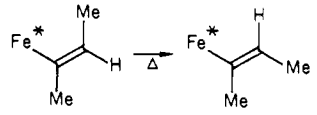
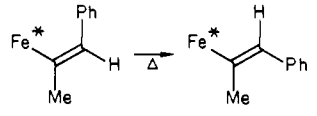
vinyl hydrogen atoms (also see the cleavage reactions and the NOE results on complex **5** outlined below).

Both compounds **1** and **3** have the larger $\beta$ substituent cis to the iron. Heating either compound in toluene solution at ca. 40 °C for 15 min causes isomerization to the presumably more stable isomers **4** and **5** (eq 2 and 3). Again, $^1$H NOE enhancement




(2)

1 4




(3)

3 5

experiments proved the stereochemistry of the products. For example, with **5**, irradiation of the vinyl hydrogen atom resonance now leads to no enhancement of the methyl resonances whereas irradiation of the phenyl resonance leads to a 22% enhancement of the methyl resonance. Note that the methyl-vinyl hydrogen coupling remains small (1.4 Hz) as expected for this isomer. Bergman has reported an analogous (probably base catalyzed) isomerization for a nickel-alkenyl complex.[11] Further investigations of these isomerization reactions are under way at present.

That these alkenyl complexes can be useful in the synthesis of alkenes is demonstrated by the fact that the alkenyl group can be cleaved by halogens with retention of stereochemistry. As shown in Scheme I, reaction of **1** with $Br_2$[12] at -78 °C in $Et_2O$ yields **6**[13] and of **2** with $I_2$[12] in warm $CS_2$ yields **7**.[14] Cleavage of **3** and **5** with $Br_2$[15] and **4**[16] and **5**[17] with $I_2$ also proceeds with retention of stereochemistry. Isolated yields of alkenes in these small-scale reactions are good (60-78%), and the Fe*-X complex is isolated nearly quantitatively. Note for the two compounds (**1** and **3**) undergoing the cis-trans isomerization reaction that either alkene isomer can be cleaved free of contamination of the other. Because the iron starting material for this chemistry, Fe*-X (X = I, Br), is inexpensive and easy to prepare on a large scale[18] (and is recovered in the last step), the reactions outlined here represent a new and potentially powerful method for preparing specifically substituted alkenes from internal alkynes, a method different in approach and result from zirconium[3b] or copper chemistry.[19] Complete development of this method for the synthesis of alkenes is under way at present.

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*Received April 28, 1980*

## Arene-Metal Complexes in Organic Synthesis. Synthesis of Acorenone and Acorenone B

*Sir:*

The development of synthesis strategies for the generation of a quaternary carbon, especially a spirocyclic ring system with good control over the stereochemistry, continues to be a challenge to organic synthesis. Among spirocyclic natural products, the spiro[4.5]decane system has been studied often because of many examples in nature and interesting elements of stereochemistry. Acorenone (**1**) and acorenone B (**2**) are members of this class of sesquiterpenes and have been synthesized by several research groups.[1] In common with most previous syntheses of spirosesquiterpenes,[2] the strategy in these efforts involved the formation of *gem*-disubstituted monocyclic ring systems and then construction of the second ring. We have reported a new approach to the formation of spiro[4.5]decenones which appears particularly attractive as the basis of a simple synthesis of the acorenones.[3]

Acorenone and acorenone B have the common structural feature of a spiro ring formed from a 2-substituted cyclohexenone and 1,3-dialkylcyclopentane. There are three centers of chirality, the carbons bearing the methyl and isopropyl groups and the spiro carbon. Our strategy (Scheme I) relies on the activating and meta-directing effects of the chromium tricarbonyl group[4] to introduce the spirocyclopentane unit by nucleophilic addition to an anisole derivative (**3**). It employs the specific exo addition to coordinated arenes[5,6] to control the configuration at the spiro carbon. Hydrogenation of an *exo*-methylene unit is proposed to introduce the cis relationship of the two alkyl groups. The execution of this strategy is outlined in Schemes II-IV, showing all isolated intermediates.

As outlined in Scheme II, the chromium complex **3** was prepared in 95% yield by heating *o*-methylanisole and chromium hexacarbonyl in dioxane at reflux with an air condenser.[5,7] Complex **3** was easily crystallized (mp 71-72 °C) and has been prepared on a 70-g scale. The first crucial bond is formed by reaction of **3** with the cyanohydrin acetal anion **4**[8] followed by oxidation with excess iodine. Treatment with aqueous acid and then base converted the cyanohydrin acetal to a ketone unit,[8] effecting formal nucleophilic substitution for hydrogen by an acyl group. The reaction produced isomer **5** (90-95% yield) contaminated by a trace (<3%) of a positional isomer.[9] The 4-carbon side chain required for cyclization (in **7**) was obtained by addition

(11) Huggins, J. M.; Bergman, R. G. *J. Am. Chem. Soc.* **1979**, *101*, 4410-4412.

(12) The $Br_2$ cleavage reactions were carried out by cooling an $Et_2O$ solution of the complex to -78 °C followed by the dropwise addition of 1 equiv of $Br_2$ in $Et_2O$, and the resultant solution was stirred cold for 2 h. The $I_2$ cleavage reactions were carried out by dropwise addition of 1 equiv of $I_2$ in $CS_2$ to a $CS_2$ solution of the complex heated to 35 °C. To either reaction is added degassed $H_2O$, the water layer is extracted with ether, the organic extracts were combined and dried over $MgSO_4$, and the filtered solution was flash evaporated into a liquid nitrogen cooled trap at low pressure. The organic compound is isolated by evaporation of the solvent from the warmed solution in the trap (60-78% yield), and they were identified by comparison of IR and $^1$H NMR data with literature values as noted. The Fe*-X complex (X = Br, I) was isolated by a brief chromatography on alumina, eluting with $CH_2Cl_2$, of the remaining residue after the flash evaporation. Note that up to the step of the flash evaporation the solutions need moderate protection from oxygen.

(13) Vidal, M.; Vincens, M.; Arnaud, P. *Bull. Soc. Chim. Fr.* **1972**, 665-681.

(14) Stereochemistry assigned by $^1$H NOE enhancement experiments. $^{13}$C and $^1$H NMR data are also consistent with the formulation.

(15) Klein, J.; Levene, R. *Tetrahedron Lett.* **1974**, 2935-2938.

(16) Matter, A. E.; Pascual, C.; Pretsch, E.; Pross, A.; Simon, W.; Sternhell, S. *Tetrahedron* **1969**, *25*, 2023-2034.

(17) Heck, R. F.; Schoenberg, A.; Bantoletti, I. J. *Org. Chem.* **1974**, *39*, 3318-3326.

(18) (a) King, R. B. In "Organometallic Synthesis"; Eisch, J. J., King, R. B., Ed.; Academic Press: New York, 1965; Vol. I., p 114. (b) Reichel, P. M.; Shubkin, R. L.; Barnett, K. W.; Reichard, D. *Inorg. Chem.* **1977**, *5*, 1177-1181. (c) Brown, D. A.; Lyons, H. J.; Manning, A. R.; Rowley, J. M. *Inorg. Chem. Acta* **1969**, *3*, 346-350.

(19) (a) Jukes, A. E. *Adv. Organomet. Chem.* **1974**, *12*, 215-323. (b) Posner, G. H. *Org. React.* (N.Y.) **1972**, *19*, 1-113.

(1) (a) G. L. Lange, E. E. Neidert, W. J. Orrom, and D. J. Wallace, *Can. J. Chem.*, **56**, 1628 (1978); (b) W. Oppolzer, K. K. Mahalanabis, and K. Battig, *Helv. Chim. Acta*, **60**, 2388 (1977); (c) M. Desaro and J-P. Bachmann, *J. Chem. Soc., Chem. Commun.*, 203 (1978); (d) H. Wolf, M. Kolleck, and W. Rascher, *Chem. Ber.*, **109**, 2805 (1976); (e) B. M. Trost, K. Hiroi, and N. Holy, *J. Am. Chem. Soc.*, **97**, 5873 (1975); (f) J. F. Ruppert, M. A. Avery, and J. D. White, *J. Chem. Soc., Chem. Commun.*, 978 (1976).

(2) (a) J. A. Marshall, S. F. Brady, and N. H. Anderson, *Fortschr. Chem. Org. Naturst.*, **31**, 283 (1974); (b) A. A. Krapcho, *Synthesis*, 77 (1978).

(3) M. F. Semmelhack, J. J. Harrison, and Y. Thebtaranonth, *J. Org. Chem.*, **44**, 3275 (1979).

(4) M. F. Semmelhack and G. Clark, *J. Am. Chem. Soc.*, **99**, 1675 (1977).

(5) M. F. Semmelhack, H. T. Hall, Jr., R. Farina, M. Yoshifuji, G. Clark, T. Bargar, K. Hirotsu, and J. Clardy, *J. Am. Chem. Soc.*, **101**, 3535 (1979).

(6) For a general discussion of nucleophilic addition to coordinated $\pi$ systems, see: S. G. Davies, M. L. H. Green, and D. M. P. Mingos, *Tetrahedron*, **34**, 3047 (1978).

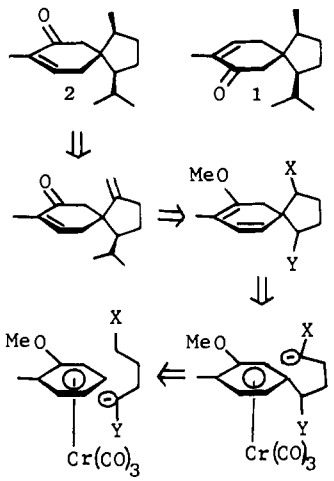
(7) B. Nichols and M. C. Whiting, *J. Chem. Soc.*, 551 (1959).

(8) The cyanohydrin acetal was prepared from isobutyroaldehyde and used according to the method of G. Stork and L. Maldonado, *J. Am. Chem. Soc.*, **93**, 5286 (1971).

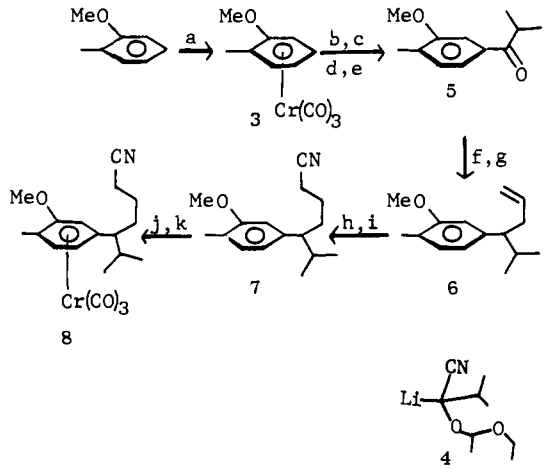
(9) Compound **5** was obtained in high purity by careful fractional distillation, 77% yield.

0002-7863/80/1502-5924$01.00/0 

Scheme I. Strategy



Scheme II[a]



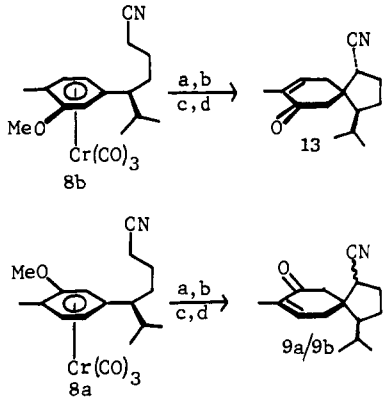
[a] Reagents: (a) $Cr(CO)_6$; (b) anion **4**; (c) $I_2$; (d) aqueous acid; (e) aqueous base; (f) allyl-MgBr; (g) $CF_3CO_2H$, $Et_3SiH$; (h) HBr; (i) KCN; (j) $Cr(CO)_6$, 2 mol equiv; (k) CO, 350 psi.

of allylmagnesium bromide to **5** followed by reduction of the resulting tertiary alcohol by using "ionic hydrogenation".[10] Anti-Markovnikov addition of hydrogen bromide followed by displacement by cyanide afforded the nitrile **7** in 77% yield overall from **5**.

Reaction of **7** with excess chromium hexacarbonyl was complete within 12–15 h at reflux in dioxane to give a mixture of **8** and the corresponding complex with a $Cr(CO)_5$ unit attached to the nitrile group.[11] Treatment of the mixture with carbon monoxide (350 psi, 25 °C, 15 h, THF) followed by chromatography on Florisil gave **8** as a mixture of diastereomers in 84% yield. The ratio of diastereomers was about 60:40 [high-pressure liquid-chromatography (high-pressure LC) and $^{13}C$ NMR spectra]. Complete separation by preparative high-pressure LC gave an easily crystallized solid (**8a**), mp 90.8–92 °C, and a low melting point solid, **8b**, each homogeneous by high-pressure LC and $^{13}C$ NMR.

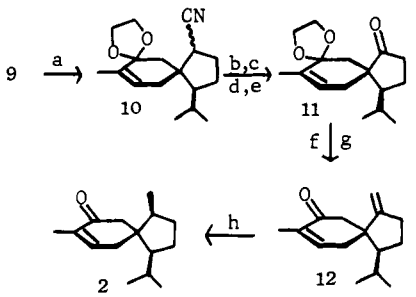
Diastereomer **8a** was treated with lithium diisopropylamide in THF at −78 °C (Scheme III). Then hexamethylphosphoric triamide (HMPT) was added, and the mixture was stirred at −78 °C for 4 h. Dropwise addition of trifluoromethanesulfonic acid (5-fold molar excess) produced a deep red solution which was poured into a mixture of concentrated aqueous ammonium hydroxide and ether (equivolume) cooled to −30 °C. From the

Scheme III. Cyclization[a]



[a] Reagents: (a) $LiNR_2$; (b) $CF_3SO_3H$; (c) $NH_4OH$; (d) aqueous acid.

Scheme IV[a]



[a] Reagents: (a) $HOCH_2CH_2OH$, acid; (b) $LiNEt_2$; (c) $O_2$; (d) $Me_2S$; (e) aqueous base; (f) $Ph_3P{=}CH_2$; (g) aqueous acid; (h) $(Ph_3P)_3RhCl$, $H_2$.

organic layer was isolated a crude product which was treated with a 5% solution of hydrochloric acid ($H_2O$–$CH_3OH$, 80 °C, 18 h). The resulting mixture of cyclohexenones (spiro and fused ring systems) was separated carefully by chromatography. It consisted of recovered arene **7** (30%), fused ring isomers (20%),[12] and two spirocyclohexenones, **9a** (40%) and **9b** (5%).

Spiro ketone **9a** was converted to the ethylene ketal **10a** and then to keto ketal **11** following the oxidative-decyanation procedure of Watt (Scheme IV).[13] Spiro ketone **9b** was converted by the same sequence to **11**, verifying that **9a** and **9b** differ in the orientation of the cyano group. Wittig olefination followed by removal of the ketal unit produced ketone **12**. Hydrogenation of the *exo*-methylene group was accomplished stereospecifically (Wilkenson's catalyst) to give racemic acorenone B, identical in $^1H$ NMR and chromatographic properties with a sample of natural (−)-acorenone B.[14] The overall yield from **9a** was ca. 45%.

The lower melting complex (**8b**) was treated in a precisely parallel way. A single spirocyclohexenone (**13**) was obtained,[15] and none of the other diastereomeric series (i.e., **9**) was detected by analytical high-pressure LC. The yield of **13** was only 15%, and it was accompanied by both unreacted **7** and fused cyclohexenones. Conversion of **13** to acorenone (**1**) was accomplished in 40% yield overall in a sequence exactly parallel with Scheme

(10) Cf.: D. N. Kursanov, Z. N. Parnes, and N. H. Loim, *Synthesis*, 633 (1974).

(11) M. F. Semmelhack, Y. Thebtaranonth, and L. Keller, *J. Am. Chem. Soc.*, **99**, 959 (1977).

(12) Full details concerning the structure of the side products will be published in the article describing this work. The primary spectroscopic data used to distinguish the fused ring from spirocyclic products are the $^{13}C$ NMR signals attributed to the spiro carbon atom. They appear as singlets (off resonance proton decoupling) of low intensity at ca. $\delta$ 50.0 in the $^{13}C$ NMR spectra.

(13) S. J. Selikson and D. S. Watt, *J. Org. Chem.*, **40**, 268 (1975).

(14) We are grateful to L. Romero Fonseca (National University of Argentina), Gordon Lange (University of Guelph, Canada), M. Pesaro (Givauden, Dubendorf, Switzerland), and James White (Oregon State University) for samples of acorenone and acorenone B. We also thank Barry Trost (University of Wisconsin) and J. Wolfe (Technical University, Braunschweig, West Germany) for spectra of synthetic samples.

(15) The trans arrangement of the nitrile and the isopropyl groups in **13** is assigned arbitrarily.

IV. The racemic acorenone was shown to be identical by $^1$H 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 ($^1$H 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.

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## Stereoselective and Regioselective Ene Reactions of Methyl $\alpha$-Chloroacrylate

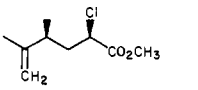
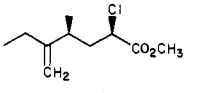
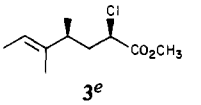
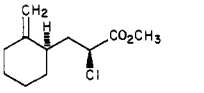
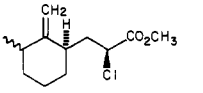
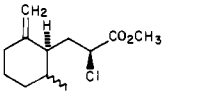
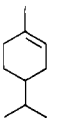
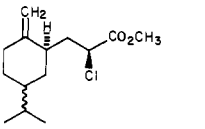
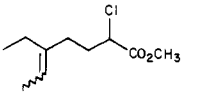
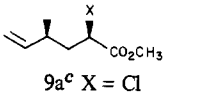
*Sir:*

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 $\alpha$ 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 $\beta$ 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 $\alpha$-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 $\alpha$-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 $^1$H 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 $^1$H 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 $^1$H 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 $\alpha$ position with substituents which are electron withdrawing by induction and resonance are, of course, reactive. Unfortunately, these compounds, such as methyl $\alpha$-cyanoacrylate, tend to undergo ionic reactions due to their ability to stabilize an anionic intermediate.

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