

THE ACTION OF GRIGNARD REAGENTS ON BENZOPYRONES

Part I. Preparation of Some Chromenes from 4-Substituted Coumarins

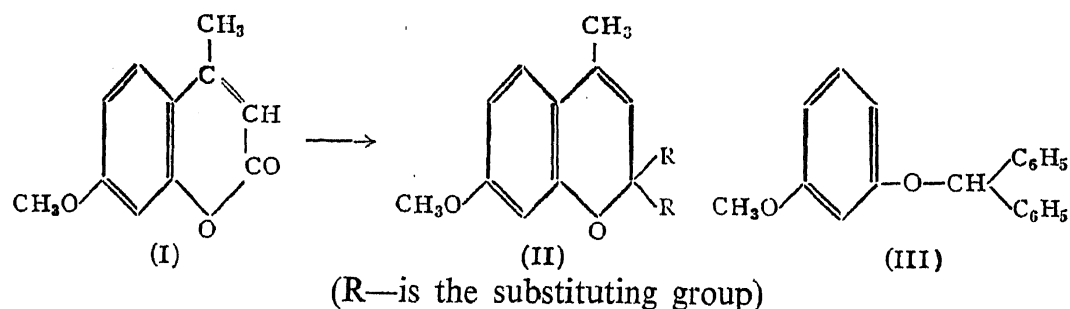
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THE present investigation was undertaken with the object of synthesising compounds expected to possess insecticidal action similar to that of deguelin. With this object in view the action of grignard reagents on coumarins was taken up. This reaction was employed by Willstätter and co-workers¹ for the synthesis of anthocyanidines. Houben,² and Lowenbein, Pongracz and Spiess³ have also recorded a large number of investigations leading to the formation of substituted chromens and suggested a mechanism for the course of the reaction employing a large excess of the grignard reagent. Heilbron and Hill⁴ investigated the action of grignard reagents on substituted coumarins with the object of synthesising flavylum chlorides containing methoxyl and hydroxyl in the 4-position; the latter being expected readily to lose hydrogen chloride and pass into flavones. They obtained only diaryl products and consequently a detailed investigation of coumarins substituted in 3- and 4-positions was initiated. These investigations led them to the definite conclusion that the course of the reaction resulting in the production of either a Δ^2 or Δ^3 chromen is influenced solely by the position of the substituent in the pyran ring.

In this communication we are reporting the condensation of methoxymethyl umbelliferone with excess of grignard reagents prepared from (a) bromobenzene, (b) *p*-brom anisol, (c) benzyl chloride, (d) α -naphthyl bromide, and (e) methyl iodide. α -Naphthocoumarin was condensed with magnesium phenyl bromide. All these condensation products are assigned the Δ^3 -chromen structure in conformity with the general conclusions arrived at by Heilbron and co-workers, that namely when the 4-position is occupied by a substituent the product formed is the Δ^3 -compound.



The 2:2-diphenyl-4-methyl-7-methoxy- Δ^3 -chromen was subjected to alkaline hydrolysis yielding the diphenyl-methyl-ether (III) thereby confirming the Δ^3 -structure.

Experimental

The general methods of reaction and processing were the same in all cases and so the details are given only in one case.

2:2-Diphenyl-4-methyl-7-methoxy- Δ^3 -chromen.—The grignard reagent prepared from 3 grams (excess) of magnesium and the equivalent amount of bromobenzene was cooled in an ice-bath and treated with 5 grams of methoxy methyl umbelliferon in dry benzene. The reaction mixture was refluxed on the water-bath for 12 hours, decomposed with iced dilute hydrochloric acid and thoroughly extracted with benzene. After removing the benzene the residue was steamed to remove volatile impurities. The residue was extracted with ether, dried and solvent removed, yielding a solid melting at 60–65°. Repeated crystallisation from 95% alcohol yielded clusters of stout flat needles melting at 93°.

(Found: C, 84.1 and H, 6.6. $C_{23}H_{20}O_2$ requires 84.1 and 6.1 respectively.)

2:2-Dianisyl-4-methyl-7-methoxy- Δ^3 -chromen.—The crude product obtained from the reaction was a reddish viscous mass and on repeated crystallisation from absolute alcohol yielded needle-like tufts melting at 110°.

(Found: C, 77.4 and H, 6.2. $C_{25}H_{24}O_4$ requires 77.3 and 6.2 respectively.)

2:2-Dibenzyl-4-methyl-7-methoxy- Δ^3 -chromen.—The product of the reaction had first of all to be pressed on to a plate to remove the persistently adhering oily impurity and then crystallised from alcohol in rosettes of colourless needles melting at 52°.

(Found: C, 84.2 and H, 6.8. $C_{25}H_{24}O_2$ requires 84.3 and 6.7 respectively.)

2:2-Di- α -Naphthyl-4-methyl-7-methoxy- Δ^3 -chromen.—The viscous semisolid reaction mass was refluxed with excess of alcohol when an impurity was dissolved out and the product solidified. This processing was repeated with fresh alcohol each time till a fine colourless powder was obtained. Final crystallisation from glacial acetic acid gave a pure product melting at 240–41°.

(Found: C, 86.7 and H, 5.7. $C_{31}H_{24}O_2$ requires 86.9 and 5.6 respectively.)

2:2:4-Trimethyl-7-methoxy- Δ^3 -chromen.—The product is a liquid boiling at 158–60°/12 mm.

(Found: C, 76.1 and H, 7.9. $C_{13}H_{16}O_2$ requires 76.5 and 7.8 respectively.)

2:2-Diphenyl-4-methyl- α -naphtho- Δ^3 -chromen.—The product on crystallisation from a large volume of 95% alcohol yielded yellow prisms melting at 126–27°.

(Found: C, 89.5 and H, 6.3. $C_{26}H_{20}O_2$ requires 89.7 and 5.8 respectively.)

Alkaline hydrolysis of 2:2-Diphenyl-4-methyl-7-methoxy- Δ^3 -chromen.—2 Grams of the substance was refluxed with 50 c.c. of 50% potassium hydroxide for 60 hours. The solid melted and remained as a viscous liquid on the top of this alkaline solution. After hydrolysis was over the reaction mixture was diluted with 200 c.c. of water, cooled and extracted with ether. The ethereal extracts were united, dried over anhydrous magnesium sulphate and the ether removed. The residue weighed 1.2 grams and solidified to a hard mass. Crystallisation from alcohol yielded needles melting at 105.5°.

(Found: C, 82.3 and H, 6.1. $C_{20}H_{18}O_2$ requires 82.7 and 6.2 respectively.)

Summary

The action of grignard reagents on methoxy methyl umbelliferone and α -naphtho coumarin was investigated to prepare compounds similar to certain naturally occurring benzopyrans.

REFERENCES

1. *Ber.*, 1924, 57, 1938, 1945.
2. *Ibid.*, 1904, 37, 489.
3. *Ibid.*, 1924, 57, 1517.
4. *J. C. S.*, 1927, 2005.