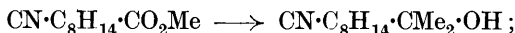


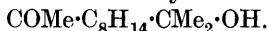
CCLXXIV.—*The Action of Magnesium Phenyl Bromide on Methyl o-Cyanobenzoate. 1 : 3-Diphenyldihydroisoindole.*

By DAVID RUNCIMAN BOYD and DONALD ERNEST LADHAMS.

It has been shown by Haller and Legagneur (*Compt. rend.*, 1925, **180**, 1621) that magnesium methyl iodide in ethereal solution reacts with the methyl ester of camphoric acid α -mononitrile to give the corresponding cyano-tertiary alcohol :



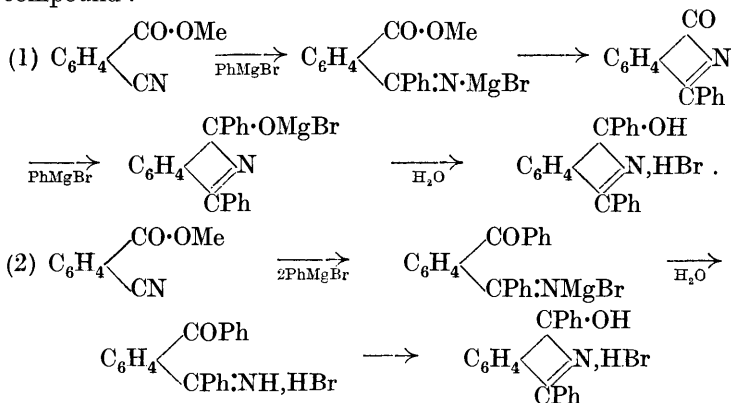
in boiling toluene solution, however, the nitrile group also is attacked, the product being the ketonic tertiary alcohol,



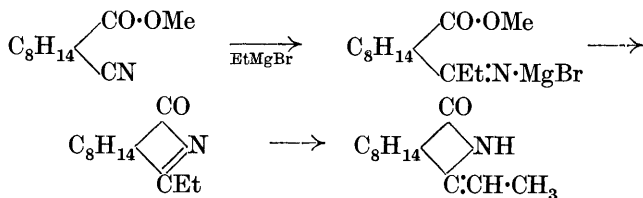
Using magnesium phenyl bromide in ethereal solution, the same authors obtained (*ibid.*, p. 881) the ketimine hydrobromide, $\text{C}_8\text{H}_{14}(\text{COPh})\cdot\text{CPh}\cdot\text{NH}\cdot\text{HBr}$. No observations appear to be on record with regard to the action of a Grignard reagent on an aromatic compound containing both a cyano- and a carbalkyloxy-group. It seemed possible that the cyano-group in such a compound would show a reactivity considerably less than that of the other competing group, and methyl *o*-cyanobenzoate was investigated by us in the hope of obtaining *o*-cyanotriphenylcarbinol.

We have found, however, that magnesium phenyl bromide in ethereal solution converts the ester almost quantitatively into the hydrobromide of a base which we consider to be 1-hydroxy-1 : 3-diphenylisoindole. No trace of the isomeric *o*-cyanotriphenylcarbinol could be detected.

Two different routes may be suggested as leading to the isoindole compound :

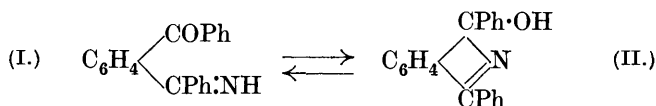


Ring formation by elimination of $\text{MeO}\cdot\text{MgBr}$, as in scheme (1), has been postulated by Salmon-Legagneur (*Ann. Chim.*, 1927, **8**, 5) to explain the formation of a nitrogen-ring compound by the action of magnesium ethyl bromide on the methyl ester of camphoric acid α -mononitrile :



In scheme (2) the *isoindole* derivative is assumed to arise from the ketimine hydrobromide by an intramolecular change.

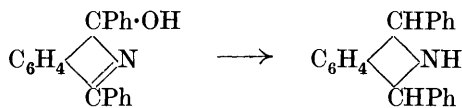
Although the *isoindole* formula * appears to us the more probable, the isomeric ketimine constitution cannot be definitely excluded. In certain solutions both forms of the compound may be present :



The comparative ease with which hydrolysis to *o*-dibenzoylbenzene takes place on boiling with dilute sulphuric acid may be regarded as evidence of the presence of (I) in the solution. On the other hand, the ring structure is supported by the following considerations :

(1) With concentrated sulphuric acid the base behaves like a tertiary aromatic carbinol, giving a solution of an intense magenta colour. In this solution the compound shows great stability; heating in a water-bath for 2 hours produced little or no alteration.

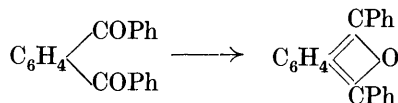
(2) The base can be reduced to 1 : 3-diphenyldihydro*isoindole* :



The reduction was effected by means of zinc dust and acetic acid, and the yield was small. Most of the base was converted into a yellow solid apparently identical with diphenylbenzofuran (Guyot and Catel, *Bull. Soc. chim.*, 1906, **35**, 1124). The appearance of this substance is attributed to hydrolysis resulting in the formation of dibenzoylbenzene, which is then reduced to the benzofuran.

* Compounds related to *isoindole* have also been obtained by Weiss and co-workers (*Monatsh.*, 1924, **45**, 105; 1927, **48**, 451) by the action of Grignard reagents on *o*-phthalonitrile.

Experiment showed that reduction of dibenzoylbenzene under similar conditions leads to the same yellow product :



Efforts to improve the yield of 1 : 3-diphenyldihydroisindole by the use of other reducing agents were unsuccessful.

1 : 3-Diphenyldihydroisindole appears to be the first example of a 1 : 3-disubstituted dihydroisindole. The parent substance and its 1-methyl derivative were described by Gabriel (*Ber.*, 1893, 26, 526, 711, 2213), but only *N*-substituted dihydroisindoles have been prepared subsequently. The compound was found to be much more stable than the unsaturated substance from which it was derived, being unattacked by boiling dilute acid or alcoholic potash, and only oxidised extremely slowly by chromic-acetic acid to dibenzoylbenzene. It behaves as a strong secondary base, giving readily crystallised salts and a *nitroso*-, a *monobenzoyl* and a *p-toluenesulphonyl* derivative (the last alkali-insoluble). From its mode of preparation it might be expected to have the *trans*-, and therefore racemic, configuration, but the material available was not sufficient for experiments on resolution.

The study of the reaction between cyanobenzoic esters and organomagnesium halides is being continued.

EXPERIMENTAL.

Methyl *o*-cyanobenzoate was prepared in 65% yield from methyl anthranilate by Clarke's modification of the Sandmeyer reaction (*J. Amer. Chem. Soc.*, 1924, 46, 1001). The oily product was distilled under reduced pressure, b. p. 154°/15 mm., and crystallised in the receiver to colourless plates, m. p. 51°.

The Action of Magnesium Phenyl Bromide on Methyl o-Cyanobenzoate.—28.6 G. of the ester (1 mol.) in 300 c.c. of ether were run slowly, with constant stirring, into the ice-cold Grignard reagent prepared from 86 g. of bromobenzene (3 mols.) and 12.2 g. of magnesium (2½ atoms) in 250 c.c. of ether. Each drop gave a yellow precipitate, so that finally a semi-solid mass was obtained. This was refluxed for an hour, cooled, and decomposed with ice and dilute sulphuric acid. The yellow solid, 1-hydroxy-1 : 3-diphenylisindole hydrobromide, was collected and washed with ether, in which it was almost insoluble. Yield, 50 g. (90%). The brown ethereal filtrate gave on evaporation a small amount of gummy material, from which unchanged ester was crystallised by rubbing with alcohol. The

hydrobromide was crystallised from chloroform-benzene, but could not be obtained pure. It decomposed above 220° . Attempts to crystallise it from alcohol converted it into *o*-dibenzoylbenzene. The free base was obtained by rubbing the hydrobromide with aqueous sodium carbonate, and a little ether to remove gummy matter (some decomposition occurred as shown by the evolution of ammonia). The prismatic crystals obtained from aqueous methyl or ethyl alcohol melted at 192.5° (decomp.) (Found: C, 83.7; H, 5.4; N, 4.9. $C_{20}H_{15}ON$ requires C, 84.1; H, 5.3; N, 4.9%). When boiled in alcoholic potash or dilute sulphuric acid for an hour, the base was quantitatively decomposed into *o*-dibenzoylbenzene, m. p. 145° (Found: C, 83.2; H, 5.1. Calc. for $C_{20}H_{14}O_2$: C, 83.9; H, 4.9%), ammonia also being formed. The *o*-dibenzoylbenzene was identified by conversion into the oxime, m. p. $149-150^{\circ}$ after crystallisation from methyl alcohol. The ketone gave a colourless solution with concentrated sulphuric acid. Guyot and Catel (*loc. cit.*) record 146° and 150° as the melting points of the ketone and oxime, and state that the solution of the ketone in sulphuric acid has a pink colour.

The free base dissolved in concentrated, or slightly diluted, sulphuric acid to give a magenta-coloured solution; the hydrobromide gave off hydrogen bromide and bromine. This solution could be boiled for some minutes or heated in the water-bath for 2 hours without any marked decomposition, as shown by cooling, pouring on ice, filtering off any traces of dibenzoylbenzene and neutralising the filtrate. An attempt was made to condense the hydroxyisoindole with phenol in the presence of sulphuric acid (Baeyer and Villiger, *Ber.*, 1902, **35**, 3018; Boyd and Hardy, this vol., p. 630). Sulphonation occurred, however, and the product was an amphoteric uncrystallisable substance.

With a view to obtaining evidence as to the constitution of the product arising in the Grignard reaction, experiments on benzoylation were carried out. Before decomposition of the Grignard complex with ice, benzoyl chloride (1 mol.) was run slowly into the well-cooled suspension, which was then refluxed for an hour, cooled, and treated with ice and ammonium chloride. A small quantity of solid remained, insoluble in the ether layer; this was extracted with alcohol, which deposited on dilution a colourless solid, m. p. 220° , containing nitrogen but giving no coloration with concentrated sulphuric acid (Found: C, 84.3; H, 5.6; N, 4.4. $C_{20}H_{15}ON$ requires C, 84.1; H, 5.3; N, 4.9%). On repeating the experiment this substance was not obtained, so that further investigation was not possible. The ethereal solution in each case contained dibenzoylbenzene, benzamide, and tarry matter.

Reduction of 1-Hydroxy-1:3-diphenylisoindole.—An acetic acid solution of the base was kept with excess of zinc dust for 2 days, with occasional warming. The filtrate exhibited a blue fluorescence (destroyed by exposure to light and air), and gave on dilution a deep-yellow solid. This could not be satisfactorily crystallised, but its m. p. of 120—125°, its oxidation by chromic-acetic acid to dibenzoylbenzene, and its behaviour in solution point to its identity with Guyot and Catel's diphenylbenzofuran, m. p. 125°. Dibenzoylbenzene was reduced under the same conditions to the same substance. The diluted acetic acid filtrate gave on neutralisation a white precipitate of 1:3-diphenyldihydroisoindole in very poor yield. The yield was increased to about 10 to 20% by adding the hydrobromide in small quantities to the boiling suspension of zinc dust in acetic acid. The colourless prisms from alcohol melted at 109° (Found: C, 87.95; H, 6.55; N, 5.1. $C_{20}H_{17}N$ requires C, 88.45; H, 6.3; N, 5.2%). The base is soluble in the usual organic solvents, and in dilute mineral acids; the solution in hot dilute hydrochloric acid gave crystals of the *hydrochloride* on cooling, m. p. 270—280° (decomp.) (Found: Cl, 11.36. $C_{20}H_{17}N, HCl$ requires Cl, 11.53%). The base was slowly oxidised by gradually adding a slight excess of chromic anhydride to an acetic acid solution heated in a water-bath. On cooling, dibenzoylbenzene crystallised.

On adding aqueous sodium nitrite to a dilute sulphuric acid solution of the base, a white precipitate of the *nitroso*-derivative, $C_6H_4(CHPh)_2N \cdot NO$, slowly formed. The crystals from alcohol were pinkish, but yellow while in the steam-oven, and melted at 175—175.5° (Found: N, 9.5. $C_{20}H_{16}ON_2$ requires N, 9.3%). This substance was unaffected by alcoholic hydrochloric acid, and could not be reduced to the corresponding hydrazine by zinc dust in acetic acid. On applying Liebermann's test it gave a green solution in the sulphuric acid-phenol mixture. The *benzoyl* derivative (Schotten-Baumann method) gave crystals very sparingly soluble in alcohol, m. p. 236° (Found: N, 3.9. $C_{27}H_{21}ON$ requires N, 3.7%). On treatment with phosphorus pentachloride (v. Braun, *Ber.*, 1904, 37, 2818) it gave an intractable tarry material. The *p-toluene-sulphonyl* derivative melted at about 255° (decomp.). It was insoluble in alkali.

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