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STEREOCONTROLLED APPROACHES TO SUBSTITUTED TETRAHYDROFURAN AND *cis*-HYDRINDENE DERIVATIVES VIA CYCLOHEXADIENE-Fe(CO)$_3$ COMPLEXES.[1]

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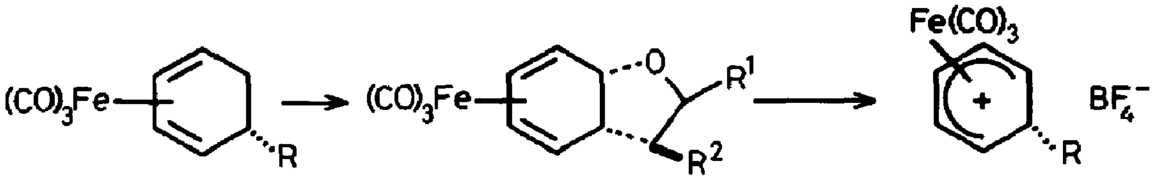
Abstract: Oxidative cyclisation of the diol complex (6) followed by removal of Fe(CO)$_3$ gives a single tetrahydrofuran derivative (7). Intramolecular nucleophile reaction of the salt (13) leads to cis-hydrindene derivative (14).

We recently described the reaction of cyclohexadiene-Fe(CO)$_3$ complex (1) with thallium(III) trifluoroacetate (TTFA), giving high yield of the oxidatively cyclised complex (2). Treatment of (2) with HBF$_4$/acetic anhydride gave the dienylium complex (3) in high yield which could be reacted stereo- and regiospecifically with sodiodimethylmalonate to give (4), but in rather low yield (30-40%).[2]



(1) $R = CH_2CH(OH)CH_3$

(5) $R = CH(CO_2Me)_2$

(6) $R = CH(CH_2OH)_2$

(2) $R^1 = Me, R^2 = H$

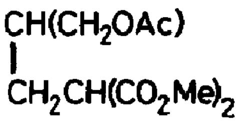
(7) $R^1 = H, R^2 = CH_2OH$

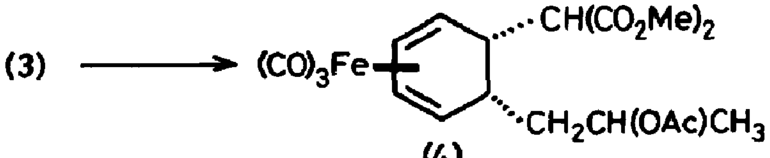
(8) $R^1 = H, R^2 = CH_2OAc$

(9) $R^1 = H, R^2 = CH_2OTs$

(10) $R^1 = H, R^2 = CH_2CH(CO_2Me)_2$

(3) $R = CH_2CH(OAc)CH_3$

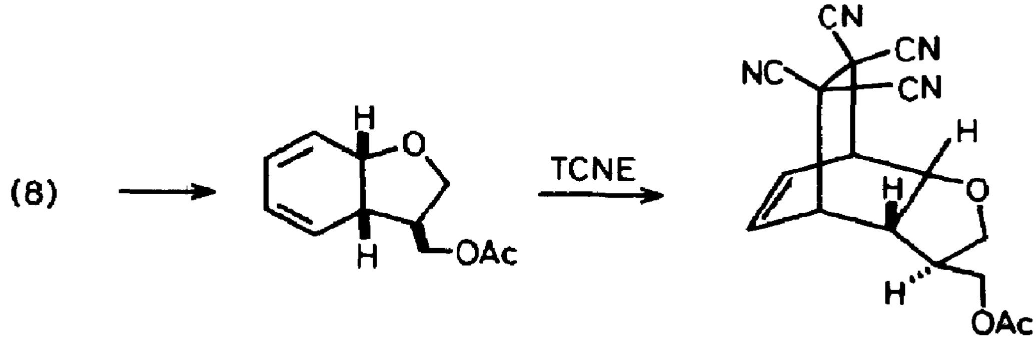
(13) R =

$CH(CH_2OAc)CH_2CH(CO_2Me)_2$



(4)

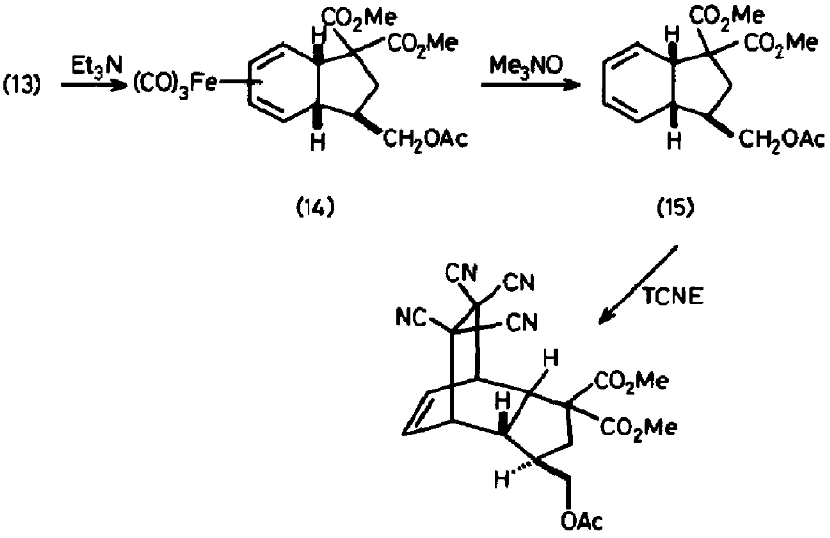
Interest in tetrahydrofuran derivatives carrying functionalised substituents with defined relative stereochemistry, owing to their potential usefulness as intermediates for a number of interesting natural products, e.g. polyether antibiotics,[3] led us to examine this reaction with a complex carrying a bifunctional substituent. Furthermore, we wished to complement our recent studies on intramolecular nucleophile additions, resulting in spirocyclisation,[4] by examining annulation reactions of salts such as (3) but bearing an enolisable group in the substituent R.

For the present model study the gem diester (5), m.p. 171-172°, was chosen as the starting point, since it was readily prepared from tricarbonylcyclohexadienyliumiron tetrafluoroborate[5] and sodiodimethylmalonate.[6,7] Reduction with DIBAL (4.8 equiv., THF, 25°C o/night, 96%) gave the diol (6), m.p. 110-111°, ν_{max} ($CHCl_3$) 3620, 3500, 2050 and 1980 cm^{-1}. Treatment of (6) with TTFA (1.7 equiv.) in the presence of $NaHCO_3$ (4.0 equiv., EtOH, -10°C) gave, after extractive work-up and chromatography, the cyclised product (7) (60%) as a single crystalline stereoisomer (n.m.r.) m.p. 121-122°, ν_{max} ($CHCl_3$) 3620, 3430, 2060 and 1985 cm^{-1}. The stereochemistry was assigned on the basis of steric considerations, the substituent R^2 occupying the less hindered face of the tetrahydrofuran ring. Acetylation of (7) (Ac_2O, C_5H_5N, 25°C, o/night) gave the acetate (8), m.p. 82.5-83.5°C. Synthesis of a tetrahydrofuran derivative would require removal of the $Fe(CO)_3$ group without aromatisation, and this was achieved in excellent yield using anhydrous trimethylamine-N-oxide[8] (benzene, 25°C, 24 h, 98%), to give the diene (11) as a colourless oil ν_{max} ($CHCl_3$) 1735 cm^{-1}. Reaction of this compound with tetracyanoethylene (benzene, 25°C, 2 h) gave the crystalline cycloadduct (12), m.p. 185-186.5°C, ν_{max} ($CHCl_3$) 2240, 1745 cm^{-1}, (60% after p.l.c.).



(11) (12)

We next turned our attention to using the primary alcohol moiety in (7) as a means of introducing an enolisable group. Conversion to the tosylate (9), m.p. 88-89°C, proceed smoothly (2 equiv. TsCl, C_5H_5N, 0°C, 3 h, 97%) and this was treated with potassiodimethylmalonate (^{t}BuOK, $CH_2[CO_2Me]_2$, 4 equiv., dioxan, reflux 24 h, 88% + 12% rec. SM) oil to afford the diester (10), ν_{max} 2060, 1980, 1750 and 1735 cm^{-1}. This compound was converted to the tetrafluoroborate (13) ν_{max} (CH_2Cl_2) 2130, 2090, 2070 cm^{-1}, using aqueous tetrafluoroboric acid in excess acetic anhydride (CARE: admixture of these two reagents is exothermic). We were now in a position to examine the cyclisation of (13), which would constitute only the second example, so far as we are aware, of <u>intramolecular</u> carbon nucleophile addition to cyclohexadienylium-Fe(CO)$_3$ complexes. Treatment of (13) with 1,5-Diazabicyclo-[5.4.0] undec-5-ene (1 equiv., CH_2Cl_2, -78°C) led to instantaneous disappearance of the infrared bands at 2130, 2090 and 2070 cm^{-1} (dienylium-Fe(CO)$_3$) with the appearance of two new bands at 2050 and 1975 cm^{-1}, and formation of one major compound (t.l.c.). Although the crude n.m.r. spectrum suggested the presence of the desired complex (14), there was also present an impurity (aromatic, δ 7.08-7.40) which persisted even after repeated preparative layer chromatography. Consequently the crude product was treated directly with Me_3NO (benzene, 25°C) to give the free ligand (15) as an oil, ν_{max} ($CHCl_3$) 1730 cm^{-1}. Treatment of this with TCNE in benzene at 25°C for 2 h gave the adduct (16) as a crystalline compound, m.p. 116-119°C. Thus, we have evolved a new annulation procedure suitable for the construction of cis-hydrindenes, a ring system present in a number of natural products, not the least important of which are the gibberellins. We are examining the generality of this procedure applied to more appropriately substituted examples.



(14)

(15)

(16)

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