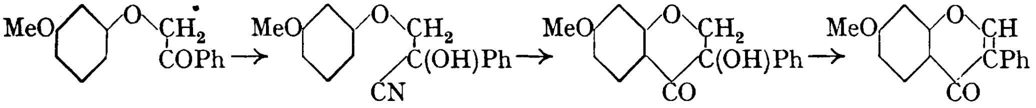
101. *Synthetical Experiments in the* iso*Flavone Group. Part VIII. Limitations of the Phenacyl Aryl Ether Cyanohydrin Method.*

By Wilson Baker, W. M. Morgans, and Robert Robinson.

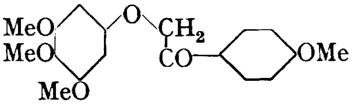
The method referred to in the title is that of Part V (J., **1929**, 1468) and may be illustrated by the scheme :—

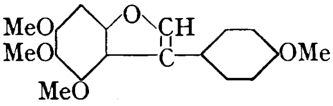


We entertained high hopes that it would prove general in its application, but the experiments now put on record show that it fails in certain cases, (a) because the cyanohydrin cannot be obtained or (b) because the ring closure in the second stage cannot be effected.

In the course of experiments preliminary to a synthesis of irigenol, *ketones* (I and II) were prepared, of which the cyanohydrins were formed with very great difficulty; that derived from (I) was ultimately obtained in an almost pure state. Unfortunately the pyran ring could not be closed, and the feeble nuclear reactivity thus indicated was confirmed by the fact that the dehydration of (I) to the *coumarone* (III) could only be accomplished by the use of phosphoric anhydride; the ketone was unchanged by solution in sulphuric acid at 0°. Attempted dehydration of (II) by means of phosphoric anhydride in benzene solution led to the formation of a substance, probably the *coumaran* derivative (IV).

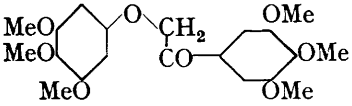
(I.)

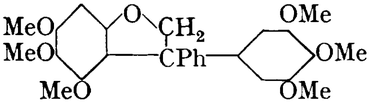




(III.)

(II.)





(IV.)

The instability of the cyanohydrins of (I) and (II) is doubtless connected with the occurrence of a methoxyl group in the *p*-position to the carbonyl (cf. Lapworth and Manske, J., **1928**, 2533; **1930**, 1976).

EXPERIMENTAL.

ω-*Diazo*-p-*acetylanisole*.—Anisoyl chloride, b. p. 140—160°/20 mm., m. p. 22°, was obtained from the acid by means of $SOCl_2$ (reflux 1 hr.). A solution of the chloride (4 g.) in anhyd. Et_2O (30 c.c.) was gradually added to one of CH_2N_2 (10 c.c. of nitrosomethylurethane) in Et_2O at 0°. After 1 hr. the Et_2O was removed in dry air, leaving yellow crystals. The *substance* separated from Et_2O in four-sided plates, m. p. 83—84° (Found : C, 61·4; H, 4·7; N, 15·9. $C_9H_8O_2N_2$ requires C, 61·4; H, 4·5; N, 15·9%), and exhibited the usual properties of the class. Treated with HBr in dry Et_2O, it gave a quant. yield of *p*-methoxyphenacyl bromide, colourless rhombohedra from Et_2O, m. p. 80—81°. Prepared in this way, the ketone is more easily purified than is the product of the alternative Friedel–Crafts condensation of anisole and bromoacetyl bromide (Kunckell and Scheven, *Ber.*, 1898, **31**, 173).

3 : 4 : 5-*Trimethoxyphenyl* p-*Methoxyphenacyl Ether* (I).—A solution of *p*-methoxyphenacyl bromide (2·9 g.) in acetone (20 c.c.) was added to one of antiarol (2·3 g.) (Chapman, Perkin, and Robinson, J., 1927, 3032) in NaOH aq. (0·5 g. in 10 c.c. H_2O), and the mixture heated on the steam-bath for 1 hr. After being worked up, the oily product solidified (4 g.) and crystallised from EtOH in colourless woolly needles, m. p. 110—111° (Found : C, 64·9; H, 6·1. $C_{18}H_{20}O_6$ requires C, 65·1; H, 6·0%), readily sol. in acetone, $CHCl_3$, and CS_2 and sparingly sol. in Et_2O and light petroleum.

Many trials of the prepn. of the *cyanohydrin* were made and the derivative was obtained as follows :—Solutions of the ketone (6 g.) in EtOAc (50 c.c.) and of KCN (7 g.) in H_2O (30 c.c.) were mixed, cooled to 0°, and very gradually treated with 30% H_2SO_4 (30 c.c.) during 2 days with shaking. After keeping for 24 hr. longer, the EtOAc layer was washed, dried, and concentrated in a current of air. The residual solid crystallised from $CHCl_3$–light petroleum, ultimately in colourless rhombs, m. p. 126—127°, which could not be completely freed from traces of unchanged ketone (Found : C, 62·8; H, 5·9; N, 3·3. $C_{19}H_{21}O_6N$ requires C, 63·5; H, 5·8; N, 3·9%). With EtOH–$AgNO_3$, AgCN was pptd. Under all conditions the attempted ring closure of the cyanohydrin failed. ω-Diazo-*p*-nitroacetophenone (Bradley and Schwarzenbach, J., 1928, 2907) was converted into *p*-nitrophenacyl bromide (cf. Engler and Zielke, *Ber.*, 1889, **22**, 204), but this bromide could not be used for the prepn. of an ether with antiarol as second component.

4 : 5 : 6 : 4′-*Tetramethoxy*-3-*phenylcoumarone* (III).—The dehydration of the trimethoxyphenyl *p*-methoxyphenacyl ether was effected in boiling C_6H_6 solution by means of an excess of P_2O_5 for 2—3 hr. The C_6H_6 was decanted and concentrated, leaving an oil which crystallised in contact with light petroleum; recryst. from EtOH, it gave colourless needles, m. p. 104—105° (Found : C, 68·7; H, 5·5. $C_{18}H_{18}O_5$ requires C, 68·8; H, 5·7%).

ω-*Diazo*-3 : 4 : 5-*trimethoxyacetophenone*.—*O*-Trimethylgalloyl chloride, m. p. 77°, was obtained by the action of $SOCl_2$ on the acid and was brought into reaction with CH_2N_2 (2 mols. under the usual conditions in dry Et_2O : yield almost theoretical). This *substance* is readily sol. in C_6H_6, acetone, and $CHCl_3$, but sparingly sol. in Et_2O and light petroleum. Recryst. from C_6H_6–light petroleum, it separated in pale yellow needles, m. p. 97—98° (Found : C, 56·0; H, 4·8; N, 12·1. $C_{11}H_{12}O_4N_2$ requires C, 55·9; H, 5·1; N, 11·9%).

3 : 4 : 5-*Trimethoxyphenacyl Bromide*.—Diazotrimethoxyacetophenone (10 g.) was decomposed by dry HBr in cold Et_2O; the product crystallised from Et_2O–light petroleum in colourless compact rhombohedra, m. p. 51—52° (Found : Br, 27·5. $C_{11}H_{13}O_4Br$ requires Br, 27·7%).

3 : 4 : 5-*Trimethoxyphenyl* 3 : 4 : 5-*Trimethoxyphenacyl Ether* (II).—Solutions of antiarol (1·7 g.) in NaOH aq. (0·38 g. in 20 c.c.) and of trimethoxyphenacyl bromide (2·75 g.) in acetone (20 c.c.) were gently heated for 1 hr. and then the acetone was removed by distillation. The product, after solidifying, crystallised from EtOH (charcoal) in colourless rhombohedra (1·45 g.), m. p. 135—136° (Found : C, 61·1; H, 6·1. $C_{20}H_{24}O_8$ requires C, 61·2; H, 6·1%).

4 : 5 : 6 : 3′ : 4′ : 5′-*Hexamethoxy*-3 : 3-*diphenylcoumaran* (IV).—This substance was obtained from the foregoing by dehydration in hot C_6H_6 by means of P_2O_5; it crystallised from EtOH in colourless slender needles, m. p. 112—113° (Found : C, 68·5; H, 6·4. $C_{26}H_{28}O_7$ requires C, 69·0; H, 6·2%).

Direct evidence of the presence of C_6H_6 in this specimen could not be obtained and thus the hypothesis that it is the coumarone with 1 C_6H_6 is excluded. The formation of the substance is evidently the result of attack of a benzene molecule by the carbonyl of the phenacyl ether.

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