

Stable Carbocations. Part 22.¹ Stereochemistry of the Deprotonation of Ferrocenylalkylium Ions, and of the Protonation of Alkenylferrocenes

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In the absence of adverse steric effects, ferrocenylalkylium ions of the type $\text{FcC}^+(\text{R})\text{CH}(\text{Ph})\text{Me}$ (Fc = ferrocenyl) undergo preferential *exo*-deprotonation upon reaction with a base and a similar *exo*-stereoselectivity is associated with protonation of the resulting alkenes $\text{FcC}(\text{R})=\text{C}(\text{Ph})\text{Me}$ in trifluoroacetic acid.

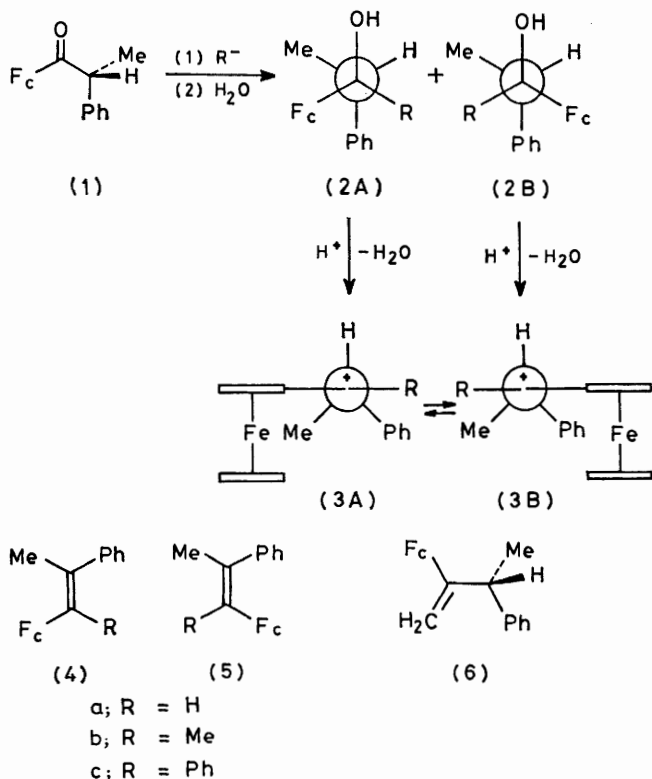
It is well established² that ferrocenyl (Fc) substrates of the type $\text{FcC}(\text{X})\text{R}^1\text{R}^2$ undergo heterolysis by preferential *exo*-departure of the leaving-group (X^-) and that nucleophilic additions to ferrocenylalkylium ions $\text{FcC}^+\text{R}^1\text{R}^2$ proceed preferentially from the *exo*-face of the pentafulvene-like ligand. Steric factors must be important in deprotonation of these carbocations since anti-Saytzeff products often predominate,³ but little is known concerning the stereoselectivity of such proton transfers, *i.e.* whether *exo*- or *endo*-deprotonation is favoured. The

a study of the stereochemistry of deprotonation of ferrocenylalkylium ions and of the reverse reaction.

RESULTS AND DISCUSSION

In principle, the diastereoisomeric carbocations (3A) and (3B) are suitable systems for investigation since β -alkyl proton loss from the *exo*- and *endo*-sides gives in each case different alkenes (4) and (5). These diastereoisomers interconvert by rotation around the $\text{Fc}-\text{C}^+$ bond (Scheme 1)⁷ but this process occurs sufficiently slowly in $\text{CF}_3\text{CO}_2\text{H}$ to be followed by ^1H n.m.r. spectroscopy, tertiary carbocations [*e.g.* (3B) and (3C)] undergoing more rapid rotation than secondary analogues [*e.g.* (3A)].[†] This isomerisation problem is circumvented with homo-annularly bridged systems [*e.g.* (9A) and (9B)] where $\text{Fc}-\text{C}^+$ rotation is precluded (Scheme 2).

Synthetic Methods.—Reactions of the racemic ketone (1)⁷ with LiAlH_4 , MeLi , and PhLi , followed by hydrolysis, gave in each case mixtures of the corresponding diastereoisomeric alcohols (2A) and (2B) in which one isomer predominated ($\geq 90\%$); these major products are assigned the stereochemistry (2A) from Cram's rule.⁸ Similar treatment of the racemic cyclic ketones (7a–d)⁹ with $\text{PhCH}(\text{Me})\text{Li}$ gave mixtures of the diastereoisomers (8A) and (8B) by exclusive *exo*-addition of the organometallic reagent to the carbonyl groups. Regioselective *exo*-addition is well recognised¹⁰ for reactions of homo-annularly bridged acylferrocenes, and is established by the presence of a strong intramolecularly Fe-bonded hydroxy-absorption in the i.r. spectra of the alcohols. Substantial amounts of both diastereoisomers were formed in reactions of the ketones (7a) and (7b), as shown by ^1H n.m.r. spectroscopy. However, reactions of the ketones (7c) and (7d) gave predominantly ($>90\%$) one diastereoisomer. In these reactions, stereoselectivity results from the presence of a pseudo-axial 2-*exo*-methyl group adjacent to the carbonyl group which produces an energy separation between the alternative diastereoisomeric transition states for *exo*-addition of the lithio-reagent. Inspection of molecular models and assessment of steric interactions in these states suggests that formation of the diastereoisomers (8A,c) and (8A,d) would be



SCHEME 1 Only one enantiomer of each chiral species is shown; all were racemic mixtures

former mode would be sterically less hindered, but stereoelectronic control may be important and intra-ionic metal-assisted deprotonation is possible,⁴ because Fe-protonated ferrocene and its alkyl derivatives have been identified spectroscopically.⁵ In this paper, we describe⁶

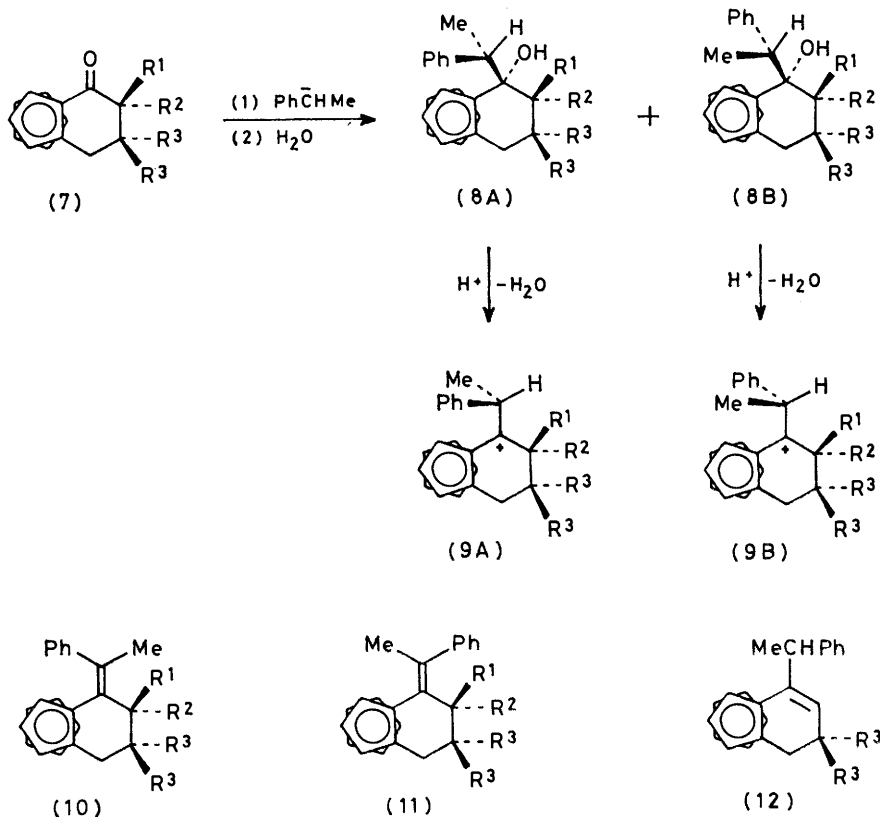
[†] Rotational barriers of *ca.* 85 and 70 kJ mol^{-1} have been measured⁷ for secondary and tertiary ferrocenylalkylium ions, respectively, in $\text{CF}_3\text{CO}_2\text{H}$.

favoured; this assignment is supported by identification of the carbocations resulting upon acid-promoted heterolysis (see later).

We were unable to separate these mixture of diastereoisomeric alcohols by chromatography. They were dehydrated by dissolution in $\text{CF}_3\text{CO}_2\text{H}$ and the resulting solutions of the carbocations (3A, 3B) and (9A, 9B) were quenched with aqueous Na_2CO_3 . Under these conditions, little alcohol was regenerated. The mixtures of alkenes [(4a) + (5a) and (4c) + (5c)] obtained from

type $\text{FcC}(\text{R}^1)=\text{C}(\text{R}^2)\text{Ph}$ have distinctive spectroscopic properties. Cyclopentadienyl proton-resonance patterns in the ^1H n.m.r. spectra are particularly diagnostic; thus, a *cis*-arrangement of ferrocenyl and phenyl groups [*e.g.* (5) and (10)] causes a marked shielding of the α -proton(s) of the substituted cyclopentadienyl ring but this effect is absent in the spectra of the *trans*-styryl analogues [*e.g.* (4) and (11)].

Carbocations of the diastereoisomeric pairs [(3A), (3B)] and [(9A), (9B)] also have distinctive ^1H n.m.r.



- a; $\text{R}^1 = \text{R}^2 = \text{R}^3 = \text{H}$
 b; $\text{R}^1 = \text{R}^2 = \text{H}, \text{R}^3 = \text{Me}$
 c; $\text{R}^1 = \text{R}^2 = \text{Me}, \text{R}^3 = \text{H}$
 d; $\text{R}^1 = \text{Me}, \text{R}^2 = \text{Ph}, \text{R}^3 = \text{H}$

SCHEME 2 See footnote to Scheme 1

the corresponding alcohols were separated cleanly by repetitive t.l.c. on SiO_2 . However, dehydration of the alcohols (2b), (8a), and (8b) gave mixtures of three isomers, [(4b) + (5b) + (6)], [(10a) + (11a) + (12a)], and [(10b) + (11b) + (12b)], respectively, in which the anti-Saytzeff products [(6), (12a), and (12b)] largely predominated (^1H n.m.r.). These mixtures could not be separated, nor could we obtain pure alkenes from dehydridation of the alcohols (8c) and (8d). However, isomer mixtures containing mainly the *Z*-alkenes (10c) and (10d) were obtained by t.l.c.

Stereochemical Assignments.—We have previously shown¹¹ that *E*- and *Z*-isomers of alkenylferrocenes of the

spectra in $\text{CF}_3\text{CO}_2\text{H}$. For each pair studied, the C_5H_5 singlet and $\text{CH}(\text{Ph})\text{Me}$ doublet resonances of one diastereoisomer appeared well down-field of the corresponding resonances of the other (Table 1). Because acid-promoted heterolysis of (1-hydroxyalkyl)ferrocenes proceeds stereospecifically by *exo*-departure of the protonated hydroxy-group,² the major products (2A,a—c) described earlier are cleanly converted into the corresponding carbocations (3A,a—c) which are characterised by the lower-field cyclopentadienyl and methyl resonances. This distinction identified the stereostructures of the carbocations [(9A,c) and (9B,c)] and [(9A,d) and (9B,d)] and confirmed that the major di-

astereoisomeric products from the reactions of the ketones (7c) and (7d), described earlier, have the structures (8A,c) and (8A,d), respectively.

Stereochemistry of Proton Transfer.—The alkenes (4a) and (5a) underwent stereoselective *exo*-protonation in

TABLE 1
¹H N.m.r. chemical shifts (τ) for carbocations ^a

Carbocation	C ₅ H ₉ ^b	CHMe ^c
(3A,a)	4.79	8.11
(3B,a)	5.22	8.31
(3A,b)	4.96	8.02
(3B,b)	5.30	8.26
(3A,c)	4.85	8.02
(3B,c)	5.01	8.35
(9A,a)	5.37	8.35
(9B,a)	5.02	8.09
(9A,b)	5.51	8.37
(9B,b)	5.16	8.06
(9A,c)	5.54	8.28
(9B,c)	4.98	8.15
(9A,d)	5.42	8.40
(9B,d)	4.88	8.35

^a In CF₃CO₂H with SiMe₄ as internal reference; chemical shifts and multiplicities of resonances of other protons were unexceptional. ^b Singlet. ^c Doublet (*J ca.* 7.5 Hz).

cold CF₃CO₂H to give the carbocations (3A,a) and (3B,a), respectively, as shown by ¹H n.m.r. spectroscopy. Quenching of these freshly prepared solutions with a large excess of aqueous Na₂CO₃ gave mixtures of the alkenes (4a) and (5a) in which the product of *exo*-deprotonation predominated (Table 2) in each case, *i.e.* (4a) from (3A,a) and (5a) from (3B,a). The relative proportions of these isomeric alkenes were determined by integration of the well separated methyl doublet resonances¹¹ in the ¹H n.m.r. spectra of the product mixtures. The proportion of the minor alkene formed in these reactions was significantly greater than that of the alternate diastereoisomeric cation present in solution (through Fc-C⁺ rotation) immediately before quenching

TABLE 2
Alkene \rightleftharpoons carbocation interconversions ^a

Precursors ^b	Reagents ^c	Products ^b
(4a)	A	(3A,a) (>97), (3B,a) (<3)
(5a)	A	(3A,a) (<3), (3B,a) (>97)
(3A,a) (>97), (3B,a) (<3)	B	(4a) (86), (5a) (14)
(3A,a) (<3), (3B,a) (>97)	B	(4a) (9), (5a) (91)
(4c)	A	(3A,c) (90), (3B,c) (10)
(5c)	A	(3A,c) (12), (3B,c) (88)
(3A,c) (90), (3B,c) (10)	B	(4c) (20), (5c) (80)
(3A,c) (12), (3B,c) (88)	B	(4c) (18), (5c) (82)
(10c) (85), (11c) (15)	A	(9A,c) (57), (9B,c) (43)
(10c) (75), (11c) (25)	A	(9A,c) (55), (9B,c) (45)
(10c) (58), (11c) (42)	A	(9A,c) (52), (9B,c) (48)
(9A,c) (92), (9B,c) (8)	B	(10c) (75), (11c) (25)
(9A,c) (55), (9B,c) (45)	B	(10c) (58), (11c) (42)
(10d) (96), (11d) (4)	A	(9A,d) (8), (9B,d) (92)
(9A,d) (94), (9B,d) (6)	B	(10d) (96), (11d) (4)
(9A,d) (8), (9B,d) (92)	B	(10d) (89), (11d) (11)

^a Each experiment was carried out at least twice and reproducible results were obtained. ^b Percentage compositions, determined by ¹H n.m.r. spectroscopy (see text), are given in parentheses. ^c A, Cold CF₃CO₂H (-10 °C, initially); B, ice-cold aqueous Na₂CO₃ (2*M*) in large excess.

(Table 2) suggesting that some product arises by *endo*-deprotonation. Alternatively, or as a contributing effect, the Fc-C⁺ rotational barriers separating the diastereoisomers (3A,a) and (3B,a) may be lowered (*e.g.*

by ion-pairing with base¹²) prior to proton transfer such that both alkenes arise by *exo*-deprotonation.

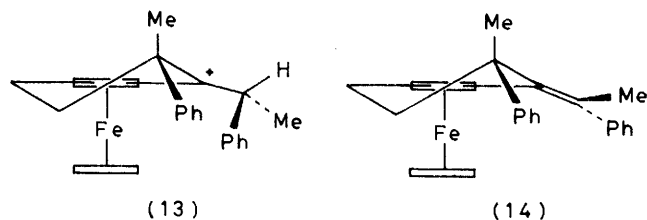
The alkenes (4c) and (5c) also dissolved in CF₃CO₂H to give predominantly the products of *exo*-protonation, (3A,c) and (3B,c), respectively. These tertiary carbocations interconvert much more rapidly than their secondary analogues, however, and the initial ¹H n.m.r. spectra showed the presence of a small proportion (*ca.* 10%) of the alternate diastereoisomer in each case. When these solutions were quenched as before, mixtures of the alkenes (4c) and (5c) were formed in which the latter predominated (Table 2), irrespective of the relative proportions of (3A,c) and (3B,c) present initially in solution. The kinetically favoured product (5c) may result either from *exo*-deprotonation of (3B,c) or *endo*-deprotonation of (3A,c). However, because these cations may interconvert rapidly by rotation prior to proton loss (see above), and may undergo deprotonation at different rates, the proportions of alkenes arising by *exo*- and *endo*-deprotonation pathways cannot be determined.

The complication of rotational isomerisation does not arise with the homoannularly bridged systems (9A) and (9B). Solutions of the carbocations (9A,c) and (9A,d), containing small amounts (<10%) of their diastereoisomers, were obtained in CF₃CO₂H from the alcohol mixtures (8A,c, 8B,c) and (8A,d, 8B,d) described earlier. Spectroscopic analysis of the products of quenching these solutions with a large excess of aqueous Na₂CO₃ showed that, while both carbocations (9A,c) and (9A,d) undergo preferential *exo*-deprotonation giving the corresponding *Z*-alkenes (10c) and (10d) as the major products, reaction of the latter proceeds with a greater stereoselectivity (Table 2).

Although pure samples of the alkenes (10c) and (11c) were not available, spectroscopic determination of the proportions of (9A,c) and (9B,c) resulting from protonation of various mixtures (Table 2) showed that these alkenes undergo both *exo*- and *endo*-protonation; the former mode is favoured (*ca.* 60%) but stereoselectivity is poor. Protonation of (10d) mixed with much smaller amounts (<5%) of (11d) gave mainly the cation (9B,d), the diastereoisomer of that (9A,d) formed as the major product of reaction of the alcohol mixture (8A,d, 8B,d) with CF₃CO₂H. Quenching experiments showed that, as with its diastereoisomer, this cation (9B,d) also undergoes deprotonation to give mainly (10d) with only small amounts of (11d) (Table 2). It follows that *exo*-proton transfer is favoured for deprotonation of (9A,d), but disfavoured for deprotonation of (9B,d) and for protonation of (10d). The transition states for these last two reactions may be sterically destabilised relative to those for corresponding *endo*-proton transfers. Thus molecular models show that *exo*-deprotonation of the cation (9B,d) would involve a very severe steric repulsion between the phenyl groups attached to the β -carbon atoms [*cf.* (13)], and *exo*-protonation of the alkene (10d) would proceed with an increase in the crowding of the allylic methyl group and the pseudo-equatorial phenyl groups [*cf.* (14)].

In summary, we conclude from these experiments that

there exists a preference for *exo*-deprotonation of ferrocenylalkylium ions and for *exo*-protonation of 1-ferrocenylalkenes over the corresponding *endo*-proton transfers, but that for particular systems this preference may be outweighed by adverse steric effects. This stereo-



selectivity may simply reflect steric factors, in that *exo*-proton transfer occurs from the less hindered face of the ligand. Alternatively, or as a contributory effect, there may be a stereoelectronic preference for the *exo*-mode.

EXPERIMENTAL

For general details, see Part 4.⁷ All new compounds gave satisfactory elemental analyses (for C and H) and ¹H n.m.r. spectra in accord with the structures assigned.

Preparation of Ketones.—Methods of synthesis of the racemic ketones (1),⁷ (7a),^{9a} (7b),^{9b} (7c),^{9b} and (7d)^{9c} have been described previously. A sample of the last compound was kindly donated by Professor R. Dabard.

Preparation of Alcohols.—Mixtures of the racemic diastereoisomeric alcohols (2A,a, 2B,a) (m.p. 103–106 °C), (2A,b, 2B,b) (viscous liquid), and (2A,c, 2B,c)⁷ (m.p. 102–104 °C) were prepared by treatment of the ketone (1) in ether with LiAlH₄, MeLi, and PhLi, respectively, using standard procedures,⁷ and were purified by chromatography (Al₂O₃) which did not separate the diastereoisomers. Attempted separation by t.l.c. (SiO₂) was also unsuccessful. The ¹H n.m.r. spectra (CDCl₃ solutions) of these mixtures showed that each contained one major diastereoisomer (≥90%) to which the structure (2A) is assigned (see Results and Discussion section).

Mixtures of the racemic diastereoisomeric alcohols (8A,a, 8B,a), (8A,b, 8B,b), (8A,c, 8B,c), and (8A,d, 8B,d) were obtained by additions of PhCH(Me)Li to the corresponding ketones (7a–d). A typical experiment is described below. All products were obtained following chromatography as viscous yellow liquids whose i.r. spectra (CCl₄ solutions) contained a strong intramolecularly Fe-bonded hydroxy-absorption¹⁰ at ca. 3 550 cm⁻¹, which establishes an *endo*-configuration for the hydroxy-groups. The ¹H n.m.r. spectra (CDCl₃ solutions) of the products (8A,a, 8B,a) and (8A,b, 8B,b) showed that these mixtures contained substantial amounts (ca. 1 : 1 and 1 : 3, respectively) of each diastereoisomer, while the products (8A,c, 8B,c) and (8A,d, 8B,d) contained one major diastereoisomer (>90%) to which the structure (8A) is assigned (see Discussion).

1-(1-Phenylethyl)-2,2-dimethyl[4](1,2) ferrocenophan-1-endo-ol (8A,c, 8B,c).—Freshly cut chips of lithium (ca. 100 mg) were added to a stirred solution of the ketone (7c) (0.56 g, 2.0 mmol) and 1-phenylethyl bromide (0.40 g, 2.2 mmol) in anhydrous ether (50 ml) under N₂. When the vigorous reaction had subsided, the mixture was stirred for 1 h and then methanol was added to remove residual lithium. The solution was washed (H₂O), dried (MgSO₄), and evaporated, and the residue was chromatographed on preparative

t.l.c. plates (SiO₂) using light petroleum (b.p. 40–60 °C) as solvent. The main yellow band gave the title compound (0.58 g, 75%) as a viscous yellow liquid. Attempts to separate the diastereoisomeric components by column chromatography (Al₂O₃) and repetitive t.l.c. (SiO₂) were unsuccessful.

Preparation of Alkenes.—The following general procedure was used. The alcohols (2A, 2B) and (8A, 8B) were dissolved in CF₃CO₂H. The resulting solutions of the carbocations (3A, 3B) and (9A, 9B), respectively, were poured with stirring into a large excess of aqueous Na₂CO₃ (10%) and the products were extracted with ether and separated by preparative t.l.c. (SiO₂). Only very small amounts of alcohols were formed; these products were not investigated. Pure samples of the alkenes (4a) (m.p. 128–130 °C), (5a) (red liquid), (4c) (m.p. 121–122 °C), and (5c) (m.p. 129–130 °C) were obtained following repetitive t.l.c. (SiO₂) of isomer mixtures using light petroleum (b.p. 40–60 °C) as solvent. The mixtures [(4b) + (5b) + (6)], [(10a) + (11a) + (12a)], and [(10b) + (11b) + (12b)] could not be separated. The mixtures [(10c) + (11c)] and [(10d) + (11d)], both obtained as red oils, contained mainly (¹H n.m.r.) the *Z*-alkenes (10) but pure samples of these compounds and the corresponding *E*-isomers (11c, d) were not obtained. The ¹H n.m.r. spectra of these alkenes, which permit differentiation between *E*- and *Z*-isomers, have been discussed¹¹ elsewhere.

Carbocation Equilibration Experiments.—Interconversion of the diastereoisomers (3A) and (3B) by Fe–C⁺ rotation can be followed by ¹H n.m.r. spectroscopy (CF₃CO₂H solutions) as discussed⁷ previously for (3A,c) ⇌ (3B,c). Rates of equilibration increased through the series (3A, 3B) R = H < Me < Ph. Corresponding spectra of cations of the series (9A,a–d, 9B,a–d) were unchanged with time. The ¹H n.m.r. chemical shifts of protons of the C₅H₅ and Me groups, which permit differentiation between cations of the type (3A), (9B) and those of the type (3B), (9A), are in Table 1.

Carbocation Quenching Experiments.—Solutions of carbocations of the series (3A, 3B) and (9A, 9B) enriched in one diastereoisomer (see Results and Discussion section) were obtained by dissolution of various samples of the alcohols (2A, 2B) and (8A, 8B) and alkenes [(4), (5)] and [(10), (11)] in CF₃CO₂H, and the diastereoisomeric compositions were determined independently by ¹H n.m.r. spectroscopy (Table 2). For those systems which undergo rotational isomerisation, cold solvent (–10 °C) was used to slow the interconversion. These solutions were quenched immediately following their preparation by pouring them into a large excess of vigorously stirred ice-cold solution of aqueous Na₂CO₃ (ca. 2M), and the alkene products were isolated as described earlier. Alkene isomer ratios were determined (Table 2) from the ¹H n.m.r. spectra of the total products by integration of the allylic methyl proton signals, which are well separated¹¹ for each isomeric pair. Independent experiments established that the alkenes do not isomerise during this work-up procedure.

A series of similar experiments was carried out in which solutions of the cations (3A,a, 3B,a) and (3A,c, 3B,c) in CF₃CO₂H were quenched with large excesses of the following bases (2M): NaOH (H₂O), NaOMe (MeOH), and KOBu^t (Bu^tOH). Although the proportions of addition and elimination products varied, ratios of isomeric alkenes formed in each case were similar, and little different from those found using Na₂CO₃ (H₂O) as quenching solution.

Alkene Protonation Experiments.—The pure alkenes (4a), (4c), (5a), and (5c), and the impure *Z*-alkenes (10c) and (10d) (each containing small proportions of the *E*-isomers) were dissolved in cold $\text{CF}_3\text{CO}_2\text{H}$ (-10°C , initially) and the ^1H n.m.r. spectra of the resulting solutions were recorded immediately. The proportions of diastereoisomeric cations present were determined (Table 2) from the relative intensities of suitable proton resonances.

We thank the National Science Foundation and the Petroleum Research Fund administered by the American Chemical Society for support of this work, Professor R. Dabard, Université de Rennes, for a sample, and the Northern Ireland Department of Education for postgraduate grants (to W. C. and N. C.).

[9/1837 Received, 19th November, 1979]

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