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THE FIRST FULL RESOLUTION OF 2-METHOXYTRICARBONYLCYCLOHEXADIENYLIRON HEXAFLUOROPHOSPHATE, AN EXAMPLE OF A SYNTHETIC ORGANIC EQUIVALENT IN THE SERIES OF CHIRAL CYCLOHEX-2-ENONE-4-CATIONS.

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A superior method, using Hunig base in CH_2Cl_2, converts complexed cations of type (1) into type (2) by the action of nucleophiles HXR', and permits the optical resolution of the title salt via the ethers of (2,R=OMe,R' = (-)-menthoxy).

The direct formation of a new asymmetric centre in full resolution and of known absolute configuration is an important capability of reactions on a resolved chiral olefin complex of a transition metal.[3] Removal of the metal abolishes the original chirality to leave that of the new organic molecule. To be able to use this in synthesis requires the ability to produce resolved complexes, particularly of cations since these undergo a wide range of fruitful nucleophilic reactions. A particular case is the class of 2-methoxytricarbonylcyclohexadienyliron salts (1), since these are synthetic organic equivalents of cyclohex-2-enone-4-cations (3) and provide for further organic synthesis[3,4]. The formulae shown for the enantiomers of resolved salt (1,R=OMe) represent the absolute configurations.

The presence of functional groups such as CO_2H permits classical resolution[5], but in their absence the cation itself can act as the functional group, given that a number of nucleophiles which react with it can eventually be removed by acid. As a preliminary to examination whether the diastereoisomeric mixture of ethers resulting from reaction with an optically active alcohol can be separated, it was necessary to examine the experimental conditions for reacting the cations with nucleophiles HXR'. Although these have been used to form uncharged dienyl complexes (X=O,S[6],N[7]) yields of isolated product were often poor. The following procedure is a general one, with examples shown in Table 1, which gives good yields under very mild conditions.

To the PF_6 salt of the cation (1 mmole) in CH_2Cl_2 is added HXR' (3 mmole) at 0° followed by Hunig base (1.1 mmole). When the solution is a clear yellow (10 min to 2 h according to the reactivity of the salt[8]) the product is purified in light petroleum either by passage through a short column of alumina (alkaline, activity 4) or crystallisation, as appropriate. On a 10-20 g scale no difficulties were found.

TABLE 1

Salt (1)	HXR'	Product (2)	Characteristics
R=H	HOPh	R=H,R'=OPh (85%)	Known[9]
	HSPh	R=H,R'=SPh (92%)	Known[10]
	$HSC_6H_4NO_2$-p	R=H,R'=$SC_6H_4NO_2$-p (93%)	m.p. 106-108°, anal.CHNS
	HSePh	R=H,R'=SePh (94%)	m.p. 53-54°, anal.CHSe
R=Me	$HOCHMe_2$	R=Me,R'=$OCHMe_2$ (77%)	oil ($CDCl_3$) 2.12 (2-Me)
R=OMe	(-)-menthol	R=OMe,R'=menthoxy (88%)	oil ($CDCl_3$) 3.68 (2OMe)
		(diastereoisomers)	(C_6D_6) 3.00 (OMe) 2.97 (OMe)

In the last example the use of C_6D_6 permits spectral definition of isomer ratios. Standard spectra in all cases support the assigned structures; proton couplings[11] indicate the α-stereochemistry of the entering group. No evidence of formation of position isomers was noted with the unsymmetrical cations.

The role of the Hunig base, and the reason for its superiority over others such as triethylamine or K_2CO_3, is not certain. It reacts with the unsubstituted salt to form a soluble product with IR bands at 2050, 1980 cm^{-1} for an uncharged iron complex, but the α-stereochemistry of (2) is to be expected of direct reaction of the nucleophile with the cation, not of displacement of quaternary nitrogen. The solution of the adduct in CH_2Cl_2 reacts with MeOH, in contrast to an analogous stable pyridinium derivative. Separation of the diastereoisomers of (2,R=OMe,R'=menthoxy) was accomplished using medium pressure liquid chromatography[12] on SiO_2 in ethyl acetate-hexane (1:9) (Table 2). Although the (±)-cation (1,R=Me) reacted smoothly with (-)-menthol, the resulting mixture was much more difficult to separate and was only partially accomplished, e.g. a specific rotation of (+)15.7° was obtained for (1,R=Me) which based on earlier observations[13] corresponds to approximately 60% optical purity. The purities of the 2-OMe ethers were assessed in C_6D_6 by ^1H and ^{13}C NMR, at 100 and 16.4 MHz respectively, as greater than 95%.

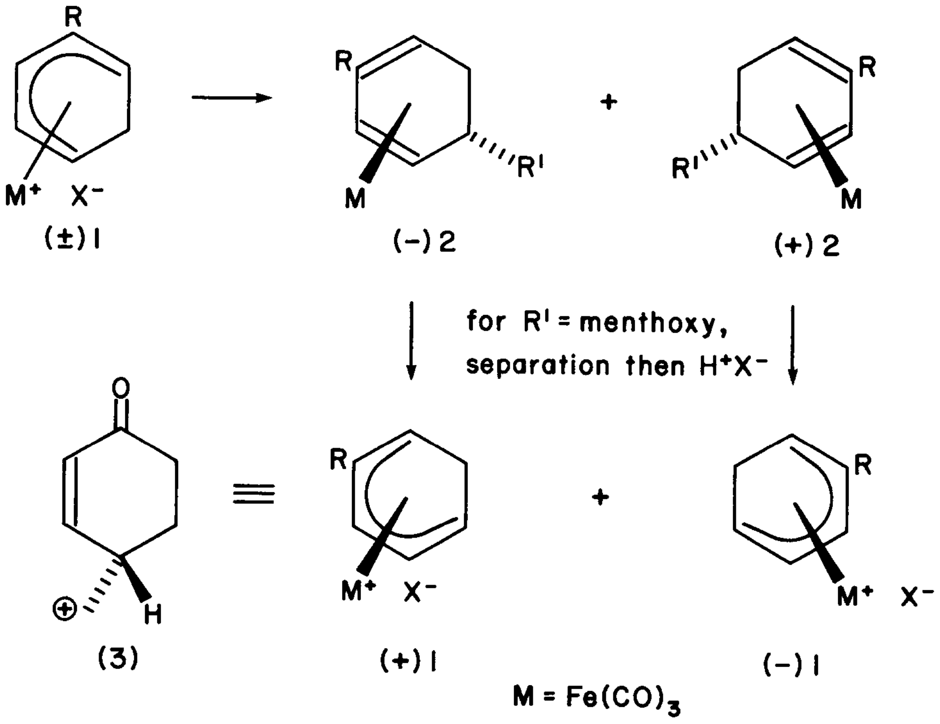
Other available optically active alcohols examined, such as borneol and ethyl lactate, although forming ethers, did not permit separation of the diastereoisomers by this method.

Conversion of ethers into the salt was accomplished in about 90% isolated yield by adding a solution of HBF_4 or HPF_6 (1 ml) dropwise at 0° to a solution in propionic anhydride, (1 g in 10 mls) followed by a mixture of ether and CH_2Cl_2 (1:1) to precipitate the salt. The rotations are shown in Table 2. The differences between the BF_4 and PF_6 salts are notable, and must be taken into account in assessing extent of resolution by other processes.

TABLE 2. Specific Rotations for 2-OMe Series.

Chromatogram Fraction		$[\alpha]_{589}$	
	Menthoxy	BF_4Salt	PF_6Salt
1	(-)132°	(+) 136°	(+) 116°
	(c=1.2,hexane)	(c=0.6,MeCN)	(c=0.6,MeCN)
2	(+) 3.9°	(-) 139.4°	(-) 120.9°
	(c=1.1,hexane)	(c=0.3,MeCN)	(c=0.3,MeCN)

Characteristics of the method for resolution of the 2-OMe salt, which contrast with previous approaches,[14] are that there is no difficulty on a preparative scale, it is rapid and quantitative in principle, the resolving agent is readily available and can be recovered. Extensions to substituted derivatives are being examined, but it should be noted that the ether formation fails in cases where a substituent containing CH is attached terminally to the cation. Base-catalysed elimination then occurs to form a triene complex.



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