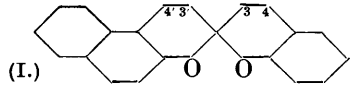
CXXIV.—*Styrylpyrylium Salts. Part XI. The Determination of the Reactive Group in Ketones of the Type* $CH_3 \cdot CO \cdot CH_2R$ *by Means of the Benzo-β-naphtha*spiro*pyran Colour Change.*

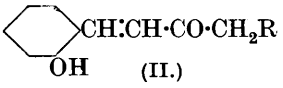
By Isidor Morris Heilbron and Francis Irving.

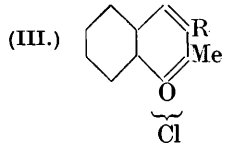
It is generally accepted that in aldehyde–ketone condensations in which the ketone contains both a methyl and a methylene group the former or the latter is reactive according as an alkali or an acid is used as the condensing agent (compare Goldschmiedt and Knöpfer, *Monatsh.*, 1897, **18**, 437; 1898, **19**, 406; Harries and Müller, *Ber.*, 1902, **35**, 966; Harries and Bromberger, *ibid.*, p. 3088; Auwers, *Ber.*, 1912, **45**, 2764). For instance, from salicylaldehyde and a ketone of the type $CH_3 \cdot CO \cdot CH_2R$ alkali condensation would produce (II), from which (IV) is obtained by the action of hydrogen chloride, isomeric with (III) formed by direct acid condensation (compare Decker and Fellenberg, *Annalen*, 1909, **364**, 1).

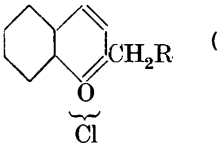
By further condensation of (III) and (IV) with 2-naphthol-1-

aldehyde, the isomeric 3- and 3′-substituted benzo-β-naphtha*spiro*pyrans are respectively obtained (I).

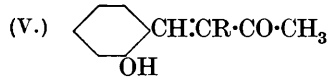


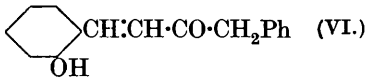




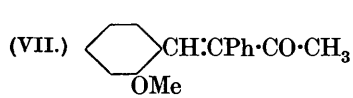


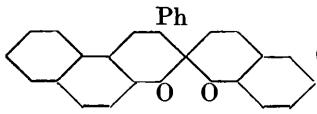
It has been shown that, whereas benzo-β-naphtha*spiro*pyrans substituted in the 3-position ionise on being heated in inert solvents, giving coloured solutions, the isomeric 3′-substituted compounds fail to show this phenomenon (Dickinson and Heilbron, J., 1927, 1699). This reaction can therefore be utilised in deciding between the structures (II) and (V), and affords a readier method than the oxidation and reduction reactions used previously (compare Goldschmiedt and Krczmar, *Monatsh.*, 1901, **22**, 659; Harries and Müller, *loc. cit.*; Harries and Bromberger, *loc. cit.*; Stoermer and Wehln, *Ber.*, 1902, **35**, 3549; Gheorghiu and Arwentiew, *J. pr. Chem.*, 1928, **118**, 295).





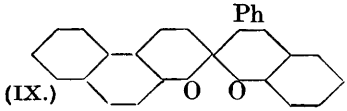
In order to illustrate this method for the determination of structure we have again examined the ketone obtained by Dickinson (J., 1926, 2234), by condensing salicylaldehyde with benzyl methyl ketone in presence of piperidine. This compound (A) was regarded as 2-hydroxystyryl benzyl ketone (VI), since its methyl derivative was not identical with the *ketone* (B) prepared by condensing *o*-methoxybenzaldehyde with benzyl methyl ketone by means of hydrogen chloride, which from analogy with known reactions was designated 2-methoxy-α-phenylstyryl methyl ketone (VII).



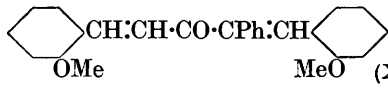


We have now prepared the phenylbenzo-β-naphtha*spiro*pyran from (A) and find that it develops a purple colour in boiling xylene and other higher-boiling inert solvents, and also that it differs in melting point from the isomeric, non-ionising *spiro*pyran obtained by Dilthey, Berres, Hölterhoff, and Wübken (*J. pr. Chem.*, 1926, **114**,

179). From its method of preparation the latter compound must have the structure (VIII), and consequently the *spiro*pyran derived from (A) must be 3-*phenylbenzo*-β-*naphtha*spiro*pyran* (IX).



(IX.)



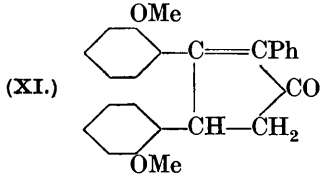
(X.)

The same compound is obtained by condensing the pyrylium salt (III; R = Ph), prepared from salicylaldehyde and benzyl methyl ketone, with 2-naphthol-1-aldehyde. The effect of piperidine is thus, contrary to Dickinson's contention (*loc. cit.*), identical with that of hydrogen chloride in inducing activation of the methylene group in benzyl methyl ketone in preference to the methyl radical. A similar and equally unexpected reaction has recently been recorded by Lovett and Roberts (J., 1928, 1975) in the case of ω-phenylacetylacetophenone and salicylaldehyde, whereby the methylene next to the phenyl group is activated.

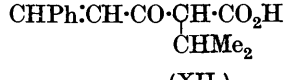
As a direct consequence of the above proof, it follows that the ketone (A) must be represented by formula (VII) and hence (B) must have some other constitution. This compound (m. p. 145°) has again been investigated in greater detail, and it has been found, as shown in the following table, that analytical values alone are insufficient evidence of structure.

Aldehyde + Ketone		−Water.	Mol. formula.	Mol. wt.	% C.	% H.	% OMe.
(*a*) 1 mol.	1 mol.	1 mol.	$C_{17}H_{16}O_2$	252	80·9	6·4	12·3
(*b*) 2 mols.	1 mol.	2 mols.	$C_{25}H_{22}O_3$	370	81·1	5·95	16·8
(*c*) 1 mol.	2 mols.	1 mol.	$C_{26}H_{26}O_3$	386	80·8	6·7	8·0

Recourse has now been made to the determination of both molecular weight and methoxyl content, and satisfactory proof provided that (B) has actually been formed according to reaction (*b*). It is doubtful, however, whether substance (B) is the normal distyryl ketone (X), as an isomeric *compound*, m. p. 180°, has been obtained by direct condensation, by means of hydrogen chloride, of the aldehyde and the ketone in the requisite molecular proportion. These two compounds may be stereoisomerides, or one of them (probably B) may have a *cyclo*pentenone structure such as (XI) (compare Japp and Maitland, J., 1904, **85**, 1473).



(XI.)



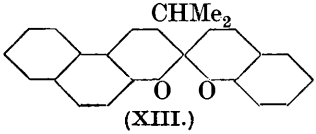
(XII.)

The application of the *spiro*pyran colour reaction has thus led to definite conclusions regarding the structure of these ketones.

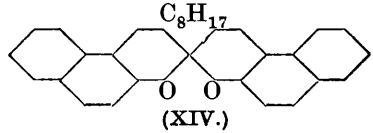
The rule that condensation involves the methyl group or the methylene group according as alkali or hydrogen chloride is used is not without exceptions. Stoermer and Wehln (*loc. cit.*) have shown that the condensation of benzaldehyde with phenoxyacetone invariably occurs at the methylene group. On the other hand, Gheorghiu and Arwentiew (*loc. cit.*) found that with methyl *iso*butyl ketone and benzaldehyde the use of either alkali or hydrogen chloride gave rise to styryl *iso*butyl ketone, the structure of which they proved by oxidation to benzoic and *iso*valeric acids. We have added the final proof by synthesising this compound from *iso*propylacetoacetic ester: by condensation with benzaldehyde in presence of alkali, *γ-benzylidene-α-isopropylacetoacetic acid* (XII) was obtained (compare Ryan and Shannon, *Proc. Roy. Irish Acad.*, 1924, **36**, B, 322); this, on being heated with copper powder, readily gave styryl *iso*butyl ketone, the semicarbazone of which gave no depression in melting point when mixed with that obtained from the alkali condensation product.

We have also been able to confirm the changes in colour of the semicarbazone under the influence of light noted by Gheorghiu and Arwentiew (*loc. cit.*). This case adds a further interesting example to the phenomenon of " reversed phototropy " originally observed by Heilbron and Wilson (J., 1914, **105**, 2892).

Methyl *iso*butyl ketone has now been condensed with salicylaldehyde in presence of alkali, and the resultant *2-hydroxystyryl isobutyl ketone* converted into 3′-iso*propylbenzo-β-naphtha*spiro*pyran* (XIII), this structure being confirmed by the inability of the compound to acquire colour in high-boiling solvents. The same *spiro*pyran has been obtained by the condensation of salicylaldehyde



(XIII.)



(XIV.)

with methyl *iso*butyl ketone in presence of hydrogen chloride, followed by the condensation of the pyrylium salt with 2-naphthol-1-aldehyde and subsequent hydrolysis. This reaction affords independent proof that methyl *iso*butyl ketone condenses with aldehydes at the methyl radical whether acid or alkali is used as catalyst.

*3′-Octylbenzo-β-naphtha*spiro*pyran* has been prepared from 2-hydroxystyryl nonyl ketone (Heilbron and Irving, J., 1928, 2323) and in conformity with the general rule fails to show colour development. On the other hand, *3-octyldi-β-naphtha*spiro*pyran* (XIV) reacts normally, giving a purple colour in xylene.

The preparation of benzo-β-naphtha*spiro*pyrans by first condensing the ketone with salicylaldehyde by means of hydrogen chloride and then adding 2-naphthol-1-aldehyde to the solution of the pyrylium salt is usually difficult. Frequently the corresponding di-β-naphtha*spiro*pyran alone is isolated; probably the salicylaldehyde forms in the first place the 2-hydroxystyrylbenzopyrylium salt, leaving half the ketone free to react with the other aldehyde. The use of low temperature (−5° or −10°) in carrying out the first stage is beneficial.

We have failed to find any relation between the readiness with which the *spiro*pyrans are transformed to pyrylium salts and the development of the colour change as suggested by Dilthey and Wübken (*Ber.*, 1928, **61**, 963; compare also Dickinson, Heilbron, and O'Brien, J., 1928, 2077). Whereas (XIII) fails to give evidence of ion formation even in boiling diphenyl ether, 3-iso*propyldi*-β-*naphtha*spiro*pyran* gives a purple solution in boiling xylene. Both substances, however, give marked pyrylium salt colorations in glacial acetic acid.

EXPERIMENTAL.

3-*Phenylbenzo*-β-*naphtha*spiro*pyran* (IX).—(1) A solution of 2-hydroxy-α-phenylstyryl methyl ketone (compound A, 1·5 g.) and 2-naphthol-1-aldehyde (1 g.) in absolute alcohol (15 c.c.) was saturated with dry hydrogen chloride. After a short time, the separated pyrylium salt was dissolved in aqueous acetone and hydrolysed with the minimum amount of dilute ammonia solution, giving the *spiro*pyran, which was recrystallised from acetone and then from benzene.

(2) A cold solution of salicylaldehyde (2 g.) and benzyl methyl ketone (2·2 g.) in absolute alcohol (5 c.c.) was slowly saturated with dry hydrogen chloride. The mixture was kept at 0° for a few hours, and a solution of 2-naphthol-1-aldehyde (3 g.) in absolute alcohol (10 c.c.) then added. More hydrogen chloride was passed in and after standing in the cold for a few hours the separated pyrylium salt was treated in the manner described above.

The pure spiro*pyran* forms colourless crystals melting at 208—209° to a purple liquid which loses its colour on cooling. A colourless solution of the compound in cold xylene becomes faintly coloured on heating. A more pronounced colour change is visible in higher-boiling solvents; in nitrobenzene, for example, a strong reddish-blue colour is produced (Found : C, 86·5; H, 5·0. $C_{27}H_{18}O_2$ requires C, 86·6; H, 4·8%). The isomeric 3′-phenylbenzo-β-naptha*spiro*pyran has m. p. 147—148° (Dilthey, Berres, Hölterhoff, and Wübken, *loc. cit.*).

Compound B (m. p. 145°).—This compound was prepared accord-

ing to Dickinson's method (*loc. cit.*). The product failed to decolorise a solution of bromine in chloroform, and dissolved in concentrated sulphuric acid to give a yellow solution which darkened slightly on long standing [Found: C, 81·05, 81·0; H, 6·0, 6·0; MeO, 15·4; *M* (Menzies), 387, 378, 390. $C_{25}H_{22}O_3$ requires C, 81·1; H, 5·95; MeO, 16·8%; *M*, 370].

The Isomeric Compound, m. p. 180° (X ?).—A solution of *o*-methoxybenzaldehyde (5 g.) and benzyl methyl ketone (2·5 g.) in absolute alcohol (40 c.c.) was slowly saturated with dry hydrogen chloride at −5°. After standing for 4 hours at 0°, the solution was poured into water and neutralised with sodium carbonate, and the product extracted with ether. The ethereal solution was dried and the residue, after removal of solvent, taken up in hot alcohol. The crude *ketone* which separated on cooling was recrystallised from ethyl acetate, giving pale yellow rhombs, m. p. 180°, which dissolved in concentrated sulphuric acid to a cherry-red solution (Found: C, 80·7; H, 5·9; MeO, 16·5. $C_{25}H_{22}O_3$ requires C, 81·1; H, 5·95; MeO, 16·8%).

γ-Benzylidene-α-isopropylacetoacetic Acid (XII).—A suspension of benzaldehyde (7 g.) and *iso*propylacetoacetic ester (10 g.) in water (200 c.c.) was shaken for 11 days and during this period six portions (each of 5 c.c.) of 8% sodium hydroxide solution were added. Unchanged material was then removed by means of ether, and the aqueous portion acidified with acetic acid. The pure *acid* separated from dilute alcohol in colourless crystals, m. p. 134° (decomp.), readily soluble in the usual organic solvents (Found: C, 72·6; H, 7·1; *M*, 245. $C_{14}H_{16}O_3$ requires C, 72·4; H, 6·9%; *M*, 232).

Styryl iso*Butyl Ketone Semicarbazone*.—γ-Benzylidene-α-*iso*propylacetoacetic acid (2 g.) was heated in presence of copper powder at 130—140° for 1½ hours. The oil obtained was dissolved in alcohol, and the semicarbazone prepared directly from the solution in the usual manner. After recrystallisation from alcohol, the pure substance melted at 167° and was found by means of a mixed m. p. determination to be identical with the semicarbazone obtained by Gheorghiu and Arwentiew (*loc. cit.*).

2-*Hydroxystyryl* iso*Butyl Ketone*.—To a solution of salicylaldehyde (12·2 g.) and methyl *iso*butyl ketone (10 g.) in alcohol (100 c.c.), sodium hydroxide (60 c.c. of 20% solution) was added. After 5 days, the dark red solution was nearly neutralised with acetic acid and diluted with an equal volume of water, and the product precipitated with carbon dioxide. The *ketone* crystallised from methyl alcohol (with freezing) in yellow rhombs, m. p. 104° (Found: C, 76·3; H, 7·9. $C_{13}H_{16}O_2$ requires C, 76·5; H, 7·8%).

3′-iso*Propylbenzo-β-naphtha*spiro*pyran* (XIII).—(1) A solution

of 2-hydroxystyryl *iso*butyl ketone (2 g.) and 2-naphthol-1-aldehyde (1·7 g.) in absolute alcohol (17 c.c.) was slowly saturated with dry hydrogen chloride and kept at 0° for 1 day. The pyrylium salt obtained was treated with dilute ammonia solution in presence of ether until the colour was discharged. The dry ethereal solution was evaporated, and the *spiro*pyran obtained from the oily residue by freezing and scratching in presence of a small quantity of acetone and methyl alcohol. Recrystallisation from a mixture of equal volumes of these solvents gave faintly yellow rhombs, m. p. 118°.

(2) A solution of salicylaldehyde (1 g.) and methyl *iso*butyl ketone (0·8 g.) in absolute alcohol (4 c.c.) was slowly saturated with dry hydrogen chloride at −10°. The mixture was kept at 0° for 15 hours to allow the primary condensation to reach completion; a solution of 2-naphthol-1-aldehyde (1·7 g.) in alcohol was then added and the whole again saturated with hydrogen chloride. The pyrylium salt, which separated after standing in the cold for 24 hours, was treated as described under (1), the same spiro*pyran* being obtained. The compound gave colourless solutions in boiling veratrole and diphenyl ether and dissolved in glacial acetic acid to a deep red solution (Found: C, 84·6; H, 6·2. $C_{24}H_{20}O_2$ requires C, 84·7; H, 5·9%).

3-iso*Propyldi*-β-*naphtha*spiro*pyran*.—A solution of 2-naphthol-1-aldehyde (3·4 g.) and methyl *iso*butyl ketone in absolute alcohol (30 c.c.) was saturated with a slow stream of dry hydrogen chloride. The deep blue solution was kept over-night at 0° and the separated pyrylium salt was then dissolved in aqueous acetone and treated with sufficient dilute ammonia solution to discharge the colour. The product on recrystallisation from benzene formed colourless prisms which melted to a purple liquid at 204° (Found: C, 86·0; H, 5·9. $C_{28}H_{22}O_2$ requires C, 86·1; H, 5·6%). Solutions in cold xylene or veratrole are colourless, but become purple at the boiling point. The spiro*pyran* dissolves in glacial acetic acid, forming a blue solution of the pyrylium salt.

3′-*Octylbenzo*-β-*naphtha*spiro*pyran*.—A solution of 2-hydroxystyryl nonyl ketone (1·5 g.) and 2-naphthol-1-aldehyde (1 g.) in absolute alcohol (15 c.c.) was saturated with dry hydrogen chloride and maintained at 0° for 2 days. The pyrylium salt which had then separated was suspended in ether and treated with sufficient dilute ammonia solution to remove the colour. The ethereal layer was evaporated and the product recrystallised from aqueous acetone, colourless needles being obtained, m. p. 101—102°. Solutions of the compound in boiling xylene or boiling diphenyl ether remained colourless (Found: C, 84·8; H, 7·2. $C_{29}H_{30}O_2$ requires C, 84·9; H, 7·3%).

3-*Octyldi*-β-*naphtha*spiro*pyran* (XIV).—A solution of methyl nonyl ketone (1 g.) and 2-naphthol-1-aldehyde (2 g.) in absolute alcohol (15 c.c.) was saturated with dry hydrogen chloride and kept at 0° for 2 days. The separated pyrylium salt was dissolved in aqueous acetone, and the solution treated with sufficient dilute aqueous ammonia to effect hydrolysis. The *product* was recrystallised from benzene, giving colourless needles, m. p. 157° (Found : C, 85·9; H, 7·2. $C_{33}H_{32}O_2$ requires C, 86·1; H, 7·0%). Its solution in xylene was colourless in the cold, but became purple on boiling; the colour disappeared when the solution was cooled.

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