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by

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Regioselectivity of Addition of Nucleophilic Raegents to α,β—Unsaturated Carbonyl Group in Cyclic Systems

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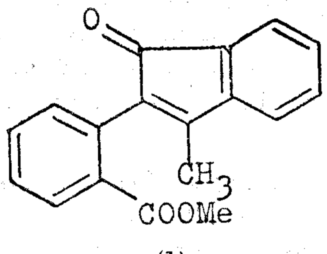
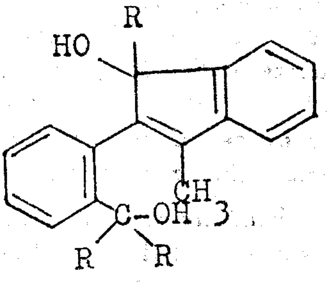
2-0- Carbomethoxyphenyl -3- methyl-indenone reacts with different Grignard reagents, to give in each case, the 1,2-addition product 0- [1-hydroxy -1- aryl (or alkyl) -3- methyl-ind-2-enyl] phenyl-diaryl (or alkyl) carbinol. The same product is also obtained when the reaction is carried out in presence of cuprous bromide.

The structure of the products is discussed in the light of their I.R., U.V., n.m.r., and mass spectra.

This work was carried out to study the regioselectivity of the addition of nucleophilic reagents to α,β-unsaturated carbonyl compounds. 2-o- carbomethoxyphenyl-3-methyl-indenone (1) was used as an example of cyclic α,β-unsaturated carbonyl compound. Different Grignard reagents were used in excess to react with this indenone system. Methyl magnesium iodide, benzyl magnesium chloride; phenyl; o,p-tolyl; o- and p-anisyl magnesium bromides were used as different Grignard reagents. In each case, o- [1-hydroxy -1- aryl (or alkyl) -3- methyl -ind--2- enyl] -phenyl-diaryl (or alkyl) carbinol (2a-h) was obtained; indicating a 1:2-mode of addition to the carbonyl group.



(1)



(2)

a; R = CH_3

b; R = CH_2Ph

c; R = C_6H_5

d; R = o-CH_3-C_6H_4-

e; R = p-CH_3-C_6H_4-

f; R = o-OCH_3-C_6H_4

g; R = p-OCH_3-C_6H_4

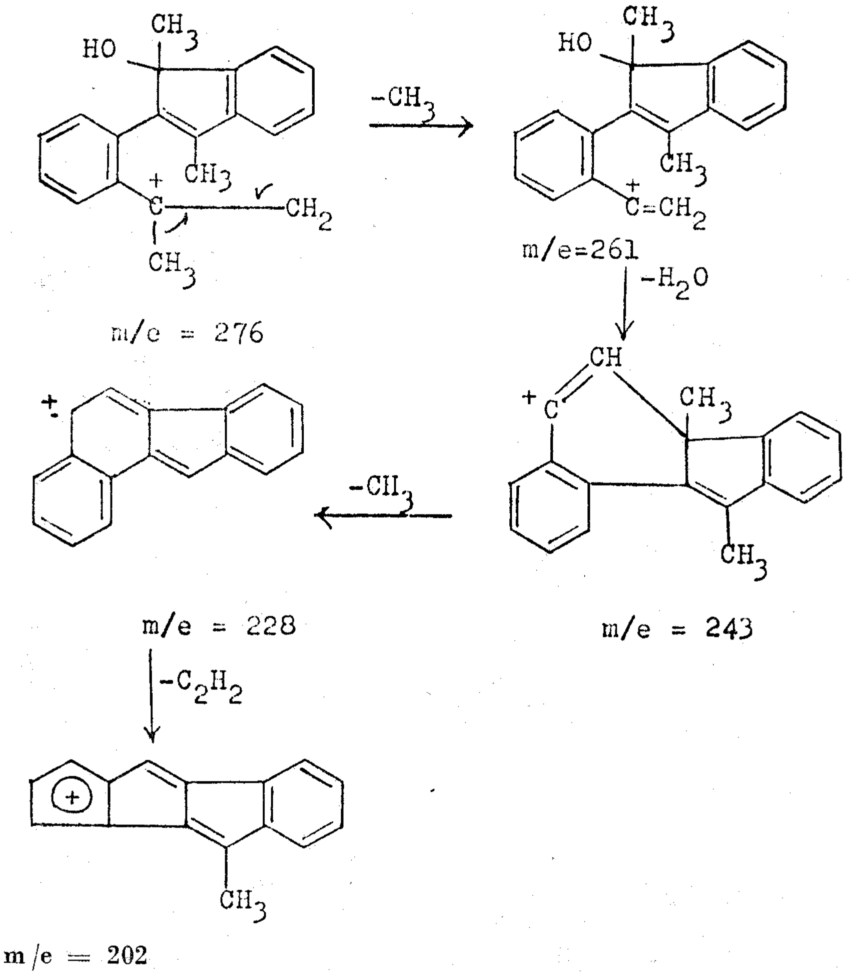
The structure assignment of these products was based on the following: i) their elemental analysis ii) Their I.R. spectra which show a broad absorption in the 3μ region, and the disappearance of the carbonyl absorption. iii) The electronic spectra of compounds 2b, 2c and 2e show absorption maxima at λ_{max} 277, 273; 274, 277; and 280 nm respectively with ϵ_{max} 10875, 16630; 7080, 7008; and 6872 respectively. These values are consistant with a trans-stilbene structure[1], although a hypsochromic shift is attributed to a partial out of plane rotation of the o-substituted phenyl groups. This rotation is not complete since the absorption is still at longer wave length compared to styrene[1]. iv) The nmr spectra of 3b and c support this structure. Beside the aromatic multiplet, compound 3b exhibits the following signals: a) a singlet at δ 1.115 ppm for the 3-methyl protons. b) Two singlets at $\delta = 2.299$ and 2.25 ppm for the methylene protons of the benzyl groups.

Similarly compound 3 c shows a signal at δ 1.085 ppm for the three methyl protons. v) The mass spectra of all the above obtained products were characterised by the same feature, which is the disappearance of the molecular ion, and the predominance of a base peak corresponding to $(M\text{-}H_2O)^+$. This supports their alcoholic structure[2]. The fragmentation of compounds 2a and c are given as representative examples of this study.

Compound 2a gives, under electron impact, the following cations: m/e 276 (96 %) due to $(M\text{-}H_2O)^{\cdot+}$., the latter loses CH_3 giving rise to an ion of m/e 261 (100 %), which loses H_2O to yield a peak of m/e 243 (78 %); loss of $CH^{\cdot}_3$ yields a peak of m/e 228 (47 %), which in turn eliminates C_2H_2 giving an ion of m/e 202 (29 %). Cations of mass/e 43 (49 %); 128 (10 %) and 114 (10 %) for acetyl, 2- methyl indenyl, and indenyl cations respectively were also detected. The following chart represents this fragmentation.

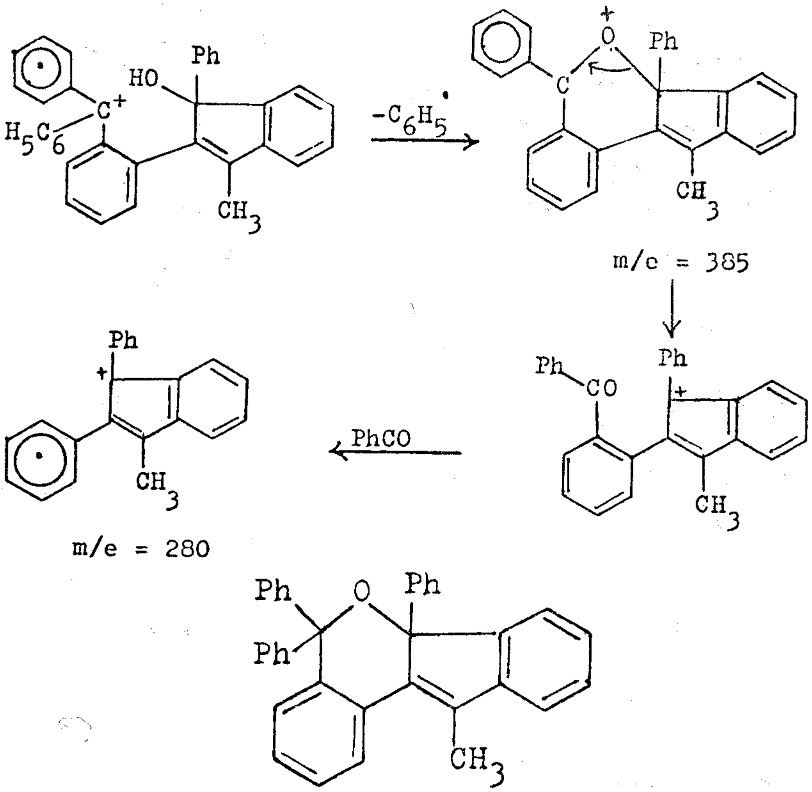
Similarly when (2c) was subjected to electron impact, the base peak was due to $(M\text{-}H_2O)^{\dot{+}}$ and appears at m/e 462, loss of $C_6H^{\cdot}_5$ gave a cation of m/e 385 (25 %) followed by charge transfer which is transformed to an isomeric form that eliminates C_6H_5CO, or C_6H_5CHO yielding cations of m/e 280 and 279 respectively, which by elimination of C_2H_2 gave the cation of m/e 254.

vi) A further support for the structure of (2) was carried out chemically by heating 2 c with concentrated sulphuric acid, cyclisation



dehydration took place between the two hydroxy groups, and 1- phenyl -3- methyl -indano [1,2-b] -benz- [1,2-c] -2,2- diphenyl-dihydropyran (3) was obtained.

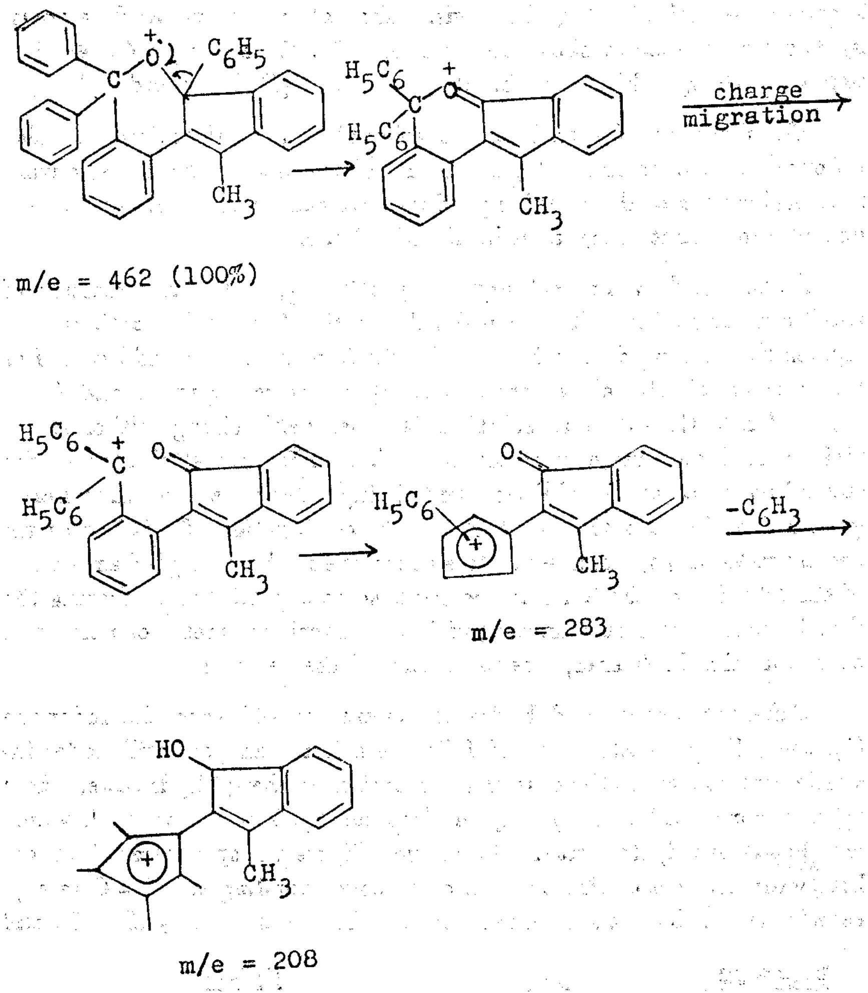
The structure of the latter was based on: i) its elemental analysis, ii) its i.r. absorption spectrum which lake any absorption in the functional group region, and the appearance of a peak at 1240 cm^{-1} for the ether linkage. iii) Its pale yellow colour and its electronic absorption spectrum which shows a peak at λ_{max} 309 nm ($\epsilon_{max} = 3518$), which when



(3)

compared with (2c) show a bathochromic shift due to the planarity of the system after cyclization. iv) when subjected to electron impact, (3) gave the following cations: The molecular ion at m /e (462) base peak, m /e 231 indicates a doubly charged ion. The molecular ion looses a phenyl radical giving rise to a cation of m /e = 385 (31 %) followed by charge migration and the conversion to a substituted cyclopentadienyl cation of m /e = 283 which in turn looses C_6H_3 giving rise to the radical ion of m /e 208 (53 %).

It is to be mentioned that when phenyl magnesium bromide reacts with (1), two different products were obtained. The elemental analysis of both of them fits with the presence of one molecule of ethanol of crystallisation in each of them. These two products differ slightly in their i.r. spectra. The lowest melting one (2c) may be converted to the second



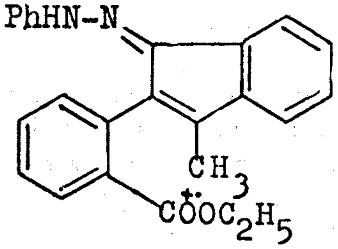
(2c′) by fusion. They gave identical fragmentation patterns when subjected to electron impact. These two products may be considered as conformers arising from partial restricted rotation around the sigma bond joining the indenyl skeleto nto the o-substituted phenyl group by the presence of three bulky o-substituents around this bond.

The presence of a molecule of ethanol of crystallisation in (2c and 2c′) was supported by: i) Their nmr spectra which exhibit the absorption spectrum of ethanol together with the above mentioned signals. ii) Their mass spectra show the presence of cations of m/e 46 (40 %); m/e 45 (100 %) which may be attributed to $C_2H_5OH^{+\cdot}$ and $C_2H_5O^{+\cdot}$

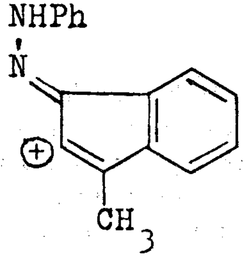
The presence of a molecule of ethanol of crystallisation was also observed in the reaction of p-bromoanisyl magnesium bromide, during recrystallisation of the reaction product, two compounds were separated, one of them containing a molecule of ethanol.

As reported by Kharash and many others [3,4,5], the introduction of small amounts of transition metal salts to the Grignard reactions, activates the olefinic double bond and thus favours the 1:4 addition. For this reason, all the above studied reactions were repeated and CuBr was added to the indenone solution. No observable change either in the yield or in the course of reaction took place. This was attributed to the steric hindrance at the olefinic bond, being substituted by three bulky groups. Another deactivating factor is the conjugation of this bond with the aromatic rings, which leads to an increase in the energy of activation of the addition of the Grignard reagent, so as any trial of activating the double bond by complexation with the transition metal can not still overcome this high energy requirement of the reaction.

Different amines and hydrazines were reacted with the indenone (1), the solid products obtained failed to solidify and are still under investigation except in the case of the reaction of phenyl hydrazine, where (1) was converted to its phenyl hydrazone (4). The structure of which was based on: (i) its elemental analysis; (ii) its i.r. spectrum which exhibit only one absorption at 1710 cm^{-1} corresponding to υ C=O in aryl ester[6]; (iii) its electronic spectrum shows absorption at λ_{max} 252, 290 and



m/e = 382 (75%)



m/e = 233

396 nm with ϵ_{max} 16912, 5606 and 13339 respectively; (iv) when (4) was subjected to electron impact, the following cations were observed at m/e 382 (75 %)corresponding to the molecular ion which looses $C_2H_5O^{\cdot}$ to yield a cation of m/e = 337. Ions of m/e 309, 307, 233, 217, 203, 202, all of relatively low intensity were also detected. The base peak appears at m/e 77.

EXPERIMENTAL

I.R. (KBr) and U.V. spectra were recorded on Unicam SP 1200 infracord, and Unicam SP 1800 spectrophotometers, respectively, and n.m.r. spectra on a Varian S-60 T spectrophotometer using TMS as internal reference. Mass spectra were measured by a Mass spectrometer SM IB with data system SS 100 (Varian Mat).

Reaction of 2-o-carbomethoxyphenyl -3- methyl -ind -2- Enone (1) with Grignard reagents: -The Grignard reagent (6 mole) in ether was added dropwise, on the cold, to a solution of (1) (1 mole) in benzene, and refluxed for 3 hrs, then left overnight at room temperature, and decomposed with ice cold saturated ammonium chloride solution, extracted with ether, washed with water, dried over anhydrous sodium sulphate, and the ether removed under reduced pressure leaving a semisolid product which was solidified by light petroleum (b.p. 40-60 C) and crystallised from a suitable solvent. (cf. Table).

Reaction of (1) with Grignard reagent in presence of cuprous bromide.

The Grignard reagent (6 moles) in ether was added to a solution of 1 mole of (1) and 0.5 mole of cuprous bromide in benzene, and the reaction mixture refluxed for 3 hrs, then left overnight at room temperature, and then decomposed with cold saturated ammonium chloride solution, then worked up as usual.

Cyclisation of (2c) to 1- phenyl -3- methyl-indano - [1,2-b]- benz- [1,2-c] -2,2- diphenyl-dihydropyran (3).

0.5 g of (2c) was refluxed with 5 ml of 50 % sulphuric acid for 2 hrs. The solution was then cooled, poured on ice-water. The precipitated solid was crystallised from ethanol.

Characterization data of the products 2,3 and 4

Nr.	M.p. (Solvent of cryst.)	Yield %	Formula (M.Wt)	Analysis Found / Calc.		
				C%	H%	N%
2a	163–4° lp. 80	76	$C_{20}H_{22}O_2$ (294)	81.54 81.63	7.57 7.48	
2b	211–2° Ethanol	66	$C_{38}H_{34}O_2$ (522)	87.43 87.35	6.70 6.51	
2c	128–130° Ethanol	32	$C_{35}H_{28}O_2C_2H_5OH$ (526)	84.61 84.09	6.62 6.81	
2c′	180–1° Ethanol	16	$C_{35}H_{28}O_2C_2H_5OH$ (526)	83.63 84.09	6.54 6.81	
2d	140–1° Methanol	37	$C_{38}H_{34}O_2$ (522)	86.64 87.35	6.68 6.51	
2e	206–208° lp. 60	69	$C_{38}H_{34}O_2$ (522)	87.17 87.35	6.85 6.51	
2f	231–33° Ethanol	59	$C_{38}H_{34}O_5$ (570)	79.45 80.00	6.16 5.96	
2g	219–21° Ethanol	39	$C_{38}H_{34}O_5$ (570)	79.32 80.00	6.16 5.96	
2h	123–5° Ethanol	27	$C_{38}H_{34}O_5C_2H_5OH$ (616)	78.32 78.17	6.12 6.18	
3	156–9° Ethanol	60	$C_{35}H_{26}O$ (462)	90.38 90.90	5.82 5.63	
4	125–6° lp. 80	92	$C_{25}H_{22}O_2N_2$ (382)	78.41 78.53	5.87 5.76	7.29 7.32

lp. 80 = light petroleum (b.p. 80-100°),
lp. 60 = light petroleum (b.p. 60-80°).

Pyrolysis of (2c).

0.5 g of o- [1-hydroxy -1- phenyl -3- methyl -ind -2- enyl]- phenyl-diphenyl-carbinol was heated to 150°C on a sandbath, and left at this temperature for 2 hrs, then cooled; a solid was obtained which was identified as 2c′ by melting and mixture melting points.

Reaction of (1) with amines:

A mixture of the indenyl ester (1) and the amine (1 mole) in acetic acid (20 ml per g ester) was refluxed for 3 hrs. The mixture was then left to cool, poured on ice cold water to precipitate the product which was crystallised from a suitable solvent.

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