the other hand, a nonparticipating group[2a] at C-2 has no directing effect on the final stereochemistry at C-1 that is determined by an interplay of additional factors as exemplified by entries 5, 9, and 10.

Mechanistically, the new glycosylation reaction is thought to proceed by the intermediate formation of an S-nitrosyl species which generates a reactive glycosyl cation that in the presence of a participating group at C-2 could get further stabilization by the formation of a dioxocarbenium cation.[2a] Finally, the reaction is completed by nucleophilic attack of the glycosyl acceptor at C-1.

The present methodology should contribute to the construction of O-glycosidic linkages in carbohydrate-containing, complex natural products. The scope of this approach, including the possible use of other potential nitrosyl donors, is under investigation in our laboratory.

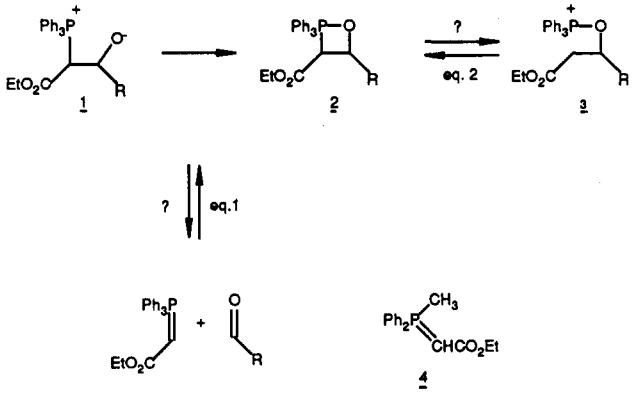
Registry No. 1, 55722-48-0; 2, 110224-77-6; 3, 79528-48-6; 4, 84635-55-2; 5, 110224-78-7; 6, 108740-74-5; 7, 110224-79-8; 8, 110224-80-1; 9, 35017-04-0; 10, 55697-53-5; 11, 14133-63-2; 12, 69558-07-2; 13, 110224-81-2; 14, 110224-82-3; 15, 110224-83-4; 16, 71348-34-0; α-17, 110224-84-5; β-17, 110224-86-7; 18, 53130-93-1; 19, 110224-85-6; $NOBF_4$, 14635-75-7.

Vince Pozsgay,* Harold J. Jennings*
Division of Biological Sciences
National Research Council of Canada
Ottawa, Ontario, Canada K1A 0R6
Received June 11, 1987

Evidence against Reversible Wittig Reaction of a Stabilized Ylide: High (*E*)-Olefin Selectivity under Kinetic Control

Summary: The betaine **10**, generated by deprotonation from deuterium-labeled **8**-*d*, decomposes stereospecifically to the (*Z*)-alkene. The corresponding Wittig reaction of ylide **4** with cyclohexanecarboxaldehyde, which gives a 95:5 (*E*)-/(*Z*)-alkene ratio, therefore occurs under kinetic control, without equilibration or Wittig reversal.

Sir: High (*E*)-olefin selectivity of carbonyl-stabilized phosphonium ylide + aldehyde reactions has been attributed to reversible formation of betaines (eq 1).[1] This

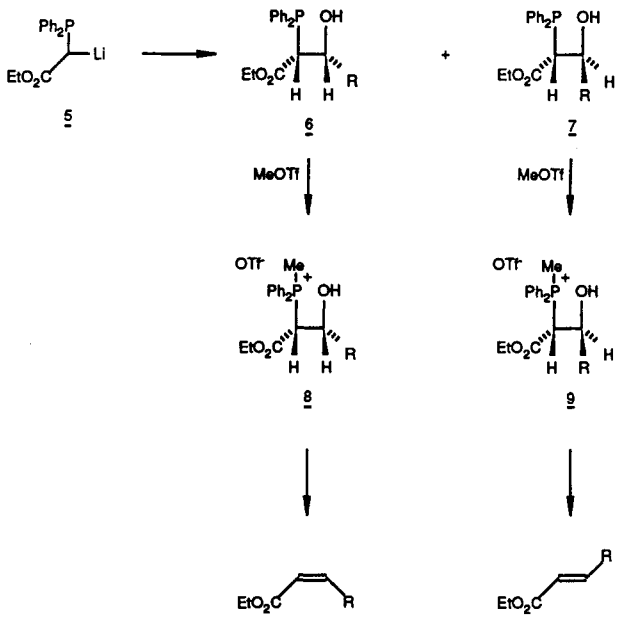


scheme has become widely accepted even though authors of the original control experiments (ethyl phenylglycidate + triphenylphosphine, refluxing ethanol, gives cinnamate with partial loss of stereochemistry) were careful not to make broad generalizations. Speziale and Bissing demonstrated *partial* reversal of intermediates using crossover experiments, but they recognized that interpretation of the results was difficult due to isomerization of product geometry and the possible intervention of other reaction pathways.[2] More recently, it has become clear that oxaphosphetanes **2** are much more stable than betaines **1**,[3] and an additional pathway for stereochemical equilibration has been suggested via the reversible formation of **3** from **2** (eq 2).[4] If either pathway (eq 1 or eq 2) is involved, then preferential decomposition of the trans-disubstituted oxaphosphetane would presumably explain the high (*E*)-olefin selectivity.

Our suspicions regarding the retro-Wittig rationale were aroused by a variety of considerations. For example, experiments in our laboratory had shown that oxaphosphetanes derived from *moderated* ylides are too short-lived at −70 °C for NMR detection or acid quenching experiments.[5] Could **2** be more resistant to olefin formation, sufficiently so for equilibration to compete? Furthermore, cis-disubstituted oxaphosphetanes corresponding to *nonstabilized ylides* decompose faster than do the trans isomers.[6] Could **2** be so different in terms of relative rates for (*E*)- vs (*Z*)-olefin formation? Since **2** cannot be detected due to its short lifetime, we have used the method of indirect oxaphosphetane formation to probe the intermediates corresponding to the stabilized ylide **4**.

As shown in Scheme I, addition of lithio phosphine **5**[8] to cyclohexanecarboxaldehyde gave a mixture of phosphines **6** and **7** (ca. 3:1 ratio[9]). The phosphines proved

Scheme I



(1) (a) House, H. O.; Rasmusson, G. H. *J. Org. Chem.* **1961**, *26*, 4278. (b) Bestmann, H. J.; Kratzer, O. *Chem. Ber.* **1962**, *95*, 1894.

(2) (a) Speziale, A. J.; Bissing, D. E. *J. Am. Chem. Soc.* **1963**, *85*, 3878. (b) Bissing, D. E.; Speziale, A. J. *J. Am. Chem. Soc.* **1965**, *87*, 2683.

(3) (a) Vedejs, E.; Snoble, K. A. J. *J. Am. Chem. Soc.* **1973**, *95*, 5778. (b) Vedejs, E.; Meier, G. P.; Snoble, K. A. J. *J. Am. Chem. Soc.* **1981**, *103*, 2823.

(4) (a) Bestmann, H. J.; Roth, K.; Eberhard, W.; Bohme, R.; Burzlaff, H. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 876. (b) Bestmann, H. J. *Pure Appl. Chem.* **1979**, *51*, 515. (c) Bestmann, H. J. *Ibid.* **1980**, *52*, 771.

(5) Vedejs, E.; Huang, W. F. *J. Org. Chem.* **1984**, *49*, 212.

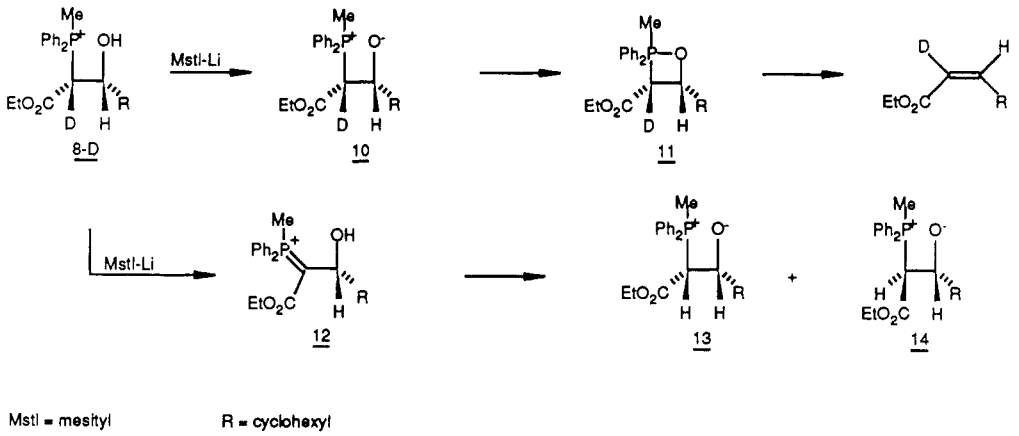
(6) (a) Vedejs, E.; Marth, C.; Ruggeri, R., submitted for publication in *J. Am. Chem. Soc.* (b) Maryanoff, B. E.; Reitz, A. B.; Mutter, M. S.; Inners, R. R.; Almond, H. R., Jr.; Whittle, R. R.; Olofson, R. A. *J. Am. Chem. Soc.* **1986**, *108*, 7664 and references therein.

(7) (a) Vedejs, E.; Fuchs, P. L. *J. Am. Chem. Soc.* **1973**, *95*, 822. (b) Vedejs, E.; Snoble, K. A. J.; Fuchs, P. L. *J. Org. Chem.* **1973**, *38*, 1178. (c) Jones, M. E.; Trippett, S. *J. Chem. Soc. C* **1966**, 1090.

(8) Reetz, M. T.; Eibach, F. *Justus Liebigs Ann. Chem.* **1977**, 242.

0022-3263/87/1952-4637$01.50/0

Scheme II



surprisingly unstable and could only be handled in solution. However, chromatographic separation was possible, and direct methyl triflate alkylation of the major chromatography fraction in the original eluent (hexane/ether/CH_2Cl_2, 8:1:1) precipitated a crystalline salt (ca. 10%) to which structure **8** is assigned on the basis of the characteristic NMR spectrum[10] and subsequent transformations. Similar treatment of the minor component (presumably, **7**) gave no crystals, and attempted purification of **9** resulted in Wittig decomposition to ethyl (*E*)-2-cyclohexylacrylate, 99:1 *E*/*Z*.

The stereochemistry of **8** was proved by treatment with $NaN(SiMe_3)_2$ in THF at −95 °C. This experiment gave highly stereospecific and rapid decomposition to the (*Z*)-alkene upon warming to −78 °C. No intermediates could be detected or intercepted by acid-quenching techniques, and there was <1% stereochemical equilibration. At higher temperatures, partial loss of stereochemistry did occur, but even at 20 °C the (*Z*)-alkene was still the major product ($NaN(SiMe_3)_2$, 61:39 *Z*/*E*; mesityllithium, 59:41 *Z*/*E*). Superficially, these observations suggest that equilibration via eq 1 or eq 2 might be involved, but this is not the case.

Deuterium-labeled phosphonium salt **8-*d*** (Scheme II) was prepared[8] starting from $Ph_2PCD_2CO_2C_2H_5$. Residual protons α to phosphorus were detected at the level of 1% by high-field NMR integration. Treatment of **8-*d*** with mesityllithium[11] in THF at 20 °C gave a significantly higher 73:27 *Z*/*E* ratio than in the case of unlabeled **8**. *All* of the (*E*)-alkene in this experiment was free of deuterium within limits of high field NMR analysis (±1% integral uncertainty). The (*Z*)-alkene contained 51% of the original deuterium (2.3:1 d_1 to d_0). The absence of label in the (*E*)-alkene can only be explained if mesityllithium removes α-deuterons and OH protons competitively as shown in Scheme II. Initial OH proton removal under kinetic control results in the betaine **10**, which decomposes with >98% retention via the oxaphosphetane **11**. Competing removal of the α-deuteron in **8-*d*** affords the hydroxy ylide **12**.[12] Further conversion to alkene can only occur via protonation of **12** by the residual OH protons. We do not know whether proton transfer is intramolecular or intermolecular. However, C-protonation is clearly not stereospecific and eventually converts **12** into both α-protiobetaine diastereomers **13** and **14** in a ratio of 1:1.4, the ratio of deuterium-free (*Z*)- and (*E*)-alkenes. In experiments performed at lower temperatures, the *Z*/*E* ratio increases and the % deuterium loss decreases. In no case have we detected deuterium-containing (*E*)-alkene starting from **8-*d***. Therefore, olefin formation from the betaine **10** and the oxaphosphetane **11** is completely stereospecific! Within the 1–2% limits of NMR detection, there is no Wittig reversal (eq 1) and no stereochemical equilibration by any other means (eq 2, etc). *All* of the equilibration in the control experiments occurs *before* **10** or **11** are formed.

The above findings lead to the conclusion that the reaction of stabilized ylide **4** ($Ph_2CH_3P{=}CHCO_2C_2H_5$) with cyclohexanecarboxaldehyde (95:5 *E*/*Z*) occurs *under kinetic control*! The long-standing belief that stabilized ylide reactions with aliphatic aldehydes involve retro-Wittig equilibration and thermodynamic control is clearly incorrect in this case. In view of the close analogy between $Ph_3P{=}CHR$ and $Ph_2MeP{=}CHR$ in terms of resistance to Wittig reversal,[3,7] it would be most surprising if the commonly used stabilized ylides such as $Ph_3P{=}CHCO_2Et$ behaved differently than does **4**.

The presence of the electron-withdrawing ester substituent accelerates oxaphosphetane decomposition at least as much as it does the retro-Wittig process. Our results rule out the ionic structure **3** in a case where the negative charge might have some stabilization. There is no further basis for invoking such intermediates in representative Wittig reactions.[4] Finally, the new findings raise serious doubts about the idea of reversibility in stabilized ylide reactions. The *irreversible* reaction of **4** with cyclohexanecarboxaldehyde is actually more *E*-selective (95:5 *E*/*Z*) than the corresponding benzaldehyde case (71:29 *E*/*Z*), where control experiments suggest partial reversal under certain (but not all) conditions.[13] Details of the kinetic preference will be discussed in a full paper. For

(9) The ratio is estimated by the *E*/*Z* ratio of alkenes obtained when **6** + **7** are methylated and the resulting **8** + **9** are decomposed at −78 °C with $NaN(SiMe_3)_3$ (kinetic control, assuming impurities do not induce formation of **12**).

(10) **8**: ^1H NMR (500 MHz, acetone-d_6) δ 1.14 (3 H, t, J = 7.10 Hz), 0.71–1.24 (m, 6 H), 1.56–2.03 (m, 5 H), 3.05 (d, J_{Me-P} = 13.95 Hz), 3.72 (ddd, J_{H3-H2} = 1.65 Hz, J_{H3-H4} = 11.85 Hz, J_{H3-P} = 11.85 Hz), 4.14 (q, d, J = 7.12, 10.85 Hz), 4.20 (q, d, J = 7.09, 10.79 Hz), 4.33 (dd, J_{H2-H3} = 1.65 Hz, J_{H2-P} = 12.85 Hz), 7.70–7.79 (m, 4 H), 7.82–7.94 (m, 2 H), 8.07–8.15 (m, 4 H); ^{31}P NMR (202.4 MHz, acetone-d_6) δ 29.97; mp 150–153 °C. **8-*d*** same as **8** but the signal at δ 4.33 disappears and the signal at δ 3.72 is dd, J_{H3-H4} = 11.85 Hz, J_{H3-HP} = 11.85 Hz.

(11) Seebach, D.; Beck, A. K.; Hoekstra, M. S. *Tetrahedron Lett.* **1977**, *18*, 1187.

(12) For previous examples of equilibration via hydroxy ylide formation involving nonstabilized ylides, see ref 7b.

(13) Control experiments similar to those in Scheme I indicate that benzaldehyde adducts of **4** undergo extensive or negligible retro-Wittig cleavage depending on conditions. The highest reversal has been detected in ether solvents (maximum 50–60%), but there is no detectable loss of stereochemistry when the cis precursor hydroxyphosphonium salt is treated with DBU at room temperature in methanol. These observations cannot be fully interpreted until labeling studies to be described in a full paper are completed.

now, we note that kinetic trans oxaphosphetane selectivity is a logical consequence of an asynchronous cycloaddition with a relatively advanced, product-like transition state because the trans oxaphosphetanes are more stable than the cis isomers in all known examples of isomer interconversion.[6] Since **4** reacts with a *kinetic* preference for (*E*)-alkenes, equilibrium arguments for related Wittig reactions of stabilized ylides with aliphatic aldehydes are neither necessary nor justified.

Acknowledgment. This work was supported by the National Science Foundation (CHE-8306121).

Registry No. **4**, 110223-71-7; **5**, 110223-68-2; **8**-OTf$^-$, 110223-70-6; **8**-*d*, 110223-72-8; cyclohexanecarboxaldehyde, 2043-61-0.

E. Vedejs,* T. Fleck, S. Hara

S. M. McElvain Laboratory of Organic Chemistry
Chemistry Department
University of Wisconsin, Madison, Wisconsin 53706

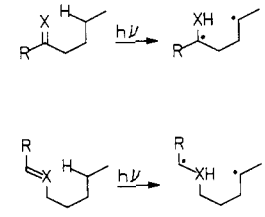
Received June 1, 1987

Photochemical 1,5-Hydrogen Transfer of 1,2-Disubstituted Acyclic Alkenes. A Novel Entry to 1,6-Diradicals

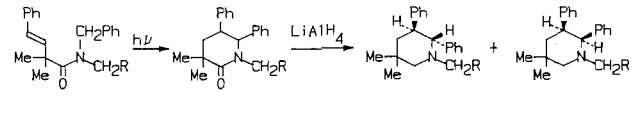
Summary: Photolysis of β,γ-unsaturated amides **1a** and **1b** gives cyclization products **2a** and **2b** via 1,6-diradical intermediates formed by 1,5-hydrogen transfer.

Sir: Photochemical 1,5-hydrogen transfer of carbonyl compounds (Norrish type II reaction),[1] thioketones,[2] and 1,1-disubstituted alkenes[3] is one of the most extensively studied photoreactions. In these reactions, the hydrogen transfer via six-membered cyclic transition states gives 1,4-diradicals (Scheme I) which undergo either elimination or cyclization to give four-membered cyclic compounds. It is well-known that 1,6-hydrogen transfer is sterically less favorable than 1,5-hydrogen transfer.[4,5] 1,7-Hydrogen transfer which gives 1,6-diradicals via eight-membered cyclic transition states (ϵ-hydrogen abstraction) is extremely rare because of highly unfavorable conformational factors.[2,6,7,8] Photochemical 1,5-hydrogen transfer of 1,2-disubstituted acyclic alkenes (or imines) via sterically favorable six-membered transition states could give 1,6-diradicals (Scheme I). However, such reactions are hitherto unknown presumably because of the presence of rapid

Scheme I



Scheme II



1		2	3	4
a: R=Ph	in MeOH	45%		17%
	in MeCN	40%		6%
b: R=H	in MeOH	39%		12%

competitive processes in the excited states, e.g., *E-Z* isomerization. We report here the first example of 1,5-hydrogen transfer of acyclic 1,2-disubstituted alkenes which produces 1,6-diradicals.[9]

When *N*,*N*-dibenzyl-2,2-dimethyl-4-phenylbut-3-enamide (**1a**) in methanol was irradiated with a low-pressure mercury lamp,[10] 3,3-dimethyl-5,6-diphenyl-1-benzylpiperidin-2-one (**2a**) was obtained. The cyclization product was a mixture of two stereoisomers which were not completely separated. The separation was achieved after conversion into the corresponding piperidines **3a** and **4a** by reduction with lithium aluminum hydride (Scheme II). Photolysis of **1a** in acetonitrile gave a similar result. The structures of **3a** and **4a** were confirmed by elemental analyses and spectral data.[11] The stereochemistry of **3a** and **4a** was assigned as shown in Scheme II on the basis of the coupling constant between the vicinal protons on C-2 and C-3 in the NMR spectrum of **4a** (6 Hz). The stereoselectivity in the photocyclization is explainable in terms of the stabilities of the products: the major isomer is presumed to be more stable than the minor one because both of the phenyl groups are equatorial.

Photolysis of an *N*-benzyl-*N*-methyl amide (**1b**) also gave the corresponding cyclization products. In this reaction, no methyl-hydrogen-abstraction products were detected. Meanwhile, an *N*,*N*-diethyl amide (1c) did not afford cyclization products on irradiation but underwent only *E-Z* isomerization.

The formation of **2** is quite reasonably explained in terms of 1,5-hydrogen transfer followed by cyclization of the resulting 1,6-diradical **5**. The regiospecific benzyl-hydrogen-abstraction in the photolysis of **1b** as well as the

(1) Wagner, P. J. *Acc. Chem. Res.* **1971**, *4*, 168. (b) Wagner, P. J. *Rearrangements in Ground and Excited States*; de Mayo, P., Ed.; Academic: New York, 1980.

(2) (a) de Mayo, P.; Suau, R. *J. Am. Chem. Soc.* **1974**, *96*, 6807. (b) Aoyama, H.; Susuki, S.; Hasegawa, T.; Omote, Y. *J. Chem. Soc., Perkin Trans. 1* **1982**, 247.

(3) Hornback, J.; Proel, G. S. *J. Am. Chem. Soc.* **1979**, *101*, 7367. Hornback, J. M.; Barrows, R. D. *J. Org. Chem.* **1982**, *47*, 4285.

(4) (a) Wagner, P. J.; Kelso, P. A.; Kempainen, A. E.; Zepp, R. G. *J. Am. Chem. Soc.* **1972**, *94*, 7500. (b) Wagner, P. J.; Giri, B. P.; Scaiano, J. C.; Ward, D. L.; Gabe, E.; Lee, F. L. *Ibid.* **1985**, *107*, 5483. (c) Aoyama, H.; Inoue, Y.; Omote, Y. *J. Org. Chem.* **1981**, *46*, 1965. Thiones undergo 1,6-hydrogen transfer preferentially; see ref 2a.

(5) For a recent theoretical study on hydrogen transfer via six- and seven-membered transition states, see: Dorigo, A. E.; Houk, K. N. *J. Am. Chem. Soc.* **1987**, *109*, 2195.

(6) Meador, M. A.; Wagner, P. J. *J. Org. Chem.* **1985**, *50*, 419.

(7) Carless, H. A. J.; Fekarurhobo, G. K. *Tetrahedron Lett.* **1984**, *25*, 5943.

(8) Aoyama, H.; Arata, Y.; Omote, Y. *J. Chem. Soc., Chem. Commun.* **1985**, 1381.

(9) For a review on the photochemistry of alkenes, see: Kropp, P. *J. Org. Photochem.* **1979**, *4*, 1.

(10) The unsaturated amide (300 mg) in methanol (60 mL) was irradiated with a low-pressure mercury lamp (Rayonet Photochemical Reactor RPR 2537 A, the Southern New England Ultraviolet Co) for 4.5 h.

(11) **3a**: mp 112–113 °C; ^{1}H NMR ($CDCl_3$) δ 0.88 (s, 3 H, Me), 1.26 (s, 3 H, Me), 1.52–1.72 (m, 2 H, CH_2), 1.92 and 2.64 (AB q, 2 H, J = 11 Hz, NCH_2), 2.81 and 3.77 (AB q, 2 H, J = 14 Hz, benzylic), 2.96–3.24 (m, 2 H, 2-H and 3-H), 6.6–7.8 (m, 15 H, Ph); ^{13}C NMR ($CDCl_3$) δ 24.4 (q), 29.7 (q), 30.6 (s), 46.1 (t), 48.6 (d), 59.3 (t), 64.3 (t), 74.7 (d), 125.8–128.0, 140.0 (s), 142.8 (s), 143.5 (s); mass spectrum (EI) m/z 355 (M^+). **4a**: bp 150–160 °C (0.1 Torr (bath temperature)); ^{1}H NMR ($CDCl_3$) δ 1.09 (s, 3 H, Me), 1.15 (s, 3 H, Me), 1.43 (dd, 1 H, J = 3 Hz and J = 13 Hz, 4-H), 2.19 (t, 1 H, J = 13 Hz, 4-H), 2.33 and 2.72 (AB q, 2 H, J = 11 Hz, NCH_2), 3.34 and 3.49 (AB q, 2 H, J = 14 Hz, benzylic), 3.4–3.7 (m, 1 H, 3-H), 4.00 (d, 1 H, J = 6 Hz, 2-H), 6.7–7.4 (m, 15 H, Ph); ^{13}C NMR ($CDCl_3$) δ 26.4 (q), 30.2 (q), 31.4 (s), 37.2 (t), 42.7 (d), 58.1 (t), 59.6 (t), 69.3 (d), 125.7–130.1, 139.7 (s), 139.9 (s), 142.7 (s); mass spectrum (EI), m/z 355 (M^+). The compounds **3a** and **4a** gave satisfactory analytical data (0.25%).

0022-3263/87/1952-4639$01.50/0