Pergamon

Tetrahedron Letters, Vol. 35, No. 24, pp. 4215-4218, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $7.00+0.00

0040-4039(94)E0749-N

Stereoselective Addition of Silyl Enol Ethers to α-Ferrocenylcarbenium Ions

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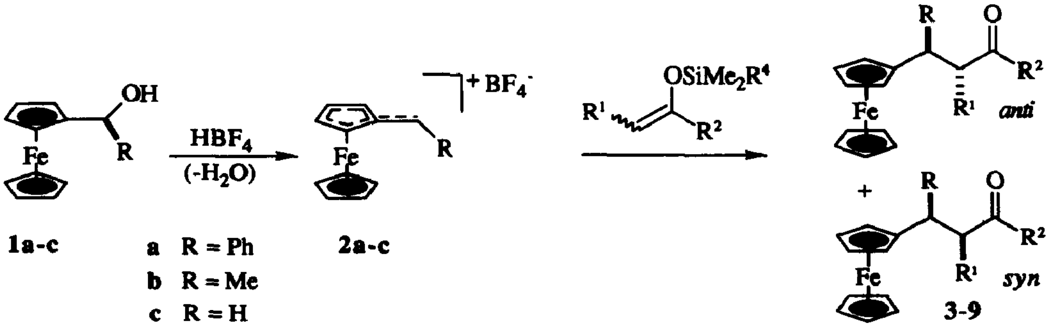
Abstract: 1-Ferrocenylalcohols are readily converted into their corresponding α-ferrocenylcarbenium tetrafluoborate salts. These react cleanly with silyl enol ethers to give alkylated products with up to 6 : 1 selectivity for the *anti* diastereoisomer.

Ferrocene based ligands systems, incorporating both tetrahedral and planar chirality, have found successful application in numerous asymmetric catalytic processes.[1] A feature of existing ligands is their common synthesis from N,N-dimethyl-1-ferrocenylethylamine derivatives by stereospecific replacement of dimethylamine by other secondary amines.[2] These reactions proceed *via* configurationally stable α-ferrocenylcarbenium ions, which also form adducts with a wide range of other heteroatom nucleophiles.[3]

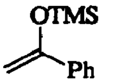
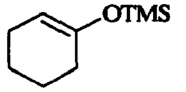
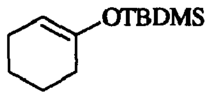
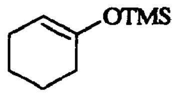
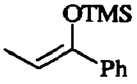
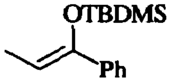
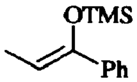
It has been previously reported that a number of transition metal stabilised carbenium ions including (propargyl)dicobalt hexacarbonyl ions,[4] (η^5-cyclohexadienyl)iron tricarbonyl salts[5] and cationic (η^6-chloroarene)iron and ruthenium cyclopentadienyl complexes,[6] react with silyl enol ethers to give alkylated products. Attracted by the possibile application of this alkylation methodology to the synthesis of novel ferrocene derivatives, we sought to investigate the reaction between silyl enol ethers and α-ferrocenylcarbenium ions. Our preliminary results are reported in this letter.

α-Ferrocenylcarbenium ions were conveniently generated by the addition of HBF_4 to diethyl ether solutions of 1-ferrocenylalcohols **1a-c**, in a modification of a procedure previously reported by Allenmark.[3a,7] Subsequently, **2a** was dissolved in CH_2Cl_2 and to this was added, at low temperature, an excess of 1-(trimethylsiloxy)styrene. The addition was accompanied by an almost instantaneous change in colour from very dark red to yellow. After work up, the adduct **3** was isolated by chromatography in excellent yield (Scheme 1, Table 1).



Scheme 1

Table 1[a]

Entry	Substrate	Silyl enol ether	Product	anti : syn[b]	Yield[c] (%)
1	**1a**		**3** R = R^2 = Ph R^1 = H	–	88
2	**1b**	"	**4** R = Me R^1 = H R^2 = Ph	–	93
3	**1c**	"	**5**[d] R = R^1 = H R^2 = Ph	–	85
4	**1a**		**6** R = Ph R^1/R^2 = $-(CH_2)_4-$	2.5 : 1	90
5	**1a**		**6**[e] R = Ph R^1/R^2 = $-(CH_2)_4-$	1 : 1.3	98
6	**1b**		**7** R = Me R^1/R^2 = $-(CH_2)_4-$	1 : 1	90
7	**1a**		**8** R = R^2 = Ph R^1 = Me	6 : 1	89
8	**1a**		**8**[f] R = R^2 = Ph R^1 = Me	6 : 1	95
9	**1b**		**9** R = R^1 = Me R^2 = Ph	2.7 : 1[g]	95

a) All reactions were performed according to the standard procedure[7] unless otherwise stated. b) As determined by ^1H NMR spectroscopy. c) Isolated yield, calculated from **1**. d) **2c** generated and washed at -30 °C. e) Reaction mixture stirred at -78 °C for 1h. prior to quenching. f) Reaction mixture warmed to -40 °C over a period of 1h. prior to quenching. g) Relative configuration assigned by analogy with entries 4 and 7.

Similarly, compounds **4** and **5** were prepared from **2b** and **2c** respectively, showing that the sucess of the reaction is independent of the relative stability of the intermediate α-ferrocenylcarbenium ion.

Alkylation of **2a** with 1-(trimethylsiloxy)cyclohexene (entry 4) resulted in a modest 2.5 : 1 selectivity for one diastereoisomer of **6**. After purification by chromatography and recrystallisation, the relative configuration of the major isomer was found to be *anti* by an X-ray crystal structure analysis (Figure 1).[8]

Interestingly, use of the corresponding *tert*-butyldimethylsilyl enol ether (entry 5) gave a 1.3 : 1 excess of the *syn* diastereoisomer, and addition of 1-(trimethylsiloxy)cyclohexene to **2b** (entry 6) gave **7**, as a 1 : 1 mixture of diastereoisomers. In contrast (*Z*)-enol ethers, derived from propiophenone, added to **2a** with 6 : 1 selectivity for one diastereoisomer of **8**. In this instance selectivity was observed to be independent of the alkyl groups attached to silicon (entries 7 and 8). The minor isomer was removed by recrystallisation and the relative configuration of the major isomer was determined as *anti*, again by an X-ray crystallographic analysis (Figure 2).[9] Finally, alkylation of **2b** by (*Z*)-1-phenyl-1-(trimethylsilyloxy)propene proceeded with 2.7 : 1 diastereoselectivity to give **9** (entry 9).

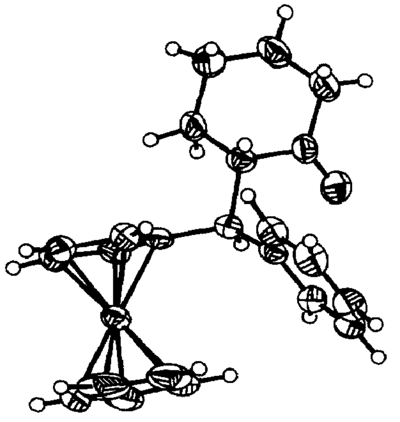


Figure 1 Molecular structure of *anti* **6**

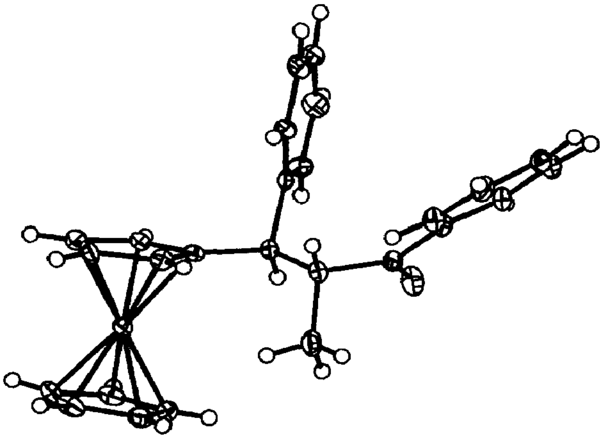
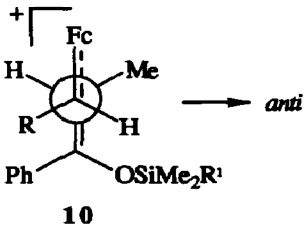
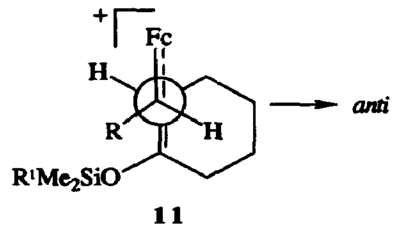


Figure 2 Molecular structure of *anti* **8**

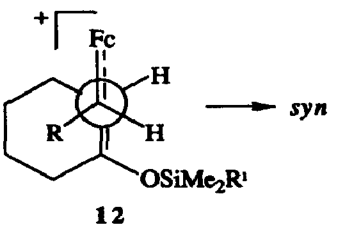
To account for the observed stereoselectivity, it is proposed that the reactions proceed predominantly *via* the extended acyclic transition states **10** and **11** for the (*Z*)- and (*E*)-silyl enol ethers respectively. In model **10**, the trialkylsiloxy group is remote from other sterically demanding groups and, as a result, a change in the size of this group has no effect upon the diastereoselectivity (entries 7 and 8). In contrast, for **11**, the trialkylsiloxy group is proximal to carbenium ion substituent R such that the alternative transition state **12** is increasingly favoured by a change from trimethylsilyl to *tert*-butyldimethylsilyl (entries 5 and 6).



10



11



12

The observed *anti* selectivity is opposite to that expected by application of topological rules for the combination of two prochiral π-systems.[10] These require a *gauche* relationship of the donor and acceptor π-systems, which in the above cases would lead to a predominance of the *syn* diastereoisomers. It is of note that in a related process, cobalt complexed propargylic ethers were observed to give *syn* alkylated products with silyl enol ethers in the presence of a Lewis acid, a reaction that is believed to proceed *via* the intermediacy of a carbenium ion.[11] However, it appears that for the addition of silyl enol ethers to α-ferrocenylcarbenium ions, the relative bulk of the donor and acceptor systems dictates that an *anti* relationship is preferred, such that electrostatic repulsions are minimised.[12]

In summary, we have demonstrated that alkylation of 1-ferrocenylalcohols proceeds in excellent overall yield, and in certain instances, with good *anti* diastereoselectivity. We are currently applying this methodology to the synthesis of novel ferrocene based catalyst systems.

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7. Standard procedure: Under a nitrogen atmosphere, a commercial 54% solution of tetrafluoroboric acid in Et_2O (0.22 ml) was added dropwise to a yellow solution of **1** (0.7 mmol) in dry Et_2O (4 ml). The resulting orange/brown precipitate was filtered under nitrogen (canular), washed with dry ether (2 x 5 ml) and dried under a stream of nitrogen to give **2**. This was dissolved in dry CH_2Cl_2 (4 ml) to give a dark red solution, cooled to -78 °C and to this was added silyl enol ether (1.4 mmol) in dry CH_2Cl_2 (2 ml) over a period of approximately 1 minute. After stirring for a further 5 min., the resulting yellow reaction mixture was quenched with sat. $NaHCO_3$(aq) and warmed to room temperature. The CH_2Cl_2 layer was separated and the aqueous layer was washed with a further 10 ml of CH_2Cl_2. The combined organic layers were dried (Na_2SO_4), filtered and evaporated, and the residue flash chromatographed (EtOAc/40-60 petrol) to give the product as a yellow crystalline solid.
8. Crystal data: ***anti* 6**, $C_{23}H_{24}FeO$, M = 372.30, triclinic; P1-, a = 6.0439(8), b = 10.569(3), c = 14.609(2) A, α = 96.349(5)°, β = 93.567(8)°, γ = 92.320(9)°, Z = 2, Mo-K_α radiation λ = 0.71069 A. R = 0.0495 for 4122 observed ($I/\sigma I$ > 2.0) reflections (R_w = 0.1242).
9. Crystal data: ***anti* 8**, $C_{26}H_{24}FeO$, M = 408.30, monoclinic; P21/n a = 11.886(2), b = 5.8613(5), c = 27.9960(13) A, β = 99.43(2)°, Z = 4, Mo-K_α radiation λ = 0.71069 A. R = 0.0360 for 7499 observed ($I/\sigma I$) > 2) reflections (R_w = 0.0730).
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(*Received in UK* 16 *February* 1994; *accepted* 15 *April* 1994)