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STEREOCHEMISTRY OF PROTON TRANSFER TO ALKENYLFERROCENES AND OF DEPROTONATION OF FERROCENYLALKYLIUM IONS

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Ferrocenylalkylium ions ($Fc\overset{+}{C}R_2$) add nucleophiles preferentially from the exo-direction and for the reverse reaction, heterolysis of $FcCR_2X$ (X = AcO, H_2O^+, etc.), exo-departure of the leaving-group (X^-) is favoured.[1] Such cations can also be generated reversibly by protonation of 1-ferrocenylalkenes and rate constants of addition and deprotonation have been determined for cations of the type $Fc\overset{+}{C}PhCH_2R$.[2] We now report on the stereochemistry of the protonation and deprotonation reactions.

The alcohol (2c), formed as the major diastereoisomer (ca. 95%) by addition of PhLi to the racemic ketone (1), undergoes stereospecific heterolysis (exo-departure of protonated OH) in CF_3CO_2H giving the cation (3Ac) which slowly (a few hours) equilibrates with its diastereoisomer (3Bc) by rotation around the $Fc-C^+$ bond[3] (Scheme 1). The alcohols (2a) and (2b), obtained as the major diastereoisomers (> 90%) in reactions of (1) with $LiAlH_4$ and MeLi respectively (cf. Cram's rule[4]), behave similarly in CF_3CO_2H giving initially the corresponding cations (3Aa) and (3Ab). Since $Fc-C^+$ rotational barriers for secondary ferrocenylalkylium ions are appreciably higher than those for tertiary analogues,[3] the equilibration of (3Aa) $\rightleftarrows$ (3Ba) is slower than for (3Ab) $\rightleftarrows$ (3Bb) and (3Ac) $\rightleftarrows$ (3Bc). In all cases, the equilibrium mixtures contained 50 ± 10% of each diastereoisomeric cation at 33°C. The progress of these equilibrations was readily followed by ^1H n.m.r. spectroscopy; for each system, the sharp Cp singlet and Me doublet (J_{MeCH}, 7Hz) resonances of cations of the (3A) series appeared 0.15-0.35 p.p.m. downfield of the corresponding signals of their (3B) diastereoisomers.

When an equilibrium mixture of the cations (3Aa) and (3Ba) in CF_3CO_2H was quenched with a large excess of aqueous Na_2CO_3, the product consisted almost entirely of the isomeric alkenes (4a) and (5a) with only traces of alcohol.

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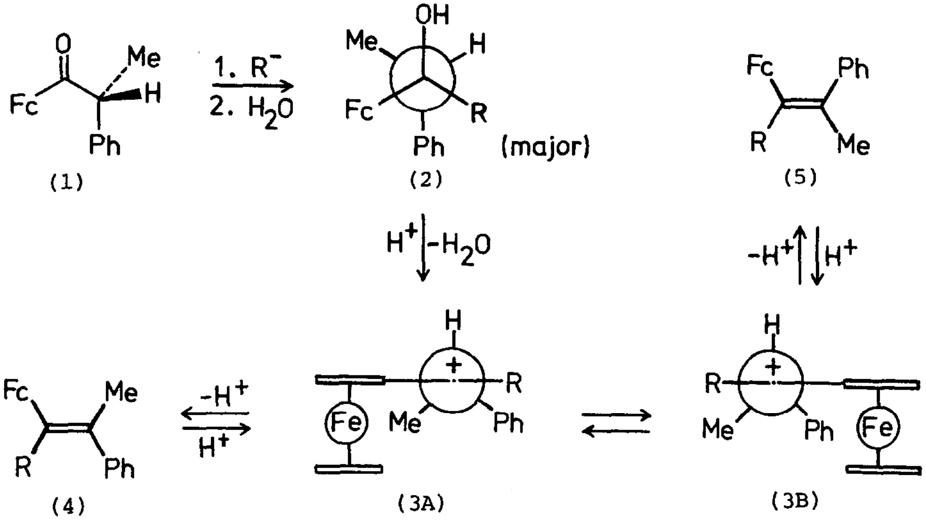
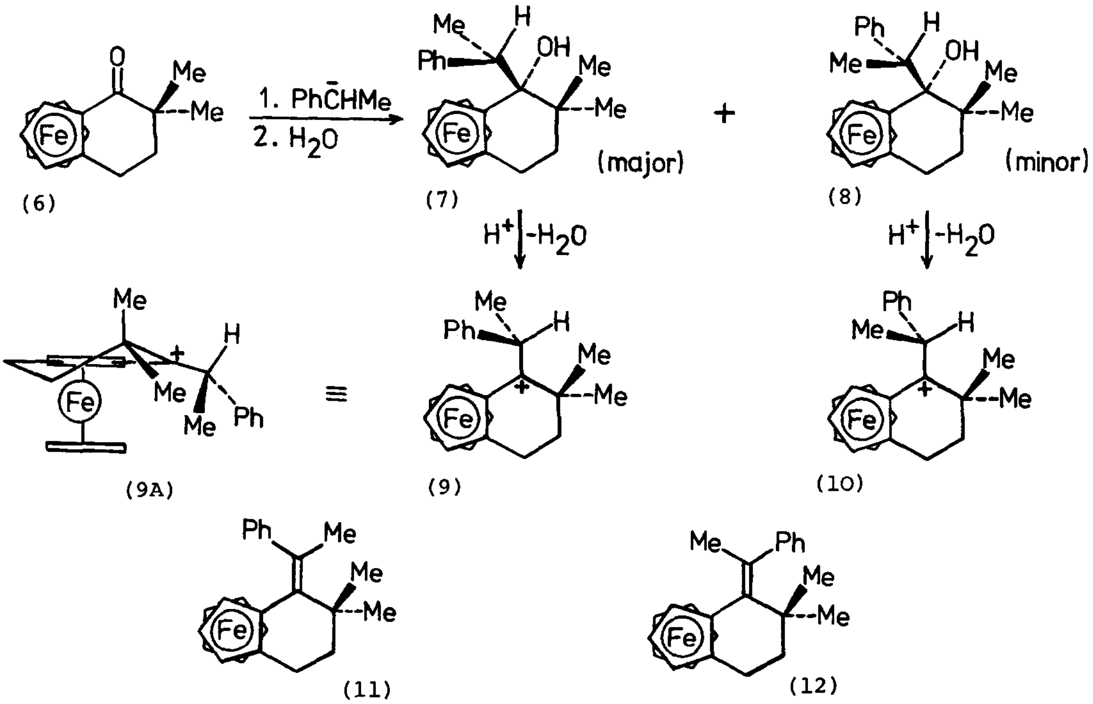
Scheme 1[†]



a; R = H b; R = Me c; R = Ph

Scheme 2[†]



[†] Only one enantiomer of each chiral species is shown; all were racemic mixtures.

These alkenes and (4c) and (5c), which were prepared similarly by dehydration of the alcohol (2c), could be separated by preparative t.l.c. (SiO_2). Deprotonation of the cation (3Ab)/(3Bb), however, gave a mixture of (4b), (5b), and mainly the terminal alkene FcC(=CH_2)CHMePh, which could not be separated. The structures of the alkenes (4a), (5a), (4c), and (5c) were assigned by comparison of their ^1H n.m.r. and u.v./visible spectra with those of related compounds of known constitution e.g. trans-FcCH=CHPh, FcCPh=CH_2. The electronic spectra were particularly characteristic. The trans-styrylferrocene chromophore gives rise to a strong absorption (logϵ, ca. 4.3) around 310 nm; with cis-styryl isomers, steric inhibition of extended π-conjugation causes a hypsochromic shift and reduction in intensity of this band which appears around 285 nm (logϵ, ca. 4.0).

The alkenes (4a) and (5a) underwent regiospecific exo-protonation in CF_3CO_2H; the ^1H n.m.r. spectra of freshly prepared solutions showed that (4a) is converted cleanly into (3Aa) and (5a) into (3Ba) (Scheme 1). A similar preference for exo-protonation was found for the alkenes (4c) and (5c) which gave initially (3Ac) and (3Bc) respectively. These diastereoisomers equilibrate more rapidly in CF_3CO_2H than their secondary analogues, however, and the initial ^1H n.m.r. spectra showed the presence of a small proportion of the alternate diastereoisomer (ca. 10%) in each case, resulting from Fc-C^+ rotation.

Immediate quenching (aqueous Na_2CO_3 or $KOBu^t/HOBu^t$) of the cation (3Aa), prepared by dissolving (4a) in cold CF_3CO_2H, gave mixtures of (4a) and (5a) in which the former predominated (85-90%). Similar treatment of the cation (3Ba), prepared from (5a), gave mixtures of the same alkenes in which (5a) predominated (85-90%). The proportions of the isomeric alkenes in these mixtures were found by integration of the well-resolved Me doublet ($J_{Me/CH}$, 2Hz) resonances of (4a) (τ7.78) and (5a)(τ7.95) in the ^1H n.m.r. spectra of the total product in $CDCl_3$. The proportion of the minor alkene product from these reactions was significantly greater than the the proportion of the alternate diastereoisomeric cation present in the CF_3CO_2H solutions (through Fc-C^+ rotation) immediately before quenching, suggesting that the cations (3Aa) and (3Ba) undergo both exo- and endo-deprotonation with the former mode favoured. Alternatively, or as a contributing effect, the Fc-C^+ rotational barrier may be lowered (e.g. through a medium effect and/or by ion-pairing with base) prior to proton transfer such that both alkene stereoisomers arise by exo-deprotonation (Scheme 1). In accord with the latter interpretation, deprotonation of mixtures of the cations (3Ac) and (3Bc) gave mixtures of the alkenes (4c) and (5c) in which the latter always predominated (ca. 90%) irrespective of the relative proportions (from 1:9 to 9:1) of the two cations in the CF_3CO_2H solution before quenching. With these tertiary carbocations, whose Fc-C^+ rotational barriers in CF_3CO_2H are much lower than those of their secondary analogues, an increase in the rotational rate during quenching but before proton transfer could lead to a loss of product selectivity, the relative proportions of the alkene products being then determined by the energies of the preceding transition states (Curtin-Hammett principle[5]). In this situation, formation of the derivative (5c) is kinetically favoured.

The behaviour of a related system in which Fc-C^+ rotation is prevented was also studied (Scheme 2). Addition of PhCHMeLi to the racemic ketone (6)[6] gave a mixture of the diastereoisomeric endo-alcohols (7) and (8) in the ratio 10:1 respectively.[‡] These were not separated. The corresponding 10:1 mixture (^{1}H n.m.r.) of diastereoisomeric cations (9) and (10), formed from the alcohol mixture in CF_3CO_2H, underwent deprotonation on quenching (KOBu^t/HOBu^t) giving a mixture of the alkenes (11)[§] and (12)[§] in the ratio 3.5:1 respectively (^{1}H n.m.r.). The major cation (9), therefore, must react both by exo- and endo-deprotonation with the former kinetically favoured. The presence of a pseudo-axial exo-Me group in the preferred conformation (9A) of this cation may introduce some steric hindrance to exo-deprotonation. Although we were unable to separate the alkenes (11) and (12), determination (^{1}H n.m.r.) of the relative proportions of the cations (9) and (10) formed in CF_3CO_2H from various mixtures of these alkenes of differing compositions showed that (11) and (12) undergo preferential but not exclusive exo-protonation.

In summary, alkenylferrocenes of the type FcCR=CMePh undergo preferential exo-protonation in CF_3CO_2H giving ferrocenylalkylium ions which undergo preferential exo-deprotonation on reaction with a base.

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[‡] Diastereoisomeric selection in this reaction results from the presence of the pseudo-axial exo-Me group in the ketone precursor (6). The corresponding reaction of the related ketone lacking the Me substituents gives approximately equal amounts of the diastereoisomeric alcohol products.

[§] The structures of these alkenes were established by comparison of their ^{1}H n.m.r. spectra with those of alkenes of the types (4) and (5).