3$) (lit.[8] mp 193–195 °C, $[\alpha]^{25}_D$ +52° ($CHCl_3$)).[9]

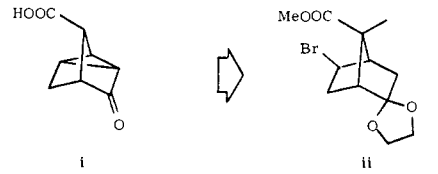
Acknowledgments. This investigation was supported by a Public Health Service Research Grant (CA 13689-07) from the National Cancer Institute, the National Institutes of Health NMR Facility for Biomedical Studies (RR-00292), and, in part, by G. D. Searle and Co. We thank Mr. George Majetich and Mr. Robert Bittner for recording the 250-MHz NMR spectra.

References and Notes

(1) For a review on sterol side chain construction, see Piatak, D. M.; Wicha, J. *Chem. Rev.* **1978**, *78*, 199.

(2) For recent approaches and solutions to this problem, see the following. Bolton, I. J.; Harrison, R. G.; Lythgoe, B. *J. Chem. Soc. C.* **1971**, 2950. Wicha, J.; Bal, K. *J. Chem. Soc., Perkin Trans 1* **1978**, 1282. Trost, B. M.; Taber, D. F.; Alper, J. B. *Tetrahedron Lett.* **1976**, 3857. Trost, B. M.; Verhoven, T. R. *J. Am. Chem. Soc.* **1978**, *100*, 3435. Also see Ficini, J.; d'Angelo, J.; Noire, J. *ibid.* **1974**, *96*, 1213.

(3) Bromo alcohol **2**, $[\alpha]^{25}_D$ −26° (c 1.80, $CHCl_3$), was prepared (90%) by reduction ($LiAlH_4$, THF, 60 °C) of bromo ketal ester ii[4] (mp 87–88 °C, $[\alpha]^{25}_D$



i ii

−22.6° (c 1.00, $CHCl_3$)) whose synthesis from cyclopropyl keto acid i[5] (mp 137–138 °C, $[\alpha]^{25}_D$ +74° (c 1.00, CH_3OH)[6]) has previously been described.[4]

(4) Grieco, P. A.; Masaki, Y. *J. Org. Chem.* **1975**, *40*, 150. Grieco, P. A.; Pogonowski, C. S.; Burke, S. D.; Nishizawa, M.; Miyashita, M.; Masaki, Y.; Wang, C.-L. J.; Majetich, G. *J. Am. Chem. Soc.* **1977**, *99*, 4111.

(5) Bindra, J. S.; Grodski, A.; Schaaf, T. K.; Corey, E. J. *J. Am. Chem. Soc.* **1973**, *95*, 7522. We thank Dr. T. K. Schaaf (Pfizer) for providing us with the details for resolving acid i.

(6) Our $[\alpha]^{25}_D$ for optically pure i in methanol (c 1.00) was +75.2°; however, this value rapidly drops to +60°. Use of dioxane (c 1.00) gave $[\alpha]^{25}_D$ +81.8° consistently.

(7) Watenabe, W. H.; Conlon, L. E. *J. Am. Chem. Soc.*, **1957**, *79*, 2828. Dauben, W. G.; Dietsche, T. J. *J. Org. Chem.* **1972**, *37*, 1212.

(8) Littlewood, P. S.; Lythgoe, B.; Saksena, A. K. *J. Chem. Soc. C* **1971**, 2955.

(9) We are indebted to Professor Basil Lythgoe for providing us with an infrared spectrum of **13** and for a generous sample of the semicarbazone of de-*AB*-cholestan-9-one (**13**).

Paul A. Grieco,* Tetsuo Takigawa, David R. Moore
Department of Chemistry, University of Pittsburgh
Pittsburgh, Pennsylvania 15260
Received February 13, 1979

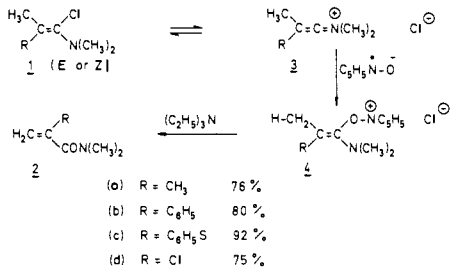
α,β Dehydrogenation of Carboxamides

Sir:

Dehydrogenation of the readily available saturated fatty acids to the synthetically more useful α,β-unsaturated deriv-

0002-7863/79/1501-4381$01.00/0

Scheme I



atives can be directly effected by several reagents.[1] However, yields are often moderate and experimental conditions are not always compatible with the presence of sensitive functional groups. The sulfenylation[2] of enolates of esters, followed by oxidation to the corresponding sulfoxides and thermolysis, offers a wider synthetic applicability and should definitely supersede the more traditional approach involving a bromination–dehydrobromination sequence. However, the method requires the formation of enolates of esters under strongly basic conditions, which precludes the presence of certain sensitive functional groups. The selenylation–deselenylation sequence[3] offers similar advantages, but suffers from the high toxicity and expense of selenylating reagents.

We describe here an alternative "one-pot" experimental procedure that effects the α,β dehydrogenation of tertiary carboxamides at room temperature and does not require the use of strong bases. Our methodology is based upon the observation that 1-chloro-*N,N*-2-trimethylpropenylamine (**1a**), which is readily available[4] from *N,N*-dimethylisobutyramide, can be smoothly converted to *N,N*-dimethylmethacrylamide (**2a**) in the presence of pyridine *N*-oxide and triethylamine.[5] This reaction has been applied successfully to the preparation of α,β-unsaturated amides **2b, 2c,** and **2d** (Scheme I). The reported yields are for pure isolated products. The reaction probably[6] involves ionization of **1** to the corresponding keteniminium chloride **3,** which then adds pyridine *N*-oxide. The adduct **4** should readily undergo 1,4 elimination under the influence of triethylamine to give **2.** The reaction works equally well with diphenyl sulfoxide, but difficulties were encountered in the isolation of the α,β-unsaturated amides from the sulfur-containing products. Trimethylamine *N*-oxide and dimethyl sulfoxide are not suitable reagents for this purpose, since they give mixtures of saturated and unsaturated amides.[7]

These results led us to develop a simple experimental procedure to effect α,β dehydrogenation of carboxamides (Scheme II). The amide **5** was first transformed into the corresponding amide chloride **6** according to known procedures.[4] Treatment of crude **6** with pyridine *N*-oxide and triethylamine gives the α,β-unsaturated amides **2** in good yield. The general procedure is as follows. A solution of **5** in dry dichloromethane (10–15% by volume) was treated overnight with 1.1–1.5 equiv of phosgene.[8-10] Removal of the solvent and excess phosgene under vacuum leaves a solid residue that is dissolved in the minimum amount of chloroform.[11] To this solution was added dropwise a mixture of pyridine *N*-oxide (1 equiv) and triethylamine (2.5 equiv) in chloroform (exothermic reaction). After

Scheme II. General Scheme for α,β Dehydrogenation of Carboxamides

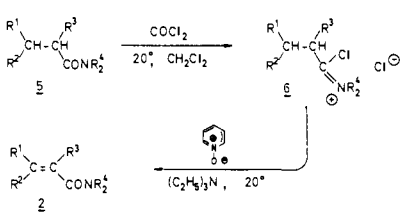
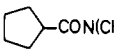
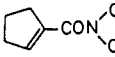
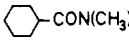
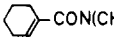
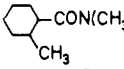
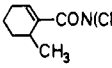
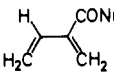
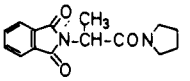
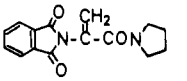
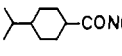
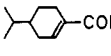
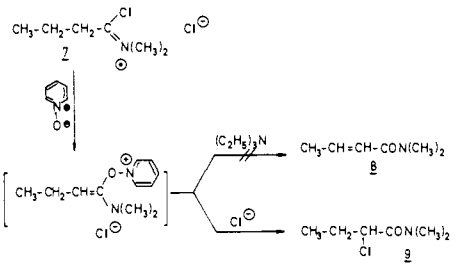


Table I. Dehydrogenation of Saturated Amides

entry	saturated amides **5**	unsaturated amides **2**	yield,[a] %
A	$(CH_3)_2CH$-CON$(CH_3)_2$	$CH_2=C(CH_3)$-CON$(CH_3)_2$	76[b]
B	C_6H_5-CH(CH_2-CH_3)-CON$(CH_3)_2$	CH_3-CH=C(C_6H_5)-CON$(CH_3)_2$	80[b]
C			65[b]
D			70[b]
E			75[b]
F	CH_3-CH=CH-CON$(CH_3)_2$		40[c]
G	CH_3-CH(Cl)-CON$(CH_3)_2$	$CH_2=C(Cl)$-CON$(CH_3)_2$	75b
H	CH_3-CH(SPh)-CON$(CH_3)_2$	$CH_2=C(SPh)$-CON$(CH_3)_2$	92[c]
I			85
J			80[c]

[a] Yields are for isolated pure products but have not been optimized. All products were characterized by spectroscopic methods. [b] Purified by distillation. [c] Purified by chromatography on neutral alumina followed by distillation.

Scheme III



we stirred the mixture at room temperature for 2 h, it was treated with petroleum ether (bp 50–80 °C). Filtration, aqueous acid workup, and normal purification procedures produce pure samples of α,β-unsaturated amides in good yield (Table I).

This simple one-pot procedure permits the smooth dehydrogenation of various carboxamides in good yield (entries A to J). In the case of substituted cyclohexylcarboxamide (entry E), dehydrogenation occurs regiospecifically to give the less substituted double bond. This method can be applied to the preparation in high yield of some useful functionalized acrylamides. The availability of the dehydroalanine derivative (entry I) obtained in 85% yield from *N*-phthaloylalanylpyrrolidinamide opens a potential new route to dehydro amino acids from saturated amino acids and demonstrates the efficiency of our approach.

A present limitation of the method is illustrated by the following observation: when the amide chloride **7** derived from *N,N*-dimethylbutyramide was treated with pyridine *N*-oxide and triethylamine according to the procedure described above, no unsaturated amide **8** was obtained. The sole product was *N,N*-dimethyl-α-chlorobutyramide (**9**)[7] (Scheme III). In spite

of this limitation, the method should be quite useful, since it nicely complements existing procedures. It uses cheap and readily available starting materials and is well suited for large-scale preparation of α-substituted, unsaturated amides. Its scope is broadened by the availability of smooth procedures allowing the conversion of tertiary amides into acids, esters, aldehydes, ketones, and amines.[12] Further applications of the newly described dehydrogenation method are under investigation.

Acknowledgment. We express our thanks to the Catholic University of Louvain (Secrétariat du Tiers Monde) and the "Institut pour l'Encouragement de la Recherche Scientifique dans l'Industrie et l'Agriculture" for fellowships to R. Da Costa, M. Gillard, and J. B. Falmagne, and the "Fonds de la Recherche Fondamentale et Collective" for financial support.

References and Notes

(1) Kasturi, T. R.; Pettit, G. R.; Jaeggi, K. A. *J. Chem. Soc., Chem. Commun.* **1967**, 644-646; Walker, D.; Hiebert, J. H. *Chem. Rev.* **1967**, *67*, 153-195; Jerusi, R. A. In "Selective Organic Transformations"; Thyagarajan, B. S., Ed.; Wiley-Interscience: New York, 1970; Vol. I, pp 315-321; Pettit, G. R.; Fessler, D. C.; Paull, K. D.; Hoffer, P.; Knight, J. C. *J. Org. Chem.* **1970**, *35*, 1398-1404; Theissen, R. J. *ibid.* **1971**, *36*, 752-757; Bierling, B.; Kirsche, K.; Oberender, H. *J. Prakt. Chem.* **1972**, *314*, 170; Marx, J. N.; Cox, J. H.; Norman, L. R. *J. Org. Chem.* **1972**, *37*, 4489-4491; Cainelli, G.; Cardillo, G.; Umani Ronchi, A. *J. Chem. Soc. Chem. Commun.* **1973**, 94-95; Thomas, A. F.; Ozainne, M. *ibid.* **1973**, 746; Trolliet, M.; Longeray, R.; Dreux, J. *Bull. Soc. Chim. Fr.* **1974**, 1484-1486.

(2) Trost, B. M.; Salzmann, T. N.; (in part) Hiroi, K. *J. Am. Chem. Soc.* **1976**, 98, 4887-4901, and references cited therein.

(3) For a recent review, see: Reich, H. J. *Acc. Chem. Res.* **1979**, *12*, 22-30.

(4) Haveaux, B.; Dekoker, A.; Rens, M.; Sidani, A. R.; Toye, J.; Ghosez, L. *Org. Syn.* in press.

(5) The use of pyridine *N*-oxide as an oxidizing agent has been reported in a few cases: Rüchardt, C.; Eichter, S.; Krätz, O. *Tetrahedron Lett.* **1965**, 233-236; Cohen, T.; Song, I. H.; Fager, J. H. *ibid.* **1965**, 237-241; Cohen, T.; Song, I. H. *J. Org. Chem.* **1966**, *31*, 3058-3059; Cohen, T.; Song, I. H.; Fager, J. H.; Deets, G. L. *J. Am. Chem. Soc.* **1967**, *89*, 4968-4975; Katritzky, A. R.; Lunt, E. *Tetrahedron* **1969**, *25*, 4291-4305. Of particular interest for the present work was the formation of 20% 2,3-diphenylpropenoic acid from the reaction of the corresponding saturated acid with pyridine *N*-oxide in the presence of acetic anhydride: Cohen, T.; Shaw, C. K.; Jenkins, J. A. *J. Org. Chem.* **1973**, *38*, 3737-3739.

(6) For a review on the chemistry of α-haloenamines and keteniminium salts, see: Ghosez, L.; Marchand-Brynaert, J. In "Advances in Organic Chemistry"; Taylor, E. C., Ed.; Wiley-Interscience: New York, 1976; Vol. 9, pp 421—532.

(7) A mechanistic study of these reactions will be reported later with the full experimental details.

(8) When R^2 = H, it is advised to saturate the solution of amide with gaseous HCl prior to phosgenation. This precludes the formation of small amounts of β-acylated product.

(9) With the more reactive amides, cooling may be necessary during the early stages of phosgenation.

(10) If the phosgenation is not completed after 24 h, a few drops of dimethylformamide and more phosgene can be added to the mixture, which is allowed to stand 2 to 3 more days at room temperature.

(11) All these experiments require complete exclusion of moisture.

(12) Borch, R. F. *Tetrahedron Lett.* **1968**, 61-65; Challis, B. C.; Challis, J. In "The Chemistry of Amides"; Patai, S.; Zabicky, J., Eds.; Interscience: New York, 1970; pp 731-857; Gassman, P. G.; Hodgson, P. K.; Balchunis, R. J. *J. Am. Chem. Soc.* **1976**, *98*, 1275-1276.

R. Da Costa, M. Gillard, J. B. Falmagne, L. Ghosez*
Laboratoire de Chimie Organique de Synthèse
Université Catholique de Louvain
B-1348 Louvain-la-Neuve, Belgium
Received December 4, 1978

Solar Energy Storage Reactions Involving Polynuclear Rhodium Isocyanide Complexes. Flash Photolysis Studies in Aqueous Sulfuric Acid Solutions

Sir:

We have recently reported[1] that 546-nm irradiation of solutions of the binuclear Rh(I) complex $Rh_2(bridge)_4^{2+}$ (bridge = 1,3-diisocyanopropane) in concentrated HX(aq) results in clean conversion to H_2 and $Rh_2(bridge)_4X_2^{2+}$ (X = Cl, Br).[2] Since these reactions are driven by visible photons, they represent one way of achieving conversion of solar to chemical energy. Recent work in our laboratory has shown that a thermal reaction between $Rh_2(bridge)_4^{2+}$ and HCl generates a blue photoactive species, $[Rh_2(bridge)_4Cl^{2+}]_n$, and hydrogen. Irradiation of $[Rh_2(bridge)_4Cl^{2+}]_n$ produces the ultimate products, according to the following scheme:

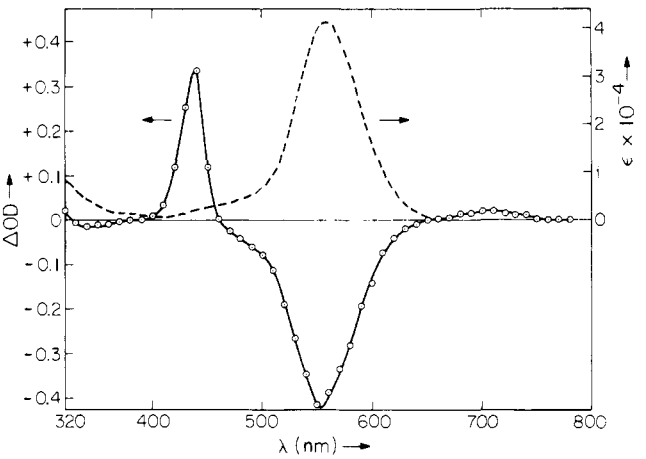


Figure 1. Absorption spectrum (- - -) and flash-generated transient difference spectrum (—) for $[Rh_2(bridge)_4^{3+}]_n$ in 1 N H_2SO_4(aq) at 25 °C.

$$Rh_2(bridge)_4^{2+} + HCl \xrightarrow[12\ M\ HCl]{\Delta} (1/n)[Rh_2(bridge)_4Cl^{2+}]_n + \tfrac{1}{2}H_2$$

$$(1/n)[Rh_2(bridge)_4Cl^{2+}]_n + HCl \xrightarrow[12\ M\ HCl]{546\ nm} Rh_2(bridge)_4Cl_2^{2+} + \tfrac{1}{2}H_2$$

Analysis of the hydrogen evolved in the separate thermal and photochemical steps has established the above stoichiometric relationships.[3] The structure of the photoactive species, $[Rh_2(bridge)_4Cl^{2+}]_n$, or that of an analogue, $[Rh_2(bridge)_4^{3+}]_n$ (prepared by oxidation of $Rh_2(bridge)_4^{2+}$ in H_2SO_4 solutions), is being actively pursued. Evidence that bears on the structural question in the case of $[Rh_2(bridge)_4^{3+}]_n$ has been obtained in a series of flash photolysis experiments, as reported herein.

Solutions of $[Rh_2(bridge)_4^{3+}]_n$ prepared by oxidation of $[Rh_2(bridge)_4](BF_4)_2$ in 1 N H_2SO_4(aq) possess an absorption maximum at 558 nm (ϵ/Rh_2 = 44 400) (Figure 1). Since the same λ_{max} is obtained for H_2O solutions with no added electrolytes, we assume that no sulfate or bisulfate is bound as a ligand to the rhodium complex.[4] Degassed H_2SO_4(aq) solutions of $[Rh_2(bridge)_4^{3+}]_n$ are indefinitely stable ($[H_2SO_4] \lesssim 20$ N). Flash photolysis reveals a transient(s), however, with absorption maxima at 438 ($\Delta\epsilon/Rh_2$ = 34 500) and 705 nm ($\Delta\epsilon/Rh_2$ = 2000) (Figure 1).[5] Extinction coefficients were calculated from the bleaching at 550–560 nm, making the assumption that transient(s) absorption is negligible at these wavelengths. The transient(s) is prompt, with a rise time of <10 ns, and undergoes clean second-order decay[6] to starting material. The rate constant in 1 N H_2SO_4(aq) is 3.3 (± 0.2) × 10^7 M^{-1} s^{-1}, where the calculation assumes that the bimolecular process involves identical reaction partners (vide infra). The rate constant is identical within experimental error in 1 N D_2SO_4 (D_2O).

Figure 2 depicts the dependence of the second-order rate constant on ionic strength.[7] The slope at low ionic strengths (+8.1) should equal the product of charges of the two reactants.[8] It is difficult to imagine how such a high product of

0002-7863/79/1501-4383$01.00/0