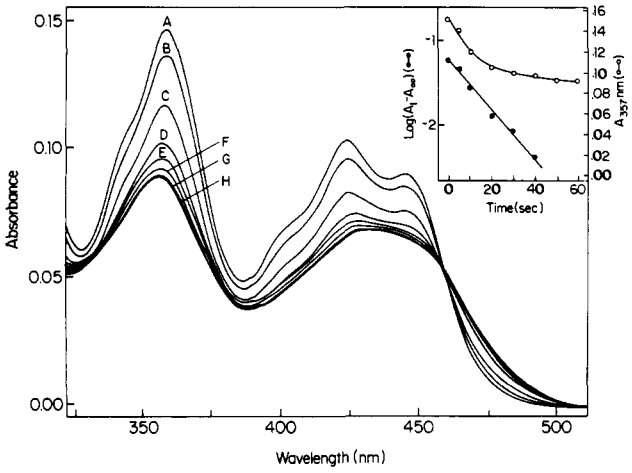

Figure 2. Visible absorption spectra at 25 °C for the photodecomposition of 3-azido-9-[[4-(diethylamino)-1-methylbutyl]amino]-7-methoxyacridine. Spectra A–H correspond to 0, 5, 10, 20, 30, 40, 50, and 60-s irradiations of a 1.078×10^{-5} M solution of the azide in 30 mM phosphate, pH 3.0. The solutions were irradiated in a Rayonet RPR-100 photochemical reactor using four RPR-3500-A lamps. The inset plots show A_{357} (○) and the logarithm of the observed A_{357} minus A_{357} observed at 60-s irradiation time (●) against time.

removed in this way. The yield of crystalline product was 50%: mp 161–162 °C, dec; ν_{max} ($CHCl_3$) 2120 cm^{-1}. Anal. Calcd for $C_{14}H_9N_4ClO$: C, 59.06; H, 3.19; N, 19.68; Cl, 12.45. Found: C, 59.04; H, 3.22; N, 19.53; Cl, 12.40.

Displacement of the chloro substituent from VIII to give the quinacrine azide analogue II was carried out by heating a mixture of the 2-amino-5-(diethylamino)pentane (1.33 equiv) with the chloroacridine (VIII) and phenol at 100 °C for 3 h. The mixture was then taken up in ether and dry hydrogen chloride gas bubbled through it to precipitate the hydrochloride salt: mp 173 °C, dec; ν_{max} ($CHCl_3$) 2110 cm^{-1}. Anal. Calcd for $C_{23}H_{29}N_6O \cdot 2HCl \cdot H_2O$: C, 55.53; H, 6.89; N, 16.89; Cl, 14.24. Found: C, 55.37; H, 6.43; N, 16.44; Cl, 13.78.

Figure 2 shows the photosensitivity of the quinacrine azide product which appears to smoothly decompose in a 60-s irradiation with 350-nm light. The inset plot for Figure 2 shows the absorbance plotted for the 357-nm maximum and log (A_i – A) plotted against time. A $t_{1/2}$ of 8–10 s is observed for the first-order photodecomposition. Similar data are obtained from the absorbances at 423 nm. An isosbestic point at 460 nm is also observed for the photodecomposition reaction. The photosensitivity of II is not pH dependent. Photodecomposition kinetics virtually identical with those seen in Figure 2 have been observed at pH 7.2 (30 mM phosphate). We have not investigated the photochemical products for the irradiation of II or any of the other azido intermediates all of which are comparably photosensitive. It is important to note that most biological systems are relatively insensitive to irradiation with 350-nm light of such intensity and duration as is needed to photodecompose II. The photosensitivity of II appears to be comparable to other organic azides which have proven useful in photochemical labeling.[26]

Both work in our laboratory and elsewhere suggest that these azides will prove useful in photochemical labeling experiments. Mair and Stevens[6] have shown that azide in the 3-position on the acridine ring gives rise on irradiation to complex mixtures of products which they assumed to result from a variety of reactions of the generated reactive nitrene. In our more biologically interesting azidoacridines there is a similar photoproduct complexity. In contrast Mair and Stevens showed that the azide in the 9-position of the acridine ring results in a long-lived nitrene. Such nitrenes may survive many collisions with solvent and form an azo dimer as a principal product. Other positions of the acridine ring do not appear to have been investigated.

(26) Chowdhry, V.; Westheimer, F. H. *Annu. Rev. Biochem.* **1979**, *48*, 293–325.

Ethylidenation of Olefins Using a Convenient Iron-Containing Cyclopropanation Reagent[1]

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Large numbers of methods have been developed previously for the synthesis of cyclopropanes, usually through use of olefins as starting materials.[2] Among the most commonly used procedures are the Simmons–Smith reaction and related methods.[2e] However, the vast majority of the cases in which these methods are employed involve the transfer of simply the methylene group to olefins to give relatively simple cyclopropanes. Some exceptions are the transfer of the benzylidene group[3] and, in a very few cases, the transfer of the ethylidene group.[3,4] However, these latter reactions commonly occur in disappointingly low yields. Certainly, alkylidene transfer in general has not been shown to be a synthetically attractive operation.

Earlier we had reported the use of reagent **1** for the methylenation of olefins.[5] The development of this methodology was

$$CpFe(CO)_2CH_2S^+(CH_3)_2\ BF_4^-$$
1

$$CpFe^+(CO)_2{=}CH_2$$
2

$$CpFe^+(CO)_2{=}CHCH_2CH_3$$
3

$$CpFe^+(CO)_2(H_2C{=}CHCH_3)$$
4

based upon previous studies of others concerned with the iron–carbene complex **2** and closely related derivatives.[6] Because of

(1) This work was presented in part at the following meetings and symposia: (a) "Abstracts of Papers", 177th National Meeting of the American Chemical Society, Honolulu, HI, April, 1979; American Chemical Society: Washington, DC, 1979; ORGN 255. (b) 9th International Conference on Organometallic Chemistry, Dijon, France, Sept., 1979, Abstract No. B4; (c) 9th Northeast Regional Meeting of the American Chemical Society, Syracuse, NY, Oct, 1979; American Chemical Society: Washington, DC, 1979, ORGN 1. (d) International Symposium on Metallo-organics in Organic Synthesis, Swansea, Wales, July, 1980.

(2) For reviews concerning the reactions, the natural occurrence, and the synthesis of cyclopropanes, see: (a) Halton, B. *Alicyclic* Chem., **1977**, *5*, 1–99 and the earlier volumes of this series. (b) Yanovskaya, L. A.; Dombrovskii, V. A. *Russ. Chem. Rev.* **1975**, *44*, 154–169. (c) Boyle, P. H. in "Rodd's Chemistry of Carbon Compounds," 2nd ed.; Ansell, M. F., Ed.; Elsevier: Amsterdam, 1974; Vol. IIA, Suppl., pp 9–47 and the earlier volumes of this series. (d) Ferguson, L. N. "Highlights of Alicyclic Chemistry"; Franklin: Palisade, NJ, 1973; Part I, pp 210–271. (e) Simmons, H. E.; Cairns, T. L.; Vladuchick, S. A.; Hoiness, C. M. *Org. React* **1973**, *20*, 1–131. (f) Wendisch, D. In "Methoden der Organischen Chemie (Houben-Weyl)", 4th ed.; Müller, E., Ed.; Georg Thieme: Stuttgart, 1971; Vol. IV, Part 3, pp 15–673. (g) Lukina, M. Y. *Russ. Chem. Rev.* **1962**, *31*, 419–439.

(3) (a) Furukawa, J.; Kawabata, N.; Nishimura, J. *Tetrahedron Lett.* **1968**, 3495–3499. (b) Furukawa, J.; Kawabata, N.; Fujita, T. *Tetrahedron* **1970**, *26*, 243–250.

(4) (a) Nishimura, J.; Kawabata, N.; Furukawa, J. *Tetrahedron* **1969**, *25*, 2647–2659. (b) Kawabata, N.; Nakagawa, T.; Nakao, T.; Yamashita, S. *J. Org. Chem.* **1977**, *42*, 3031–3035.

(5) Brandt, S.; Helquist, P. *J. Am. Chem. Soc.* **1979**, *101*, 6473–6475.

(6) (a) Jolly, P. W.; Pettit, R. *Ibid.* **1966**, *88*, 5044–5045. (b) Green, M. L. H.; Ishaq, M.; Whiteley, R. N. *J. Chem. Soc. A* **1967**, 1508–1515. (c) Sanders, A.; Cohen, L.; Giering, W. P.; Kenedy, D.; Magatti, C. V. *J. Am. Chem. Soc.* **1973**, *95*, 5430–5431. (d) Davison, A.; Krusell, W. C.; Michaelson, R. C. *J. Organomet. Chem.* **1974**, *72*, C7–C10. (e) Flood, T. C.; DiSanti, F. J.; Miles, D. L. *J. Chem. Soc., Chem. Commun.* **1975**, 336–337. (f) Brookhart, M.; Nelson, G. O. *J. Am. Chem. Soc.* **1977**, *99*, 6099–6101. (g) Stevens, A. E.; Beauchamp, J. L. *J. Am. Chem. Soc.* **1978**, *100*, 2584–2585. (h) Riley, P. E.; Capshew, C. E.; Pettit, R.; Davis, R. E. *Inorg. Chem.* **1978**, *17*, 408–414. (i) Schilling, B. E. R.; Hoffman, R.; Lichtenberger, D. L. *J. Am. Chem. Soc.* **1979**, *101*, 585–591. (j) Johnson, D. L.; Gladysz, J. A. *Ibid.* **1979**, *101*, 6433–6435. (k) Brookhart, M.; Tucker, J. R.; Flood, T. C.; Jensen, J. *Ibid.* **1980**, *102*, 1203–1205. (l) Brookhart, M.; Tucker, J. R.; Husk, G. R. *J. Organomet. Chem.* **1980**, *193*, C23-C26.

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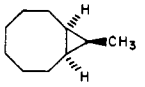
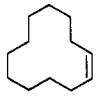
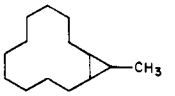
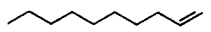
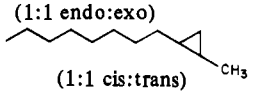
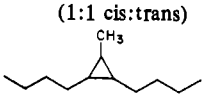
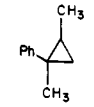
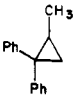
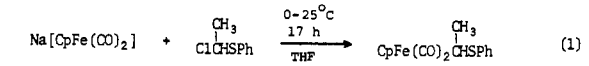
Table I. Ethylidenation of Olefins with 5

entry	olefin	cyclopropane	conversion of olefin,[a] %	corrected yield,[b] %
1			85[c]	70
2		 (1:1 endo:exo)	49	70
3		 (1:1 cis:trans)	55	70
4			62[d]	44
5			81[e]	67
6		 (41:17 *Z*:*E*)	100[f]	58
7			59	81

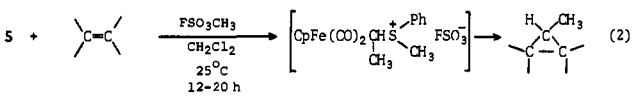
[a] These values were obtained by GLPC determination of the amount of unreacted olefin. [b] The yields of cyclopropanes were determined by GLPC using an internal standard and a sample of pure, isolated product for calibration. Yields are corrected for the amount of unreacted olefin. [c] Stereochemistry determined by ^{1}H NMR as in ref 4b. [d] Stereochemistry of this product not yet determined. [e] Stereochemistry determined by ^{1}H NMR as in ref 13; the CH_3 resonance appeared at δ 0.79. [f] The C-2 CH_3 group resonance appeared in the ^{1}H NMR spectrum at δ 0.76 for the *Z* isomer and δ 1.16 for the *E* isomer.

the limitations on other cyclopropanation reactions discussed above, we became interested in extending our method to transfer of groups other than only the methylene group. However, we were aware of the work of Rosenblum in which a propylidene complex **3** was generated as a possible intermediate as a result of an unrelated reaction; after its formation, **3** apparently underwent 1,2-hydride shift and rearrangement to give the propene complex **4**.[7] Because **3** is either identical or at least similar to intermediates that would be formed upon the extension of our methodology to alkylidene transfer, we were greatly concerned with the possibility that this rearrangement pathway would plague attempts to generalize our cyclopropanation procedure. In order to test this point, we have investigated ethylidenation reactions, and we are pleased to report that despite the unfavorable precedent cited above, we have been able to develop a useful method for ethylidene transfer.

The well-known and readily available ferrate, $Na[CpFe(CO)_2]$,[8] reacts with 1-chloroethyl phenyl sulfide[9] to give the iron-substituted sulfide derivative **5** [^{1}H NMR ($CDCl_3$) 7.1–7.5 (m, 5 H, Ar *H*), 5.0 (s, 5 H, C_5H_5), 3.6 (q, *J* = 7 Hz, 1 H, C*H*), 1.5 (d, J = 7 Hz, 3 H, CH_3)] in 78% yield after purification by "flash" chromatography[10] (eq 1). The complex **5** is a yellow, crystalline



(1)



(2)

material which may be weighed and handled in air for reasonably long periods of time, although for long-term storage the complex should be kept under an inert atmosphere. Most importantly, upon reaction with a variety of olefins in the presence of methyl fluorosulfonate (caution: this very reactive alkylating agent is highly toxic[11]) methyl-substituted cyclopropanes **7** are produced directly (eq 2).[12] These reactions proceed via formation of the sulfonium salt **6** which we do not isolate because of its lower stability in comparison with our previously developed methylene transfer reagent **1**. Instead, the sulfide **5** itself appears to be a perfectly convenient reagent for effecting ethylidenation of olefins as shown. Our results are summarized in Table I.

While the cyclopropanations using **1** require a reaction temperature of ca. 100 °C, the use of the methylphenylsulfonium group in **6** in place of the dimethylsulfonium group as in **1** permits the reactions to be performed at ambient temperatures. Typically, the cyclopropanation reactions are performed using a 1:1.25:1 molar ratio of **5**, methyl fluorosulfonate, and the olefin at a concentration of ca. 1 M in methylene chloride as the solvent at 25 °C for a period of 12–20 h. The use of 2 molar equiv of **5** leads to increases in the percent conversions of the olefins, but all of the results reported in Table I refer to the use of only 1 equiv of **5** in order to give a clearer indication of the efficiency of these reactions. The products are isolated by diluting the reaction mixtures with pentane followed by use of routine extraction and chromatographic techniques. The procedure gives acceptably good yields of cyclopropanes from monosubstituted (run 3), cis-disubstituted (runs 1,2,4), and phenylated (runs 5–7) olefins, but

(7) Cutler, A.; Fish, R. W.; Giering, W. P.; Rosenblum, M. *J. Am. Chem. Soc.* **1972**, *94*, 4354–4355.
(8) (a) King, R. B.; Bisnette, M. B. *J. Organomet. Chem.* **1964**, *2*, 15–37. (b) Reger, D. L.; Fauth, D. J.; Dukes, M. D. *Synth. React. Inorg. Metal-Org. Chem.* **1977**, *7*, 151–155.
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(10) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2925.
(11) For a description of toxic effects of FSO_3CH_3 and a suggested treatment for inhalation of this volatile reagent, see: *Chem. Eng. News* **1978**, 56.
(12) A related procedure for ethylidenation has recently been developed which employs ether derivatives analogous to our sulfide **5**: Brookhart, M., private communication.
(13) (a) Closs, G. L.; Moss, R. A. *J. Am. Chem. Soc.* **1964**, *86*, 4042–4053. (b) Mathias, R.; Weyerstahl, P. *Chem. Ber.* **1979**, *112*, 3041–3053.

the reaction fails in the case of trans-disubstituted olefins, (e.g., *trans*-5-decene, *trans*-stilbene). Other obvious types of unsaturated substrates have yet to be investigated. The observed product stereochemistries[14] (especially runs 1,4,5, and 6) may have important implications regarding the mechanism[15] of these reactions, a point which we are studying in further detail. In some cases (runs 1,2) small amounts of olefinic products (e.g., 3-ethylcyclooctene in run 1) are obtained in addition to the cyclopropanes, but we have not yet been able to establish which changes in reaction parameters are most clearly associated with the formation of these byproducts.

Having successfully developed a synthetically attractive method for ethylidenation of olefins, we are now more confident that related procedures for alkylidene transfer in general may be found.[16] Investigations are in progress in our laboratory to define the scope of these reactions with respect to the transfer of other groups, the use of several types of unsaturated substrates, and the development of reagents containing other metals in place of iron and other leaving groups in place of sulfonium salts. The complete details of this work will be described in a forthcoming full paper.

Acknowledgment. We are grateful to Professor Maurice Brookhart of the University of North Carolina for communicating his related results to us and the National Science Foundation (Grant CHE 7918019) and the donors of the Petroleum Research Fund, administered by the American Chemical Society, (Grant No. 12032-ACl, 3) for providing the financial support for this research.

(14) Although our stereochemical assignments are based upon generally accepted ^{1}H NMR correlations,[4b,13] we consider all of these assignments to be tentative until we have completed a more thorough study based upon not only spectroscopic characterization but also chemical correlations.

(15) (a) Casey, C. P.; Polichnowski, S. W. *J. Am. Chem. Soc.* **1977**, *99*, 6097–6099. (b) Casey, C. P.; Polichnowski, S. W.; Shusterman, A. J.; Jones, C. R. *Ibid.* **1979**, *101*, 7282–7292.

(16) Recently Mr. M. Thaker has found in our laboratory that the reaction of $CpFe(CO)_2CH{=}CH_2$ with HBF_4 and cyclooctene affords the same cyclopropane (direct GLPC comparison) as in run 1 of Table I. This result serves to indicate the possibility of β protonation of the vinyl ligand and provides yet an additional, potentially general route for alkylidene transfer.

Chirality Transfer via Organopalladium Chemistry. A Synthesis of Optically Active Vitamin E Side Chain from D-Glucose

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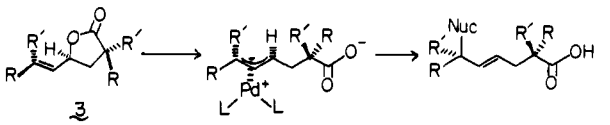
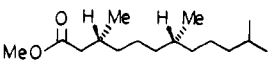
The control of stereochemistry in acyclic systems is an important methodological and synthetic challenge. We demonstrated such control of relative stereochemistry at remote chiral centers via organopalladium[1] and organocopper[2] intermediates. Success of these approaches (Scheme I) required (1) ionization of the substrate **3** from a single conformation, (2) formation of the new C–C bond faster than the rate at which the stereochemical integrity of the intermediate was lost, and (3) regioselective alkylation. In the case of palladium, such attack of the nucleophile took place from the face of the π-allyl opposite palladium. The process allowed net replacement of a C–O bond by a C–C bond with allyl inversion and retention of configuration. The advantage of this approach stemmed, in part, from the potential availability of the requisite substrates from carbohydrates[3,4] which would control

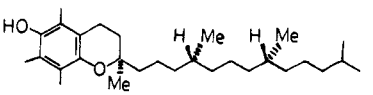
Scheme I



absolute as well as relative stereochemistry. In this paper, we realize that potential in the development of a synthesis of the side chain **1** of Vitamin E (**2**)[5,6] from D-glucose, which is also applicable to the synthesis of the side chain of Vitamin K.[1,12]

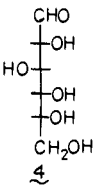


1

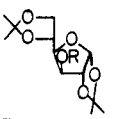


2

D-Glucose (**4**) was converted to its diacetonide **5**[7] ($ZnCl_2$, 85%,

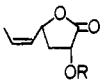


4

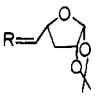


5 R=H
6 R=Ts

H_3PO_3, acetone, room temperature 3 days) and its free hydroxyl was tosylated[8] (1.5 equiv of TsCl, pyridine, 82%). Elimination of **6** to the olefin (KOH, 0.4 mm, 60 °C, 65%) followed by hydrogenation (3 atm of H_2, 10% Pd/C, EtOH, 92%) effected removal of the undesired hydroxyl group at C-3 and inversion of the C-4 center. Selective deprotection of the exo acetonide [HCl (catalytic), 1:1 MeOH:H_2O, 84%] followed by glycol cleavage [1.2 equiv of $NaIO_4$, H_2O (pH 6–7), 83%] afforded aldehyde **7**.[4d,e]



9 R=H
10 R=CO Ph



7 R=O
8 R=CHCH$_3$ (Z)

Wittig olefination ($Ph_3P{\oplus}CH_2CH_3Br{\ominus}$, KO-*t*-Bu, THF, 69%) gave entirely (*Z*)-olefin **8**[9] ($[\alpha]^{25}_D$ −49.17°, *c* 1.08, $CHCl_3$) by 270-MHz ^{1}H NMR (δ 5.56, ddq, J = 12.0, 7.0, and 1.5 Hz) and 15.04-MHz ^{13}C NMR spectroscopy (δ 12.59 for the vinyl methyl carbon).[10] Deprotection of the remaining acetonide [PTSA (catalytic), 10:1 CH_3CN:H_2O] and selective oxidation of the resulting diol (1.5 equiv of Ag_2CO_3/celite,[11] benzene, 41% over

(1) Trost, B. M.; Klun, T. P. *J. Am. Chem. Soc.* **1979**, *101*, 6756.
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