right-hand side of eq 5, 282; found, 280 ± 57). ^{31}P NMR observations are also consistent with the equilibrium proposed in eq 5.[15] The absence of metal hydrides is demonstrated by reaction of **3** with anhydrous HCl; 1- and 2-butenes are the only volatile products—no hydrogen is formed. Treatment of **3** with dry oxygen liberates butadiene. **3** reacts reversibly with PMe_3 at low temperatures. ^{31}P NMR spectra of **3** and excess PMe_3 (5 equiv/1 equiv of Zr) at −80 °C in toluene-d_8 show the presence of free dmpe (0.5 equiv/1 equiv of Zr) and an ABX pattern,[16] consistent with the formation of $(C_4H_6)_2$-Zr(dmpe)(PMe_3) as shown in eq 6. That the interaction is

$$3 + 2PMe_3 \rightleftharpoons \text{dmpe} + 2(\diagdown\!\!\diagup)_2Zr(\text{dmpe})(PMe_3) \quad (6)$$

reversible is shown by precipitation of the less soluble **3** on addition of hexane at −80 °C. Warming these solutions to room temperature results in irreversible decomposition.

In arene solvents, **3** reacts rapidly with hydrogen, forming butane and brown solutions.[17] These solutions catalyze the hydrogenation of olefins and alkynes under mild conditions. Thus, 1-octene, cyclohexene, and 2-pentyne are hydrogenated at moderate rates.[18] The trisubstituted olefin 2-methyl-2-butene is hydrogenated, at best, very slowly. ^{31}P NMR studies indicate that the toluene and benzene solutions formed on treatment of **3** with H_2 are complex.[19]

This work has two major ramifications: (1) formally di- and zerovalent zirconium complexes with electron-donating ligands are stable, particularly in the presence of π-accepting groups;[20] and (2) as shown by eq 3 and as suggested by the use of **3** as a hydrogenation catalyst, the Zr(IV) → Zr(II) and, possibly, Zr(II) → Zr(0) redox couples are not so endothermic that catalytic processes involving them are implausible.

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the National Science Foundation (CHE-75-19177) for support of this research.

References and Notes

(1) F. W. S. Benfield, M. L. H. Green, J. S. Ogden, and D. Young, *J. Chem. Soc., Chem. Commun.*, 866 (1973).
(2) (a) H. Breil and G. Wilke, *Angew. Chem.*, **78**, 942 (1966); (b) H. J. Kablitz and G. Wilke, *J. Organomet. Chem.*, **51**, 241 (1973); (c) H. J. Kablitz, R. Kallweit, and G. Wilke, *ibid.*, **44**, C49 (1972).
(3) (a) J. E. Bercaw, R. H. Marvich, L. G. Bell, and H. H. Brintzinger, *J. Am. Chem. Soc.*, **95**, 1219 (1972); (b) A. Davison and S. S. Wreford, *ibid.*, **96**, 3017 (1974); (c) G. P. Pez, *ibid.*, **98**, 8072 (1976).
(4) (a) J. E. Bercaw, *J. Am. Chem. Soc.*, **96**, 5087 (1974); (b) J. M. Manriquez and J. E. Bercaw, *ibid.*, **96**, 6229 (1974).
(5) H. O. von Oven and H. J. deLiefde Meijer, *J. Organomet. Chem.*, **23**, 159 (1970).
(6) $^{31}P\{^1H\}$ NMR (C_6D_6) δ −2.7 ppm (s); mass spectrum *m/e* 530 ($[^{12}C_{12}{}^1H_{32}{}^{31}P_4{}^{35}Cl_4{}^{90}Zr]^+$), 345 ($[P - Cl, dmpe]^+$). Anal. Calcd for $C_{12}H_{32}P_4Cl_4Zr$: C, 27.03; H, 6.05; Cl, 26.60. Found: C, 27.33; H, 6.07; Cl, 26.66.
(7) R. J. H. Clark, J. Lewis, R. S. Nyholm, P. Pauling, and G. B. Robertson, *Nature (London)*, **192**, 222 (1961).
(8) R. J. H. Clark, W. Errington, J. Lewis, and R. S. Nyholm, *J. Chem. Soc. A*, 989 (1966).
(9) $^{31}P\{^1H\}$ NMR (toluene-d_8) ABCD pattern, δ_A −20.52, δ_B − 15.7, δ_C −2.2, δ_D −0.3 ppm ($|J_{AB}|$ = 13.0, $|J_{AC}|$ = 22.1, $|J_{AD}|$ = 7.4, $|J_{BC}|$ = 11.2, $|J_{BD}|$ = 17.7, $|J_{CD}|$ = 24.2 Hz); $^1H\{^{31}P\}$ NMR (benzene-d_6) τ 4.5 (t, 1 H), 4.93 (t, 2 H), 5.75 (t, 2 H), 7.06 (d, 1 H), 7.41 (m, 1 H), 8.4–9.3 (br complex multiplet from dmpe protons); mass spectrum *m/e* 470 ($[^{12}C_{18}{}^1H_{40}{}^{31}P_4{}^{90}Zr]^+$). Anal. Calcd for $C_{18}H_{40}P_4Zr$: C, 45.84; H, 8.54. Found: C, 45.63; H, 8.33.
(10) The hydride resonance is, presumably, obscured by dmpe proton resonances: ZrH ^1H NMR resonances with chemical shifts near this and at lower fields are well documented: J. M. Manriquez, D. R. McAlister, R. D. Sanner, and J. E. Bercaw, *J. Am. Chem. Soc.*, **100**, 2716 (1978).
(11) The dehydrogenation of 1,3-cyclohexadiene to benzene and hydrogen and the disproportion indicated in eq 3 are both exothermic reactions, although the latter path is thermodynamically favored, ΔG°_{rxn} = −13.7 and −16.4 kcal/mol, respectively: G. J. Janz, *J. Chem. Phys.*, **22**, 751 (1954).
(12) *Minimum* rate at 90 °C = 16 turnovers/h at a catalyst to substrate ratio of 1:320.
(13) (a) J. E. Lyons, *Chem. Commun.*, 564 (1969); (b) K. Moseley and P. M. Maitlis, *J. Chem. Soc. A*, 2884 (1970); (c) M. Green and T. A. Kuc, *J. Chem. Soc., Dalton Trans.*, 832 (1972).
(14) $^1H\{^{31}P\}$ NMR (C_6D_6) δ 5.36 (m, 4 H), 1.42 (m, 4 H), 1.24 (s, 6 H, dmpe), 0.76 (s, 18 H, dmpe methyl groups), −0.20 (m, 4 H). Anal. Calcd for $C_{17}H_{36}P_3Zr$: C, 48.09; H, 8.55; Zr, 21.48. Found: C, 47.62; H, 8.27; Zr, 21.91.
(15) At 30 °C in toluene-d_8, two resonances are observed (−13.4 and 48.5 ppm). The high-field signal is near the chemical shift of free dmpe (49.5 ppm); addition of free dmpe shifts this line to higher field, but does not result in the appearance of a separate resonance. When the solution is cooled to −40 °C, the high-field resonance broadens and moves to lower field (~4.8 ppm). At lower temperatures, both resonances become complex; we were unable to obtain a limiting spectrum. This data is consistent with the equilibrium in eq 5: at low temperatures the exchange rate slows and the anticipated positive ΔS_{rxn} shifts the equilibrium to the left-hand side. More complex equilibria involving butadiene exchange may also occur.
(16) δ_A 10.0, δ_B 8.3, δ_x −10.3 ppm ($|J_{AB}|$ = 3.3, $|J_{AX}|$ = 9.8, $|J_{BX}|$ = 9.8 Hz.
(17) In aliphatic solvents, a zirconium mirror is deposited on the walls of the apparatus. Presumably, an arene–Zr interaction is necessary to stabilize the product.
(18) Rates are 4.3, 5.7, and 10.1 mol of substrate hydrogenated/h·mol of Zr at 27 °C and 760 mmH_2 for 1-octene, cyclohexene, and 2-pentyne, respectively. In the latter case *cis*-2-pentene is a detectable intermediate.
(19) $ZrH_3(dmpe)_2$ has been claimed by treatment of Zr(benzyl)$_4$/dmpe mixtures with high pressures of hydrogen: F. N. Tebbe, U.S. Patent 3 933 876; *Chem. Abstr.*, **84**, 165021e (1976).
(20) Indeed, a limiting zirconium(IV) metallocyclopentene resonance structure for **3** may be written, an expression of extensive π interaction. However, the similarity of the $^1H^{21a}$ and $^{13}C^{21b}$ NMR chemical shifts of the butadiene portion of **3** (39.1 and 105.6 ppm for methylene and methine carbons, respectively, relative to Me_4Si) to those for butadieneirontricarbonyl[21] suggest similar resonance forms. In particular, the values of $J_{^{13}CH}$ (146 and 156 Hz for **3**, 160 and 170 Hz for butadieneirontricarbonyl,[21b] 158 and 158 Hz for butadiene[21b]) indicate significant sp^2 character for the terminal methylene carbons in all cases, and, therefore, significant Zr(0) character in **3**.
(21) (a) H. G. Preston, Jr., and J. C. Davis, Jr., *J. Am. Chem. Soc.*, **88**, 1585 (1966); (b) H. L. Retcofsky, E. N. Frankel, and H. S. Gutowsky, *ibid.*, **88**, 2710 (1966).

S. Datta, S. S. Wreford*
Department of Chemistry, University of Toronto
Toronto, Ontario, Canada M5S 1A1

R. P. Beatty, T. J. McNeese
Department of Chemistry, Harvard University
Cambridge, Massachusetts 02138

Received July 25, 1978

Total Synthesis of α-Amino-3-chloro-4,5-dihydro-5-isoxazoleacetic Acid (AT-125), an Antitumor Antibiotic

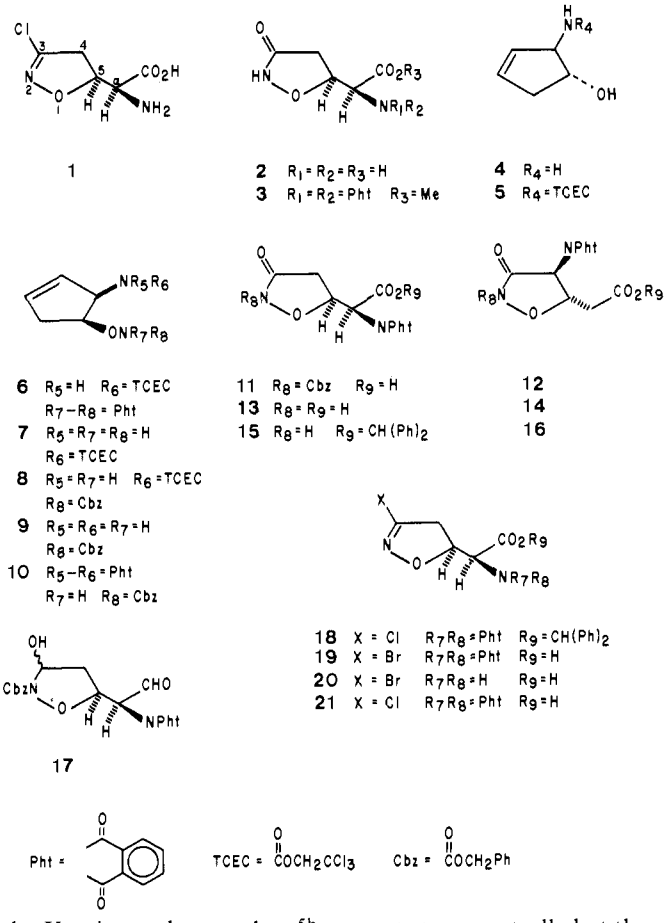
Sir:

Recently Martin et al.[1] described the isolation and structure of a novel antitumor antibiotic, (α*S*,5*S*)-α-amino-3-chloro-4,5-dihydro-5-isoxazoleacetic acid (**1**, AT-125). This material, isolated from *Streptomyces sviceus*, significantly increased the life span of tumor (L-1210 or P388) bearing mice[2] and, of even greater interest, it significantly increased the life span of immune deficient mice implanted with a solid human mammary tumor.[3] The biological activity of this material and its novel structure have already elicited a report by Baldwin et al. on an approach to its synthesis which produced nonstereospecifically a methylated analogue.[4] We report here a stereoselective, total synthesis of the racemic and optically pure isomers of AT-125.

In planning the synthesis we decided to pursue a path to AT-125 through derivatives of the known amino acid tricholomic acid (**2**).[5] In order to obtain relay material for such a route, AT-125 was hydrolyzed with 2 N NaOH to tricholomic acid identical by TLC and NMR with an authentic sample.[6] The hydrolyzed material was converted to its phthalimide methyl ester **3** (*N*-carboethoxyphthalimide[7] followed by diazomethane) which we found could be chlorinated in 65–70% yields with $(Me_2N)_3PCl_2$ in THF[8,9] to produce a material identical with the phthalimide methyl ester of AT-125. Encouraged by these results we turned our attention toward the synthesis of tricholomic acid or a suitably protected derivative thereof.

Since the synthesis of tricholomic acid previously described

0002-7863/79/1501-1054$01.00/0



by Kamiya and co-workers[5b] was not stereocontrolled at the early stages in generating a hydroxyglutamic acid backbone, we chose instead to generate the desired functionality through the opening of a cis epoxide. Thus, cyclopentadiene monoepoxide[10] was treated with methanol and ammonia to produce *trans*-3-amino-3-hydroxycyclopentene (**4**,[11a] mp 47–50 °C), an extremely water-soluble material which could readily be isolated and purified as its *p*-toluenesulfonate salt (mp 180–182 °C).[13] The amine **4** was then resolved by first removing the isomer corresponding to the unnatural configuration by crystallization of the deoxycholate salt from methanol (mp 195–197 °C). Treatment of the regenerated amine from the mother liquors with L-(+)-tartaric acid and crystallization from ethanol produced the natural antipode in 70–80% theoretical yield (mp 86.5–88.5 °C, $[\alpha]^{20}_{578}$ −42° (*c* 1.7, MeOH)).[14,15] From this point all the subsequent chemistry described was carried out on the racemic mixture and on both optical isomers.

The amine **4** was converted to its trichloroethyl carbamate **5**[11b] (natural, mp 87–87.5 °C, $[\alpha]^{25}_{D}$ −92° (c 0.14, MeOH); racemic, mp 106–107.5 °C) with CCl_3CH_2OCOCl and aqueous Na_2CO_3. Replacement of the hydroxyl of **5** was effected with Ph_3P, diethyl azodicarboxylate, and *N*-hydroxyphthalimide to produce the phthalimidoxy ether **6**[11c] (natural, mp 117–118 °C, $[\alpha]^{25}_{D}$ −26° (*c* 0.56, MeOH); racemic, mp 138.5–139.5 °C) with complete inversion.[16] The Pht protecting group was removed ($NH_2NH_2{\cdot}H_2O$) and replaced with Cbz ($PhCH_2OCOCl$ in pyridine) giving **8**[11d] (natural, mp 90–91 °C, $[\alpha]^{25}_{D}$ −33° (*c* 0.2, MeOH); racemic, mp 82–85 °C) in 80–85% overall yield. The trichloroethylcarbonyl protecting group was then removed from **8** (Zn, MeOH, $MeSO_3H$) and replaced by Pht (*o*-$CH_3O_2CPhCOCl$,[17] THF, Et_3N) to give Cbz–Pht protected material **10**[11e] (natural, mp 89–92 °C, $[\alpha]^{20}_{578}$ −150° (*c* 0.68, MeOH)) in 75–80% yield.

In devising our plans we had anticipated that oxidative cleavage of the double bond in **10** would produce a diacid which would then require further manipulation to produce cyclized materials. Thus we were pleasantly surprised to find that cleavage of **10** with $NaIO_4$ in aqueous acetone containing catalytic quantities of $RuCl_3{\cdot}xH_2O$[18a] produced instead a mixture of two monoacids. These materials were the already cyclized products **11**[11f] (natural, oil, $[\alpha]^{20}_{578}$ −78° (*c* 2.0, MeOH); racemic, mp 115–116 °C) and **12**[11g] (natural, oil; racemic, mp 160–162 °C), which could be separated chromatographically on CC-4 silica gel or better on pH 3 (phosphate) buffered silica gel. They were produced in a 4:1 ratio in over 85% combined yield.[19,20]

Since we do not consider it likely that the predicted diacid cyclized under the reaction conditions, we postulate that the double bond is first oxidized to a dialdehyde or aldehyde acid[18b] which may exist, at least partially, in the cyclized form (e.g., **17**) and it is this species which is oxidized to final product.

Independent hydrogenolysis of **11** and **12** over Pd black gave the hygroscopic tricholomic acid phthalimide isomers **13** (racemic, mp 153–155 °C) and **14**.[21] These in turn were converted to their diphenyl methyl esters, **15**[11h] and **16**,[11i] with diphenyldiazomethane.[22] In practice it was found easier to carry the **11–12** mixture through to **15–16** and separate chromatographically at this point. The overall yield of **15** from **10** obtained in this way was ~35–40% and of **16** ~10%.

The tricholomic acid derivative **15**, which is a more readily deprotected analogue corresponding to the relay methyl ester **3** described above, was chlorinated in the same manner to **18**[11j] (natural, mp 178–179 °C) in 60–65% yield.

Our initial deesterifications of **18** were conducted with HBr in nitromethane. This unexpectedly completely exchanged the chlorine for bromine in the time required to remove the diphenyl methyl ester (<5 min at 25 °C) to afford **19**[11k] (natural, mp 179–180 °C, $[\alpha]^{20}_{578}$ +70° (*c* 0.5, $CHCl_3$)).

This material was converted to the bromo analogue of AT-125, **20**,[11l] ($NH_2NH_2{\cdot}H_2O$; natural, $[\alpha]^{20}_{578}$ +1.67° (*c* 0.5, H_2O), $[\theta]^{max}_{216}$ +8900 ± 600, *m/e* 352 and 354 (M^+ − 15 of bis(TMS) derivative in the normal manner)). Both **19** and **20** show TLC mobilities extremely close to those of the corresponding chloro compounds and they produce nearly identical NMR spectra. Further, the bromo analogue **20** shows significant antibacterial and antitumor activity compared with AT-125.[24]

The desired AT-125 precursor **21**[11m] was readily prepared from **18** by cleavage of the diphenyl methyl ester with HCl in nitromethane. This in turn was converted to AT-125 by treatment with hydrazine hydrate and crystallized from butanol–water.[23] The α*S*,5*S* isomer produced by this process was found identical in all respects, including biologically, with natural AT-125. The ent isomer ($[\theta]^{max}_{217}$ −14 200 ± 900; NMR (D_2O) δ 5.3 (m, 1 H), 4.17 (d, *J* = 4 Hz, 1 H), 3.61 ppm (d, *J* = 9 Hz, 2 H)) was also prepared. This material and the bromo analogue are currently undergoing further biological evaluation.

References and Notes

(1) D. G. Martin, D. J. Duchamp, and C. G. Chidester, *Tetrahedron Lett.*, 2549 (1973).
(2) L. J. Hanka, D. G. Martin, and G. L. Neil, *Cancer Chemother. Res.*, **57**, 141 (1973).
(3) D. Hauchers, A. Ovejara, R. Johnson, A. Bogden, and G. Neil, *Proc. Am. Ass. Cancer Res.*, **19**, 40 (1978).
(4) J. E. Baldwin, C. Hoskins, and L. Kruse, *J. Chem. Soc., Chem. Commun.* 795 (1976).
(5) (a) T. Takemoto and T. Nakajiina, *Yakugaku Zasshi*, **84**, 1183 (1964); (b) T. Kamiya, *Chem. Pharm. Bull.*, **17**, 895 (1969), and references therein.
(6) We thank Takeda Chemical Industries, Ltd., for an authentic sample of tricholomic acid.
(7) G. H. L. Nefkens, G. J. Tesser, and J. F. Nivard, *Recl. Trav. Pays-Bas*, **79**, 688 (1960).
(8) (a) R. Appel and H. Scholer, *Chem. Ber.*, **110**, 2382 (1977). (b) R. Appel, K. Warming, and K. D. Ziehn, *Chem. Ber.*, **106**, 3450 (1973). (c) P. Wolkoff, *Can. J. Chem.*, **53**, 1333 (1975), reports the conversion of an acylhydrazone grouping to imidoyl chloride with $(C_6H_5)_3P$ + CCl_4 in acetonitrile.
(9) Several other reagents and solvents produced decidedly inferior results.

(10) M. Korach, D. R. Nielsen, and W. H. Rideout, *Org. Synth.*, **42**, 50 (1962).
(11) ^{1}H NMR ($CDCl_3$) for the following compounds: (a) **4**, δ 1.8–2.9 (m, 2 H), 3.5–4.2 (m, 2 H), 5.4–5.9 (m, 2 H); (b) **5**, δ 1.9–3.1 (m, 2 H), 4.0–4.6 (m, 2 H), 4.73 (s, 2 H), 5.5–6.1 (m, 2 H), 6.65–7.0 (m, 1 H); (c) **6**, δ 2.7–3.0 (m, 2 H), 4.78 (s, 2 H), 4.8–5.15 (m, 2 H), 5.7–6.1 (m, 2 H), 6.1–6.7 (m, 1 H), 7.82 (s, 4 H); (d) **8**, δ 2.35–2.7 (m, 2 H), 4.2–4.8 (m, 2 H), 4.72 (s, 2 H), 5.13 (s, 2 H), 5.5–6.1 (m, 2 H), 7.32 (s, 5 H), 8.46 (s, 1 H); (e) **10**, δ 2.65–3.0 (m, 2 H), 4.55–5.5 (m, 2 H), 5.0 (s, 2 H), 5.6–6.2 (m, 2 H), 7.27 (s, 5 H), 7.5–7.95 (m, 4 H); (f) 11 ($(CD_3)_2CO$), δ 3.17 (d, J = 7 Hz, 2 H) 5.21 (s, 2 H), 5.1–5.8 (m, 2 H), 7.37 (s, 5 H), 7.90 (s, 4 H), 9.5 (br s, 1 H); (g) **12**, δ 3.10 (d, J = 5 Hz, 2 H), 5.40 (s, 2 H), 5.1–5.7 (m, 2 H), 7.38 (m, 5 H), 7.85 (s, 4 H), 8.4 (br, s, 1 H); (h) **15**, δ 2.77 (d, J = 7 Hz, 2 H), 5.15–5.7 (m, 2 H), 6.91 (s, 1 H), 7.15 (s, 5 H), 7.26 (s, 5 H), 7.75 (m, 4 H), 8.1 (br s, 1 H); (i) **16**, δ 2.94 (d, J = 5 Hz, 2 H), 5.1–5.4 (m, 2 H), 6.80 (s, 1 H), 7.23 (s, 10 H), 7.72 (m, 4 H), 8.0 (br s, 1 H); (j) **18**, δ 3.33 (d, J = 9 Hz, 2 H), 5.2–5.9 (m, 2 H), 6.94 (s, 1 H), 7.21 (s, 5 H), 7.31 (s, 5 H), 7.80 (m, 4 H); (k) **19**, δ 3.41 (d, J = 9 Hz, 2 H), 5.2–5.8 (m, 7 H), 7.83 (m, 4 H); (l) **20** (D_2O), δ 3.40 (d, J = 9 Hz, 2 H), 3.92 (d, J = 4 Hz, 1 H), 5.15 (m, 2 H); (m) **21** ($(CD_3)_2CO$), δ 3.57 (d, J = 9 Hz, 2 H), 5.2–5.7 (m, 2 H), 7.95 (m, 2 H).
(12) To our knowledge, cyclopentadiene monoepoxide had not been opened by any amine at the start of our work. Recently, G. H. Posner and D. Z. Rogers, *J. Am. Chem. Soc.*, **99**, 8214 (1977), reported on the opening with *N*-butylamine.
(13) The free amine was readily regenerated by passage of a MeOH solution of the salt through a quaternary ammonium hydroxide ion exchange resin.
(14) This two-stage resolution is necessary since direct resolution with L-(+)-tartartic acid gives a poor yield of resolved material. The deoxycholic acid on the other hand gives about a 90% yield of optically pure ent isomer in a single crystallization from MeOH.
(15) The 3*R*,4*R* and 3*S*,4*S* isomers of **4** were assigned to their respective series after application of the benzoate sector rule (N. Harada and K. Nakanishi, *J. Am. Chem. Soc.*, **91**, 3989 (1969)) to the data obtained from their respective benzoate benzamides. The validity of the extension of this rule from vicinal glycols to vicinal hydroxy amines is shown herein by conversion of the material assigned 3*R*,4*R* to natural AT-125.
(16) E. Grochowski and J. Jurczak, *Synthesis*, 682 (1976). These authors carried out the reaction only on material in which it was not possible to detect inversion. However, the NMR coupling constants of our materials unequivocally show the cis stereochemistry for **6**. More recently, E. Grochowski, E. Falent, and J. Jurczak, *Polish J. Chem.*, **52**, 335 (1978), have shown this reaction to proceed with inversion.
(17) D. A. Hoogwater, D. N. Reinhoudt, T. S. Lie, J. J. Gunneweg, and H. C. Beyerman, *Recl. Trav. Pays-Bas*, **92**, 819 (1973).
(18) (a) G. Stork, A. Meisels, and J. E. Davies, *J. Am. Chem. Soc.*, **85**, 3419 (1963); P. E. Eaton, G. F. Cooper, R. C. Johnson, and R. H. Mueller, *J. Org. Chem.*, **37**, 1947 (1972); (b) S. Wolfe, S. K. Hasan, and J. R. Campbell, *Chem. Commun.*, 1420 (1970).
(19) The ratio was determined by chromatographic separation of the products. The structures were assigned to the products on the basis of their NMR spectra and the fact that the major product was converted to AT-125.
(20) When the corresponding TCEC–Cbz protected compound **8** was oxidized, a 1:1 ratio of natural to iso product was obtained.
(21) Acid deprotection of 11 or other protected derivatives such as those with R_8 = *t*-Boc or *p*-MeO–Cbz was not feasible owing to the fact that even such mild acids as 85% formic nearly quantitatively isomerized **13** to **14** in <1 h.
(22) (a) J. B. Miller, *J. Org. Chem.*, **24**, 560 (1959); (b) J. R. Adamson, R. Bywood, D. T. Eastlick, G. Gallagher, D. Walker, and E. M. Wilson, *J. Chem. Soc., Perkin Trans.* 1, 2030 (1975).
(23) We thank D. G. Martin for this procedure.
(24) Private communication from L. Hanka and D. G. Martin of The Upjohn Co.

R. C. Kelly,* I. Schletter, S. J. Stein, W. Wierenga*
Experimental Chemistry Research, The Upjohn Company
Kalamazoo, Michigan 49001
Received October 10, 1978

Photodisaggregation of Chlorophyll *a* and *b* Dimers

Sir:

We have recently demonstrated reversible unfolding of excited "dimers", formed by two covalently linked pyrochlorophyllide molecules, in benzene containing methanol.[1] This structure, in which the two macrocycles are pinned by OH bridges between Mg of one unit and keto carbonyl of the other,[2-5] shows characteristic absorption near 700 nm and is of special interest in view of proposals that it is a model for the reaction center, P-700, in photosynthesis.[2,3] We now report related work on 700-nm-absorbing chlorophyll *a* and *b* dimers, formed by direct aggregation of monomers at low temperature.[4,6-8]

At room temperature, chlorophyll *a* ($\sim 10^{-4}$ M) in dry methylcyclohexane containing 0.01 M methanol shows only the monomer peak at 661 nm. At −78 °C, this is partially converted to dimer, absorbing at 695 nm (Figure 1a). Flash photolysis using a 30-ns ruby laser pulse (694.3 nm)[1] selectively excites and bleaches the dimer (Figures 1b and 2). The initial difference spectrum (Figure 1b) shows also smaller bleaching in the Soret region and positive transients at 670 nm and in the triplet region, 470–600 nm.[9] These changes are completely reversible and correspond, at least semiquantitatively, to cleavage of a dimer to give triplet and ground-state units.[1] We note that the nascent monomer band at 670 nm is distinctly different from the original monomer (662), indicating a dif-

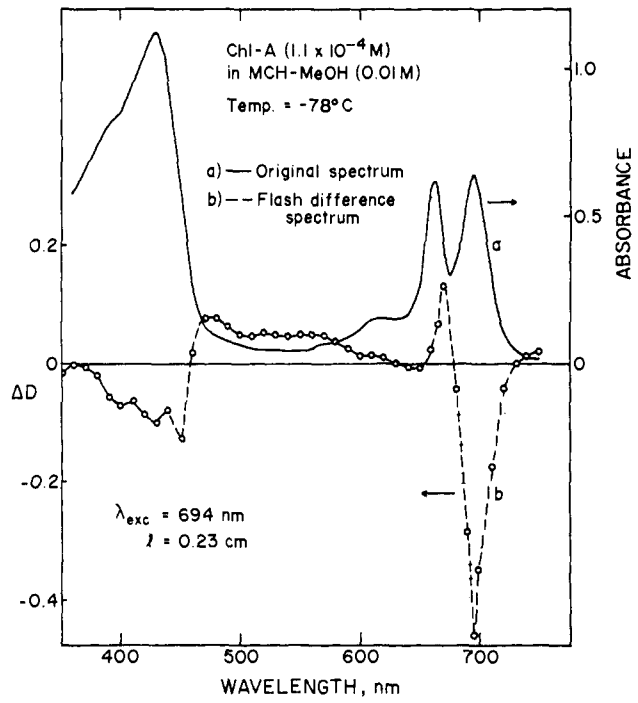


Figure 1. Absorption spectrum (curve a) and flash difference spectrum (curve b) immediately after laser flash (694.3 nm) excitation of chlorophyll *a* (1.1×10^{-4} M) in methylcyclohexane–methanol (0.01 M) at −78 °C; l = 0.23 cm; the sample was deoxygenated by argon bubbling. Arrows indicate absorbance scales for curves a and b.

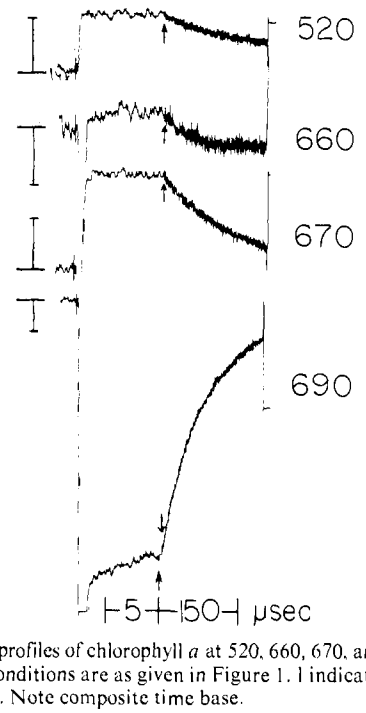


Figure 2. Flash profiles of chlorophyll *a* at 520, 660, 670, and 690 nm. The experimental conditions are as given in Figure 1. I indicates 10% change in transmission. Note composite time base.

0002-7863/79/1501-1056$01.00/0