IV. The racemic acorenone was shown to be identical by ^1H NMR and chromatographic properties with a sample of natural (−)-acorenone.[14]

The lower efficiency of these spirocyclizations compared to simpler models,[3] especially for diastereomer **8b**, was unexpected, and efforts are under way to improve the reaction. The necessity of chromatographic separation of diastereomeric complexes would be removed by selective formation of one diastereomeric complex (**8a** or **8b**), an interesting problem with little precedent.

Acknowledgments. We are pleased to acknowledge support of this work from the National Science Foundation.

Supplementary Material Available: Characterization data (^1H NMR, ^{13}C NMR, IR, UV, mass spectroscopy, and combustion analysis) on all new compounds (5 pages). Ordering information is given on any current masthead page.

(16) Fellow of the John Simon Guggenheim Foundation, 1978–1979.

M. F. Semmelhack,* A. Yamashita
Frick Chemistry Laboratory, Princeton University
Princeton, New Jersey 08544
Received April 21, 1980

Stereoselective and Regioselective Ene Reactions of Methyl α-Chloroacrylate

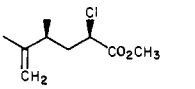
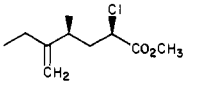
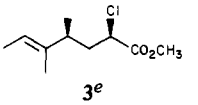
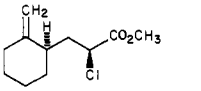
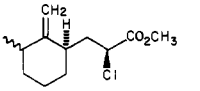
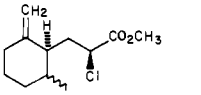
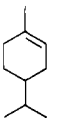
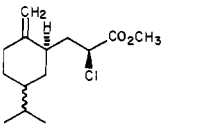
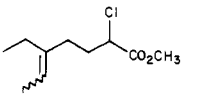
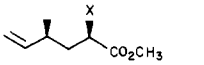
Sir:

The use of carbon–carbon double bonds as activating groups for the formation of new carbon–carbon bonds under mild conditions is of considerable interest in organic synthesis. The ene reaction provides a potential solution to this problem (Scheme I).[1] We have found that $AlCl_3$-catalyzed ene reactions of methyl acrylate[2] or methyl propiolate[3] occur at 25 °C. We have also found that $EtAlCl_2$ is a more effective catalyst for these reactions since it can also function as a proton scavenger.[3b] Lewis acid catalysis offers significant advantages over the corresponding thermal ene reactions which occur at 200–300 °C.[1]

Since the ene reactions of methyl acrylate are slow and of limited utility, we chose to activate acrylate by placing an electron-withdrawing group in the α position. This will lead to a less basic ester and therefore a more reactive Lewis acid complex. We have observed that substitution of propiolate with an electron-withdrawing group in the β position led to a more reactive Lewis acid complex.[4] Chlorine and bromine were chosen as substituents since they are inductively electron withdrawing ($\mathcal{F}$ = 0.69 and 0.73) but resonance donating ($\mathcal{R}$ = −0.16 and −0.18).[5,6]

We report here novel stereoselective and regioselective Lewis acid catalyzed ene reactions of methyl α-haloacrylates. Reaction proceeds predominantly through transition state **10**, in which the carbomethoxy group is endo and the hydrogen is transferred from the alkyl group syn to the alkenyl hydrogen. The carbomethoxy group may prefer to be endo due to secondary orbital overlap or electrostatic stabilization of a polar transition state. The alternate transition state **11**, in which the carbomethoxy group is endo and the hydrogen is transferred from the alkyl group anti to the alkenyl hydrogen, may be disfavored because of steric interaction between R_1 and the halide which is exo. As expected, methyl acrylate,

Table I. Ene Reactions of Methyl α-Chloroacrylate

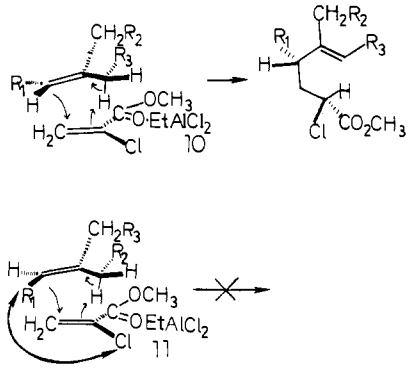
run	alkene	conditions[a] (time, days)	major ene adduct[b]	yield
1		A (1.2)	 **1**[c]	74%
2		A (0.8)	 **2**[d]	86%
3		A (0.6)	 **3**[e]	82%
4		B (2)	 **4**[f]	41%
5		B (5)	 **5**[g] (60% trans)	13%
6		B (5)	 **6**[h] (67% trans)	18%
7		B (4)	 **7**[i] (92% trans)	35%
8		B (0.5)	 **8** (≈75% *E*)	55%
9		C (2)	 **9a**[c] X = Cl	16%
10		D (3)	**b**[c] X = Br	51%

[a] (A), Alkene is 0.5 M in benzene, 0.9 equiv of MCA, 0.8 equiv of $EtAlCl_2$ at 25 °C; (B) alkene is 0.5 M in benzene, 1.8 equiv of MCA, 0.45 equiv of $EtAlCl_2$ at 25 °C; (C) MCA is 0.8 M in benzene, 6.5 equiv of *trans*-2-butene, 0.23 equiv of $EtAlCl_2$ at 67 °C; (D) MBA is 2.1 M in benzene, 5.0 equiv of *trans*-2-butene, 0.45 equiv of $EtAlCl_2$ at 70 °C. [b] All adducts were characterized by ^1H and ^{13}C NMR spectroscopy, IR spectroscopy, and elemental analysis. Isomer ratios were determined by GC and ^{13}C NMR spectra. [c] Contaminated with ≈5% of the diastereomer. [d] Contaminated with ≈5% of the diastereomer of 2 and ≈10% of the diastereomer of 3. [e] Contaminated with ≈20% of the diastereomer of 3 and ≈10% of the *Z* isomer of 3 or its diastereomer. [f] None of the other diastereomer was detectable by ^{13}C NMR. [g] The absorption of the alkene methylene group in the ^{13}C NMR spectra occurs at δ 107.6 for the trans isomer and δ 101.8 for the cis isomer. See ref 10. [h] The absorption of the methyl group in the ^1H NMR spectra occurs at δ 1.03 for the trans isomer and δ 0.94 for the cis isomer. See ref 11. [i] The absorption of the alkene methylene group in the ^1H NMR occurs at δ 4.76 (br s) for the trans isomer. In the cis isomer, it absorbs as two singlets with one hydrogen shifted upfield to δ 4.56. See ref 12.

(1) For a review, see: Hoffmann, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 556.
(2) Snider, B. B. *J. Org. Chem.* **1974**, *39*, 255. See also: Beckwith, A. L. J.; Moad, G. *Aust. J. Chem.* **1977**, *30*, 2733. Greuter, H.; Bellus, D. *Synth. Commun.* **1976**, *6*, 409. Åkermark, B.; Ljungqvist, A. *J. Org. Chem.* **1978**, *43*, 4387.
(3) (a) Snider, B. B. *J. Org. Chem.* **1976**, *41*, 3061: (b) Snider, B. B.; Rodini, D. J.; Conn, R. S. E.; Sealfon, S. *J. Am. Chem. Soc.* **1979**, *101*, 5283.
(4) Snider, B. B.; Roush, D. M. *J. Am. Chem. Soc.* **1979**, *101*, 1906. Snider, B. B.; Roush, D. M.; Rodini, D. J.; Gonzalez, D.; Spindell, D. *J. Org. Chem.* **1980**, *45*, 2773.
(5) Swain, C. G.; Lupton, E. C., Jr. *J. Am. Chem. Soc.* **1968**, *90*, 4328.
(6) Acrylates substituted in the α position with substituents which are electron withdrawing by induction and resonance are, of course, reactive. Unfortunately, these compounds, such as methyl α-cyanoacrylate, tend to undergo ionic reactions due to their ability to stabilize an anionic intermediate.

0002-7863/80/1502-5926$01.00/0

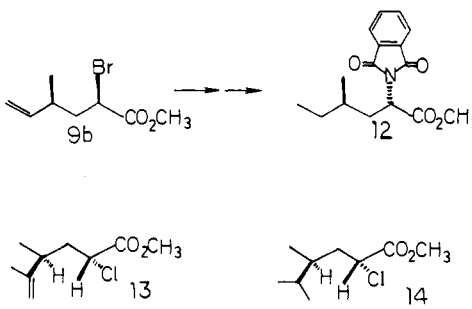
Scheme I



in which a hydrogen is exo, shows less regioselectivity. The new carbon–carbon bond is formed exclusively at the less substituted carbon of the alkene due to both electronic and steric effects.

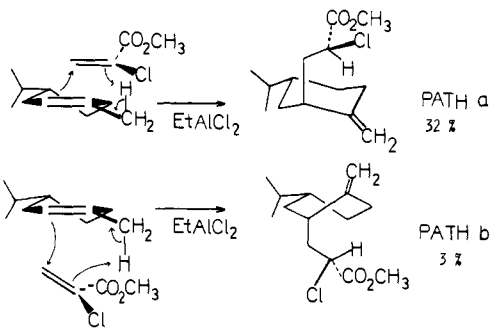
Methyl α-chloroacrylate (MCA), a readily available acrylate derivative,[7] is, as expected, considerably more reactive in $EtAlCl_2$-catalyzed ene reactions than methyl acrylate.[8] Good yields of ene adducts are obtained with 1,1-disubstituted and trisubstituted alkenes at 25 °C (See Table I). Unreactive alkenes, such as *trans*-2-butene, which do not contain a disubstituted carbon, react at higher temperatures (70 °C) and give better yields with methyl α-bromoacrylate (MBA)[9] (compare runs 9 and 10). The reactions of 1-methylcyclohexene derivatives with MCA cannot be run to high conversion since the ene adduct slowly decomposes under the reaction conditions, presumably by intramolecular proton transfer of the acidic α proton of the adduct–$EtAlCl_2$ complex to the reactive *exo*-methylene group.

The stereochemistry of the ene reaction was proven by conversion of **9b** to **12**, whose stereochemistry was proven by NMR spectral comparison with authentic samples of **12** and its diastereomer.[13] Reaction of **9b** with sodium azide with hexadecyltributylphosphonium bromide as phase-transfer catalyst (71%),[14] reduction of the azide and hydrogenation over W-2 Raney nickel (82%), and reaction with phthalic anhydride[15] give **12** (57%). Hydrolysis of the methyl ester prior to reaction with phthalic anhydride gives the unnatural diastereomer of homoleucine[13] in 75% yield.



Further confirmation of the stereochemistry of the ene reaction is obtained from examination of the ^1H NMR spectra of the major isomer (95%) of **1**, in which the methine hydrogens are both coupled to the methylene group as a doublet of doublets, J = 5.0 and 9.4 Hz. The methine hydrogens of the minor isomer (obtained by epimerization) are both coupled to the methylene group as a doublet of doublets, J = 7.5 and 7.5 Hz. The major isomer exists as the preferred conformation **13** due to attractive interactions between H-4 and the chlorine and H-2 and the double bond. Hydrogenation of **1** gives **14**, which, as expected, has no preferred conformation (H-2 absorbs as a doublet of doublets, J = 6.9 and 8.2 Hz).

Scheme II



This is the first case in which the stereochemistry of an ene reaction producing 1,3-asymmetric centers has been determined. The high degree of stereospecificity is especially remarkable since Diels–Alder reactions of MCA give mixtures of endo and exo isomers.[16] Lewis acid catalyzed ene reactions with 1,1-disubstituted enophiles may provide a general solution to the problem of control of 1,3-asymmetric centers in acyclic molecules.

The regiospecificity of the ene reactions is most clearly observed in runs 2 and 3. (*Z*)-3-Methyl-2-pentene gives a mixture of ≈85% **2**, formed via transition state **10**, ≈5% of the diastereomer of **2**, and 10% of the diastereomer of **3** via **11**. Apparently, interaction of the group adding endo with the ethyl group in **10** results in slight loss of regioselectivity. (*E*)-3-Methyl-2-pentene gives a mixture of 70% **3**, via **10**, 20% of the diastereomer of **3**, and 10% of a *Z* isomer. In this case, interaction of the ethyl group ($R_3 = CH_3$) with CO_2Me·$EtAlCl_2$ in **10** leads to loss of stereospecificity. Similar regiospecifity is observed in the reactions of 1-methylcyclohexenes (runs 4–7), in which only methylenecyclohexanes are formed. Tetrasubstituted and cis-1,2-disubstituted alkenes, in which there is no alkyl group syn to an alkenyl hydrogen, are unreactive.

This is the first example of regiospecific transfer of a hydrogen from the alkyl group syn to the alkenyl hydrogen in an ene reaction. It complements the ene reactions of β-substituted propiolates which, we have discovered, regiospecifically transfer a hydrogen from the alkyl group anti to the alkenyl hydrogen.[4]

Since the production of 2-alkylmethylenecyclohexanes from 1-methylcyclohexenes is of considerable synthetic utility, the effect of substituents on the reaction was examined. All three reactions examined (runs 5–7) are completely regiospecific. However, at longer reaction times, the product is isomerized and/or polymerized. In all three cases, MCA approaches predominantly from the side of the ring opposite to the substituent. Run 7, in which the cyclohexene is anchored[17] and the equatorial isopropyl group does not sterically interact with approaching MCA, indicates the preference for formation of the chair product (Scheme II, path a). The minor isomer is formed initially as a twist boat (Scheme II, path b). Formation of the minor isomer from the conformer with an axial isopropyl group is unlikely due to a 1,3-diaxial interaction when MCA approaches from the same side as an axial isopropyl group. The major isomer of **5** is formed as a chair

(7) Pashtushak, N. O.; Dombrovskii, A. V.; Mukhova, A. N. *Zh. Org. Khim.* **1965**, *1*, 572; *J. Org. Chem. USSR (Engl. Transl.)* **1965**, *1*, 566.

(8) Reaction of methyl acrylate with 1-methylcyclohexene under condition B (see Table I) for 6 days gives a 6% yield of ene adducts as a ≈1:1 mixture of regioisomers. Compare this to run 4 in which a single regioisomer is formed in 41% yield after 2 days.

(9) Marvel, C. S.; Cowan, J. C. *J. Am. Chem. Soc.* **1939**, *61*, 3158.

(10) Grover, S. H.; Stothers, J. B. *Can J. Chem.* **1975**, *53*, 589.

(11) Pfeffer, P. E.; Osman, S. F. *J. Org. Chem.* **1972**, *37*, 2425.

(12) Pillot, J.-P.; Dělěris, G.; Dunoguès, J.; Calas, R. *J. Org. Chem.* **1979**, *44*, 3397.

(13) Bernasconi, S.; Corbella, A.; Gariboldi, P.; Jommi, G. *Gazz. Chim. Ital.* **1977**, *107*, 95. H-2 of **12** absorbs at δ 4.82 (dd, J = 4.45, 11.2 Hz). H-2 of the diastereomer of **12** absorbs at δ 4.78 (dd, J = 6.6, 8.3 Hz). We thank Dr. Bernasconi for providing us with complete spectral data of these compounds.

(14) Reeves, W. P.; Bahr, M. L. *Synthesis* **1976**, 823. Landini, D.; Rolla, F. *Ibid.* **1976**, 389.

(15) King, F. E.; Kidd, D. A. A. *J. Chem. Soc.* **1949**, 3315.

(16) Cantello, B. C. C.; Mellor, J. M. *Tetrahedron* Lett. **1968**, 5179. Use of $EtAlCl_2$ as catalyst for these Diels–Alder reactions does not change the endo/exo ratio significantly.

(17) The *A* value for an isopropyl group is ≈2.15. See: Jensen, F. R.; Bushweller, C. H. In "Advances in Alicyclic Chemistry"; Hart, H.; Karabatsos, G. J., Ed.; Academic Press: New York, 1971; Vol. 3, pp 140–195.

(18) Fellow of the Alfred P. Sloan Foundation, 1979–1981.

cyclohexane from the conformer with a pseudoaxial methyl group and/or as a twist boat from the conformer with a pseudoequatorial methyl group to avoid the approach of MCA from the same side of the ring as the 3-methyl group.

The α-halo esters formed in these ene reactions are useful synthetic intermediates. The halide can be displaced with inversion by a variety of nucleophiles. The use of these adducts for the synthesis of δ,ϵ-unsaturated amino acids will be reported shortly.

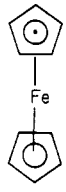
Acknowledgments. We thank the Mobil Foundation and Upjohn Corporation for financial support of this work.

Barry B. Snider,*[18] John V. Dunčia
Department of Chemistry, Princeton University
Princeton, New Jersey 08544
Received February 14, 1980

Bis(pentadienyl)iron Compounds: The "Open Ferrocenes"

Sir:

A great deal of the current interest in organometallic chemistry was spawned by the reports of the unusually stable compound ferrocene, $(C_5H_5)_2Fe$[1] (I). A very interesting molecular orbital



I

scheme involving efficient covalent interaction of iron s, p, and d valence orbitals with the cyclopentadienyl ligands' molecular orbitals has been helpful in understanding the stability of these complexes and various chemical trends.[2]

It is here noted that the molecular orbitals of a *pentadienyl* anion in a "U" configuration are quite analogous in symmetry and orientation to those of the cyclopentadienyl ligand, although the energetic orderings do differ.[3] These considerations would seem to suggest that a large class of compounds should exist in which the pentadienyl ligand replaces its more familiar cyclic counterpart. In fact, however, only relatively few metal complexes with the pentadienyl ligand are known,[4] although there would seem to be substantial advantages to a more widespread implementation

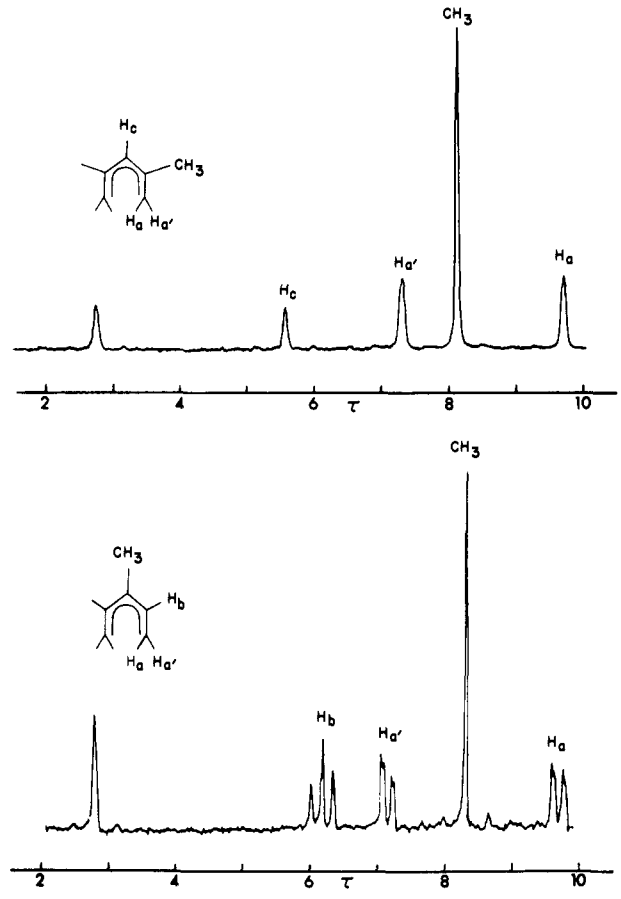
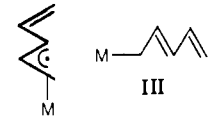


Figure 1. ^{1}H NMR spectra (C_6D_6 solvent, C_6D_5H internal standard) of (top) bis(2,4-dimethylpentadienyl)iron and (bottom) bis(3-methylpentadienyl)iron. The peaks at τ 2.77 are due to the C_6D_5H resonance.

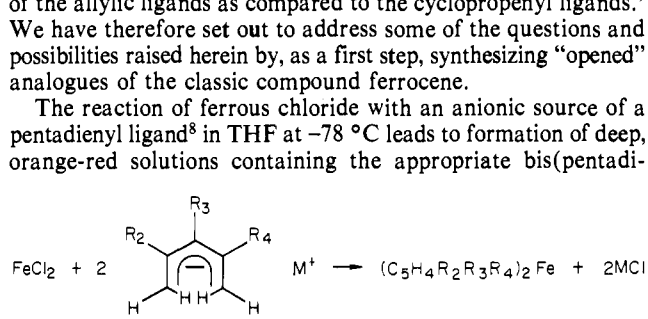
of these ligands in such complexes. For example, as this ligand is noncyclic, it should be much more prone to (reversibly) isomerize to η^3 (II) or η^1 (III) bonded configurations, a process likely to



II III

be of some chemical importance.[6] As a crude comparison in this regard, one can note the much greater versatility and application of the allylic ligands as compared to the cyclopropenyl ligands.[7] We have therefore set out to address some of the questions and possibilities raised herein by, as a first step, synthesizing "opened" analogues of the classic compound ferrocene.

The reaction of ferrous chloride with an anionic source of a pentadienyl ligand[8] in THF at −78 °C leads to formation of deep, orange-red solutions containing the appropriate bis(pentadi-



M = Li, K IV, $R_2 = R_3 = R_4 = H$
V, $R_2 = R_4 = CH_3$; $R_3 = H$
VI, $R_2 = R_4 = H$; $R_3 = CH_3$
VII, $R_2 = R_3 = CH_3$; $R_4 = H$

(1) (a) Kealy, T. J.; Pauson, P. L. *Nature (London)* **1951**, *168*, 1039. (b) Miller, S. A.; Tebboth, J. A.; Tremaine, J. F. *J. Chem. Soc.* **1952**, 632. (c) Wilkinson, G. *J. Organomet. Chem.* **1975**, *100*, 273.

(2) (a) Lauher, J. W.; Hoffman, R. *J. Am. Chem. Soc.* **1976**, *98*, 1729. (b) Sohn, Y. S.; Hendrickson, D. N.; Gray, H. B. *Ibid.* **1971**, *93*, 3603. (c) Cotton, F. A.; Wilkinson, G. "Advanced Inorganic Chemistry", 4th ed.; Interscience: New York, 1980.

(3) Streitwieser, A., Jr. "Molecular Orbital Theory for Organic Chemists", Wiley: New York, 1961.

(4) (a) Mahler, J. E.; Pettit, R. *J. Am. Chem. Soc.* **1962**, *84*, 1511. (b) Giannini, U.; Pellino, E.; Lachi, M. P. *J. Organmet. Chem.* **1968**, *12*, 551. (c) Rienacker, R.; Yoshiura, H. *Agnew Chem., Int. Ed. Engl.* **1969**, *8*, 677. (d) Krüger, C. *Ibid.* **1969**, *8*, 678. (e) A greater number of cyclohexadienyl metal complexes are known,[5] but their cyclized nature and ready reversion to arene complexes are likely to be detrimental with respect to their chemistry and σ/π-related isomerizations.

(5) For example, see: (a) Semmelhack, M. F.; Hall, H. T., Jr.; Farina, R.; Yoshifuji, M.; Clark, G.; Barger, T.; Hirotsu, K.; Clardy, J. *J. Am. Chem. Soc.* **1979**, *101*, 3535. (b) Mahler, J. E.; Pettit, R. *Ibid.* **1963**, *85*, 3955. (c) Calderazzo, F. *Inorg. Chem.* **1966**, *5*, 429. (d) Whitesides, T. H.; Lichtenberger, D. L.; Budnik, R. A. *Ibid.* **1975**, *14*, 68. (e) Khand, I. U.; Pauson, P. L.; Watts, W. E. *J. Chem. Soc.* **1969**, 2024. (f) Jones, D.; Pratt, L.; Wilkinson, G. *J. Chem. Soc.* **1962**, *4458*. (g) Bird, P. H.; Churchill, M. R. *Chem. Commun.* **1967**, 777. (h) Helling, J. F.; Braitsch, D. M. *J. Am. Chem. Soc.* **1970**, *92*, 7209. (i) Khand, I. U.; Pauson, P. L.; Watts, W. E. *J. Chem. Soc.* **1968**, 2257, 2261.

(6) (a) Tsutsui, M.; Courtney, A. *Adv. Organomet. Chem.* **1979**, *16*, 241. (b) Powell, J. *MTP Int. Rev. Sci.: Inorg. Chem., Ser. One* **1972**, *6*, 273.

(7) (a) Stone, F. G. A.; West, R., Eds. *Adv. Organomet. Chem.* **1979**, *17*, I. (b) See, however: King, R. B.; Ikai, S. *Inorg. Chem.* **1979**, *18*, 949.

(8) (a) Bates, R. B.; Gosselink, D. W.; Kaczynski, J. A. *Tetrahedron Lett.* **1967**, 199. (b) Yasuda, H.; Ohnuma, Y.; Yamauchi, M.; Tani, H.; Nakamura, A. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 2036.

0002-7863/80/1502-5928$01.00/0