Notes

Relative Stabilities of α-Phenyl and α-Ferrocenyl Vinyl Carbocations. 2

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Considerable work has been reported in the literature[1-11] relative to various methods of generating vinyl carbocations and their stability. However, controversy still remains regarding the manner of stabilization and the structure of these carbenoid intermediates. This has been especially true with α-ferrocenyl vinyl carbocations. We wish to report on our continued work with these carbocations and their unusual stability relative to that of substituted α-phenylvinyl carbocations. Our previous work[12] showed that ferrocenylphenylacetylene (**1**) was hydrated in acidic aqueous ethanol to quantitatively yield ferrocenyl benzyl ketone (**3**). As depicted in Scheme I, this result indicates that intermediate vinyl carbocation **2** was preferentially formed over carbocation **4**, thus demonstrating the superior ability of the α-ferrocenyl moiety to stabilize vinyl carbocations. Similarly it was found that ferrocenylacetylene was hydrated 10^5 times faster than phenylacetylene in acidic ethanol.

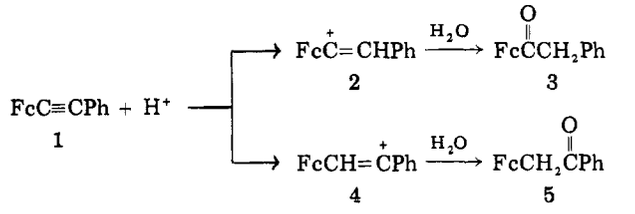
The specific purpose of the presently reported work was to prepare a ferrocenylphenylacetylene containing a benzene ring with a strong electron-releasing group in order to compare the ability of such a substituted ring with that of the ferrocenyl group to stabilize α-vinyl carbocations. Toward that end, ferrocenyl-*p*-methoxyphenylacetylene (**7**) was synthesized as shown in Scheme II.

The acid-catalyzed hydration product quantitatively obtained from **7** was ferrocenyl *p*-methoxybenzyl ketone (**9**). It is apparent, as seen in Scheme III, that α-ferrocenyl carbocation **8** is more readily formed than even the α-*p*-methoxyphenyl carbocation **10**.

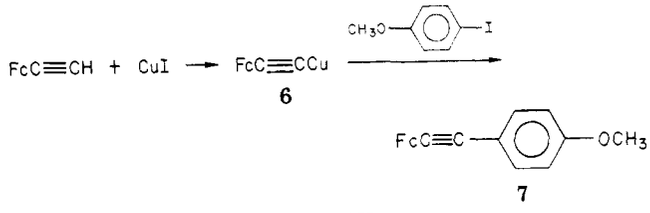
Consistent with the above result is the kinetic data obtained from the acid-catalyzed hydrations of ferrocenylacetylene (**11**) and *p*-methoxyphenylacetylene (**13**) as shown in Table I. The resultant products and the first-order kinetics observed in Table I point to an initial rate-determining protonation in these hydration reactions and confirms the great stability of the α-ferrocenyl carbocation compared to its *p*-methoxyphenyl counterpart.

This work, like that of others and our earlier efforts, adds to the list of reactions whose mechanistic pathways involve the ready formation of vinyl carbocations. We have further demonstrated the unusually large stabilizing influence of the α-ferrocenyl group on such cationic species.

Scheme I



Scheme II



Scheme III

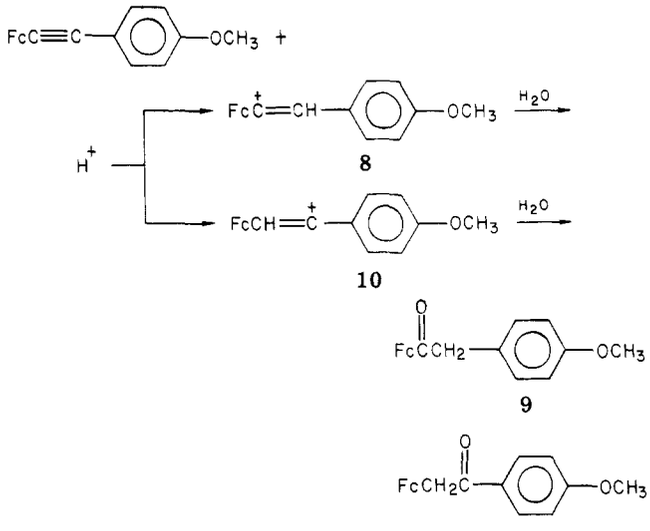
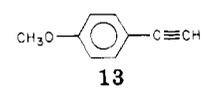
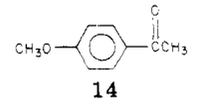


Table I. Relative Rates of Acid-Catalyzed Hydrations

compd	reaction product[a]	rate constant, s^{-1} [b,c]	rel rate
FcC≡CH (**11**)	FcCCH$_3$ (**12**)	7.65×10^{-4}	162
 (**13**)	 (**14**)	4.73×10^{-6}	1

[a] Reaction products were identified by comparing their melting points, ^{1}H NMR spectra, and infrared spectra with those of authentic samples. [b] Rates were determined by using ^{1}H NMR spectroscopy to follow disappearance of reactants. [c] Reported rates represent the average of ten determinations extending through more than three half-lives on two separate runs.

(1) M. Hanack, *Angew. Chem., Int. Ed. Engl.*, **17**, 333 (1978).
(2) L. R. Subramanian and M. Hanack, *J. Chem. Educ.*, **52** (2), 80 (1975), and extensive references cited therein.
(3) P. J. Stang, *Prog. Phys. Org. Chem.*, **10**, 205 (1973).
(4) K. Yates, G. H. Schmid, T. W. Regulski, D. G. Garratt, H. Leung, and R. McDonald, *J. Am. Chem. Soc.*, **95**, 160 (1973).
(5) G. Modena and U. Tonellato, *Adv. Phys. Org. Chem.*, **9**, 185 (1971).
(6) M. Hanack, *Acc. Chem. Res.*, **3**, 209 (1970), and extensive references cited therein.
(7) Z. Rappoport, T. Bassler, and M. Hanack, *J. Am. Chem. Soc.*, **92**, 4985 (1970).
(8) H. G. Richey and J. M. Richey, "Carbonium Ions", Vol. II, G. A. Olah and P. v. R. Schleyer, Ed., Wiley Interscience, New York, N.Y., 1970, p 899.
(9) S. A. Sherrod and R. C. Bergman, *J. Am. Chem. Soc.*, **91**, 2115 (1969).
(10) M. Cais, *Organomet. Chem. Rev.*, **1**, 435 (1966), and references cited therein.
(11) L. L. Miller and D. A. Kaufman, *J. Am. Chem. Soc.*, **90**, 7282 (1968).
(12) D. A. Kaufman and R. J. Kupper, *J. Org. Chem.*, **39**, 1438 (1974).

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Experimental Section

General. All melting points are uncorrected. IR spectra were recorded on a Perkin-Elmer 310B spectrometer; ^1H NMR spectra were obtained on a Varian A-60 spectrometer, and ^{13}C NMR spectra were recorded on a Varian XL-100 spectrometer. Mass spectra were obtained with a Hitachi RMU-60 spectrometer.

Cuprous Ferrocenyl Acetylide (6). The procedure used to prepare 6 was that used by Rosenblum et al.[13] with a 69% yield.

Ferrocenyl-*p*-methoxyphenylacetylene (7). The procedure followed was an adaptation of that by Stephens and Castro[14] in their synthesis of *p*-methoxydiphenylacetylene. In a typical preparation, 3.350 g (0.00143 mol) of *p*-iodoanisole was added to 50 mL of freshly distilled pyridine in a thoroughly dried 250-mL, three-neck, round-bottom flask which was fitted with a N_2 inlet, thermometer, and condenser leading to a mineral oil gas trap. Cuprous ferrocenyl acetylide (3.130 g, 0.0115 mol) was added in one portion to the pyridine solution. The resulting reaction mixture was allowed to stir for 10 h at 120 °C, after which time the solution had developed a dark red-brown color. After cooling, the reaction mixture was flooded with 250 mL of H_2O and extracted three times with 100-mL portions of ether. The combined ether extracts were washed successively with 10% aqueous HCl and 10% aqueous $NaHCO_3$ solutions. After drying over $MgSO_4$, the ether was removed via the rotary evaporator to yield a red-brown oil which solidified upon standing. The crude product was chromatographed from a basic alumina column with benzene to give 2.25 g (62%) of 7. When recrystallized from hexane, orange platelike crystals of 7 were obtained: mp 127–129 °C; IR 3100, 3000–2850, 1905, 1620, 1525, 1480, 1390, 1310, 1270, 1195, 1170, 1115, 1040, and 1010 cm^{-1}; ^1H NMR (CCl_3D) δ 3.8 (s, 3 H), 4.15–5.60 (m, 9 H), and 6.8–7.6 (m, 4 H); MS *m/e* 316 (M^+), 314, 301, 158, and 121; high resolution MS gave a mass for M^+ which corresponded to that of $C_{19}H_{16}OFe$ with a deviation of 0.0 ppm.

Ferrocenylacetylene (11). This compound was prepared from acetylferrocene via the method of Rosenblum et al.[13] with an overall yield of 82% and mp 53–54 °C (lit. mp 51–53 °C).

Hydration of Ferrocenyl-*p*-methoxyphenylacetylene (7). 7 (0.204 g) was added to a solution of 5 mL of acetic acid, 0.5 mL of H_2O, and 10 μL of concentrated H_2SO_4 under N_2. The resulting mixture was warmed to 75 °C for 6 h during which time there was a noticeable color change from orange to a dark red-brown. After cooling to room temperature, the reaction mixture was flooded with 25 mL of H_2O and extracted three times with 25-mL portions of CH_2Cl_2. The combined CH_2Cl_2 washings were combined, dried over $CaCl_2$, and evaporated on the rotary evaporator to yield 0.201 g (94%) of orange crystals, mp 90.5–91.5 °C. The hydration product was identified as ferrocenyl *p*-methoxybenzyl ketone by comparison of its IR, NMR, and melting point (91–92 °C) with that reported in the literature.[15]

Kinetic Data. Rates for the acid-catalyzed hydration reactions of 11 and 13 were obtained by using ^1H NMR to follow the disappearance of starting material. The reported rate constants represent the average of two separate runs with measurements being made at ten time intervals ranging through 3 half-lives. The solvent system used consisted of 5 mL of acetic-d_3 acid-*d*, 0.5 mL of D_2O, and 10 μL of concentrated H_2SO_4. Sufficient alkyne (11 or 13) was added to 0.40 mL of this solvent system to give a 0.50 M solution.

Compound 11 reacted so rapidly that significant reaction occurred during the time required for recording and integration of the appropriate peaks in its NMR spectrum. Thus the following method was employed to quench the reaction at precisely timed intervals. The requisite amount of 11 was dissolved in 5 mL of acetic-d_3 acid-*d* and 0.5 mL of D_2O, it having been determined that 11 did not undergo hydration in this solvent system. Reaction time was begun when 10 μL of concentrated H_2SO_4 was added to this solution. At precisely timed intervals, 0.4 mL of the reaction mixture was transferred with a syringe to NMR tubes containing 20 μL of pyridine, which instantly quenched the reaction. In this manner ten tubes representing ten different reaction times were prepared so that spectra and integration of each could be accurately recorded without error of further reaction.

Identification of Hydration Products (12 and 14). The hydration products listed in Table I were identified by comparison of NMR, IR, and melting point with those of authentic samples. Acetylferrocene (12) was synthesized via the method of Broadhead et al.[16] while *p*-methoxyacetophenone was purchased from Aldrich Chemical Co. (No. 11,737-4).

Registry No. 6, 53716-64-6; 7, 70659-04-0; 9, 55648-59-4; 11, 1271-47-2; 12, 1271-55-2; 13, 768-60-5; 14, 100-06-1; *p*-iodoanisole, 696-62-8.

(13) M. Rosenblum, N. Brawn, J. Papenmeier, and M. Applebaum, *J. Organomet. Chem.*, 6, 173 (1966).
(14) R. D. Stephens and C. E. Castro, *J. Org. Chem.*, 28, 3313 (1963).
(15) T. A. Woods, T. E. Boyd, E. B. Biehl, and P. C. Reeves, *J. Org. Chem.*, 40, 2416 (1975).
(16) G. D. Broadhead, J. M. Osgerby, and P. L. Pauson, *J. Chem. Soc.*, 650 (1958).

Convenient Method for the Synthesis of 25-Hydroxyvitamin D_3 Analogue. Structure Determination of Tertiary Alcohols by Carbon-13 Nuclear Magnetic Resonance Spectroscopy

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The biological importance of 25-hydroxyvitamin D, and its utilization as an intermediate for the synthesis of the medically useful 1α,25-dihydroxyvitamin D,[1] has been an incentive to search for its convenient synthesis.[2]

Most methods for the preparation of these metabolites use as starting materials naturally occurring sterols possessing an unsaturated side chain, which is degraded and rebuilt to give the side chain substituted cholesterol derivative.[3] In order to obtain the vitamin D system, it is necessary to convert the cholesterol derivative to the respective 5,7-diene which is then irradiated and thermally equilibrated.[4]

(1) Cf. H. F. DeLuca and H. K. Schnoes, *Annu. Rev. Biochem.*, 45, 631 (1976); D. R. Fraser and E. Kodicek, *Nature (London)*, 288, 764 (1970), and references cited therein.
(2) P. E. Georghiou, *Chem. Soc. Rev.*, 83 (1977).
(3) D. M. Piatak and J. Wicha, *Chem. Rev.*, 78, 199 (1978).
(4) L. F. Fieser and H. Fieser, "Steroids", Reinhold, New York, N.Y., 1959, pp 91–168; G. M. Sanders, J. Pot, and E. Havinga, *Fortschr. Chem. Org. Naturst.*, 27, 131 (1969).

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