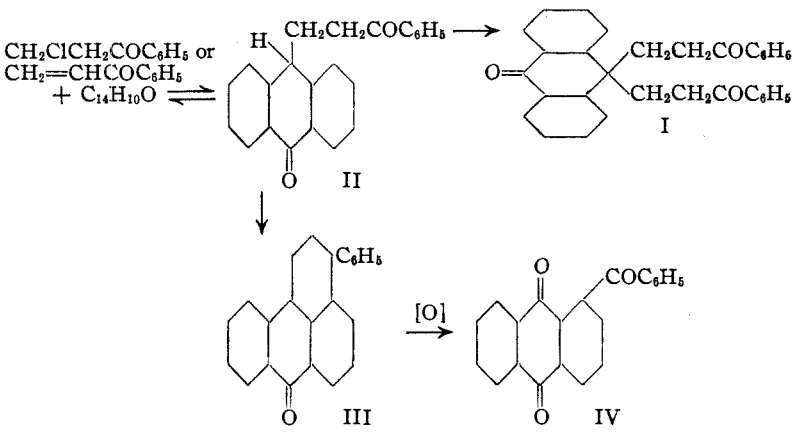
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF MCGILL UNIVERSITY]

Addition Reactions of Vinyl Phenyl Ketone. V. Anthrone

BY C. F. H. ALLEN AND S. C. OVERBAUGH

In the previous paper in this series[1] a number of trimolecular products, resulting from the addition of various substances containing nitrogen to vinyl phenyl ketone, were described. Anthrone also forms a trimolecular product (I), but by careful manipulation it is possible to isolate the primary substance (II) composed of one molecule of each substance. Both (I) and (II) are oxidized to anthraquinone and benzoic acid, and (II) adds two molecules of methylmagnesium iodide without evolution of gas, indicating the presence of two carbonyl groups.

The addition, to form (II), takes place very quickly in 70% sulfuric acid; if the action is prolonged or more concentrated acid used, ring-closure takes place and Bz-1-phenylbenzanthrone (III) is produced.



The latter can be obtained directly from the components without isolation of the intermediate. The position of the phenyl group in (III) is confirmed by the production of α-benzoylanthraquinone on oxidation.

The preparation of Bz-1-phenylbenzanthrone by two general methods is covered by numerous patents, but most of the intermediates have not been described elsewhere. In the first method[2] of which the preparation described above is an example, the intermediate (II) was not obtained but only "a condensation product," m. p. 186°,[3] which from the data given is obviously the trimolecular product (I). In our work, better yields were secured by the second method[4] and the manipulations involved were simpler. By this procedure, anthrone and cinnamic aldehyde are condensed, with or without the isolation of the intermediate cinnamalanthrone.[5]

The mechanism of the formation of benzanthrones from anthrones has been considered to be similar to the Skraup quinoline synthesis, which takes place under identical conditions. The two methods of preparation described in this paper and which lead to the same product, suggest that with aldehydes the process involves 1,2-addition to the carbonyl group, whereas with ketones 1,4-addition occurs.

In support of the first mechanism, Bally and Scholl[6] suggested that the first step was an aldol condensation, followed by dehydration. The last step, dehydrogenation, was, doubtless, brought about by some component of the mixture, since the yield of benzanthrone was only 50–60%; this indicated that the dihydrobenzanthrone itself may have acted as a hydrogen acceptor in the last step. This series of reactions resembles the older mechanism for the Skraup synthesis. It is supported by the production of Bz-1-phenylbenzanthrone (III) from cinnamic aldehyde and anthrone for the following reasons. The presence of the phenyl group in the Bz-1-position would be anticipated if an aldol condensation had taken place (barring a molecular rearrangement). The isomeric Bz-3-phenylbenzanthrone is known and

(1) Allen and Bell, *Can. J. Res.*, **11**, 40 (1934).

(2) English Patent 268,830, *Chem. Abs.*, **22**, 1366 (1928); English Patent 286,685, *ibid.*, **23**, 1138 (1929); French Patent 631,995, *Chem. Zentr.*, **99**, I, 2210 (1928); German Patent 552,269, *ibid.*, **103**, II, 2736 (1932); Nakanishi, *Proc. Imp. Acad.* (Tokyo), **9**, 394 (1933), no experimental details.

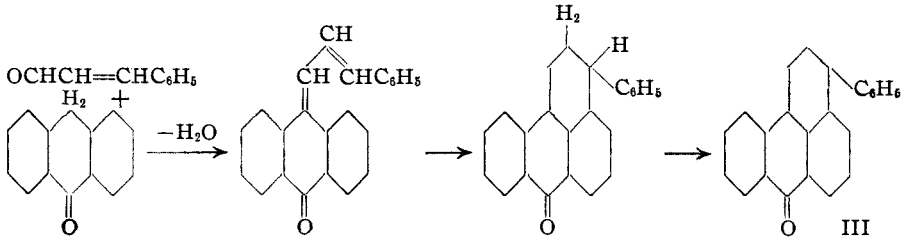
(3) German Patent 488,608, *Chem. Zentr.*, **101**, II, 3860 (1930).

(4) U. S. Patent 1,713,571, *Chem. Abs.*, **23**, 3479 (1929); U. S. Patent 1,736,061, *ibid.*, **24**, 628 (1930); U. S. Patent 1,749,519, *ibid.*, **24**, 2148 (1930); Swiss Patent 126,579, *Chem. Zentr.*, **100**, I, 447 (1929); Swiss Patent 127,033, *ibid.*, **100**, I, 146 (1929); Swiss Patent 133,994, *ibid.*, **101**, I, 1373 (1930).

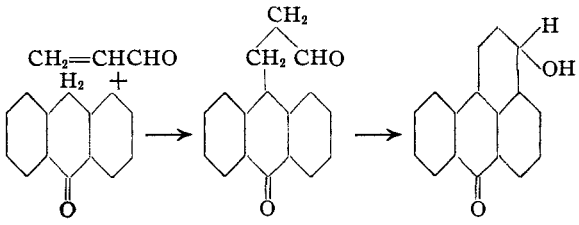
(5) U. S. Patent 1,713,590, *ibid.*, **100**, II, 1073 (1929); English Patent 297,129, *ibid.*, **100**, I, 447 (1929).

(6) Bally and Scholl, *Ber.*, **44**, 1656 (1911).

is different.[7] The tendency of groups in the Bz-ring to shift is always to the 2-position.



In suggesting the second mechanism, Meerwein[8] proposed a process involving 1,4-addition of anthrone to the unsaturated aldehyde, because he found that anthrone added in such a manner to several α,β-unsaturated compounds; he was unable, however, to secure such a substance with the available aldehydes. This series of reactions represents the at present generally accepted mechanism for the Skraup reaction.[9]



A great variety of α,β-unsaturated compounds has been mentioned in the patents, as reacting with anthrones to form benzanthrones, the suggested mechanism being addition to the conjugated system, followed by ring closure. Our work confirms this, since the primary product was isolated, as described above. This is of interest in view of the fact that certain of the patent claims could not be confirmed by other investigators.[10]

The Grignard reagent acts upon Bz-1-phenylbenzanthrone as on benzanthrone itself[11] with the production of ketones, having the substituent group in position 4, further instances of 1,4-addition involving a benzene ring. The structure of five of the ketones was carefully determined. Benzylmagnesium chloride gave 4-benzyl-(Bz-1-phenyl)-benzanthrone (V), which was oxidized to the known 1,4-dibenzoylanthraquinone (VI). Ethyl, *n*-butyl, *n*-hexyl, β-styryl, cyclohexyl and β-phenylethylmagnesium halides gave 4-substituted derivatives; the structures of the first four were determined by oxidation to the keto acid (IX). Usually the intermediate benzoylanthraquinone (VIII) was isolated. It was found impossible to oxidize the ketone from phenylmagnesium bromide; the phenyl group in position 4 apparently stabilized the Bz-ring so that it was not attacked by the reagents.

As in the case of benzanthrone, *t*-butylmagnesium chloride gave a carbinol (X) (1,2-addition). Oils only resulted from the action of methyl, *n*-heptyl and *i*-propylmagnesium halides.

Experimental

Preparation of Bz-1-phenylbenzanthrone (III). (First Method.)—When anthrone and β-chloropropiophenone were heated with 70% sulfuric acid, hydrogen chloride was evolved rapidly and the liquid soon solidified. The solid was a mixture of the bimolecular and trimolecular addition products. Only the latter was obtained when two equivalents of the ketone were used. It was impossible to confine the addition and secure only the bimolecular product. Preliminary attempts to bring about the reaction using an alkaline catalyst gave traces of the trimolecular product, but large quantities of dianthrone, even when air was excluded.

The structures of the substances were shown by formation of only anthraquinone and benzoic acid on oxidation, indicating that all side chains were on the *meso* carbon atoms. Bromination of the bimolecular product gave anthraquinone; presumably a little hydrogen bromide present caused the reversal of the addition reaction, as was observed previously with the addition product from anthrone and benzalacetophenone. With hydroxylamine the trimolecular product gave a dioxime; as it is well known that anthrones do not form oximes by the usual methods, in this instance the oximino groups are presumably on the two side chains. The bimolecular product gave a small amount of the same dioxime, owing to its ready reversibility into its components.

The bimolecular product was easily cyclicized by 80% sulfuric acid, to give Bz-1-phenylbenzanthrone; the latter could also be obtained from the components above by a longer period of heating.

A mixture of 12 g. of anthrone and 10 g. of β-chloropropiophenone in 50 cc. of 70% sulfuric acid was heated in a boiling water-bath with constant stirring; the oily

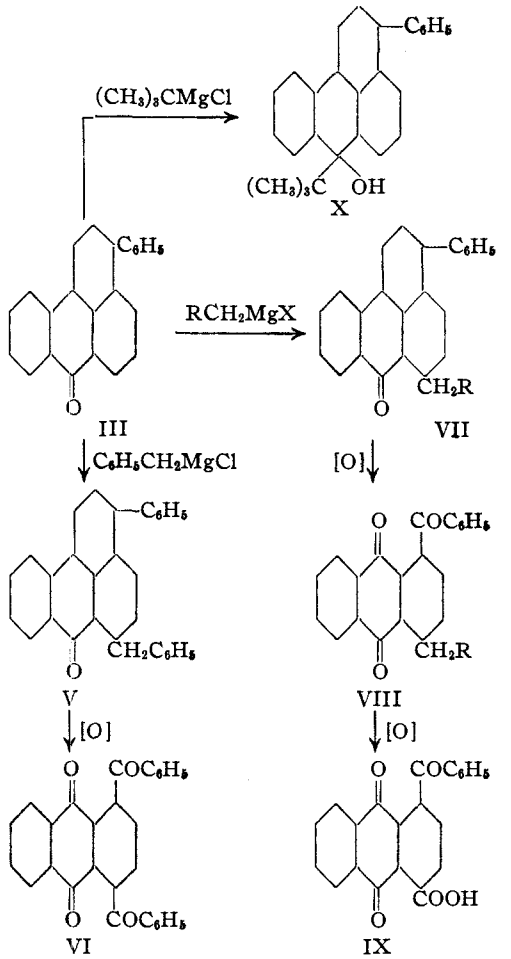
(7) German Patent 552,269, *Chem. Zentr.*, **103**, II, 2736 (1932).

(8) Meerwein, *J. prakt. Chem.*, **97**, 235 (1918).

(9) Unfortunately, many textbooks, even in the later editions, still include the older mechanism, which has been rendered extremely improbable by the work of C. Beyer, *J. prakt. Chem.*, [2] **33**, 424 (1886); v. Miller, *Ber.*, **25**, 2072 (1892); Blaise and Maire, *Bull. soc. chim.*, [4] **3**, 671 (1908); König, *Ber.*, **56**, 1853 (1923).

(10) Gagnon and Gravel, *Can. J. Res.*, **8**, 600 (1933); Vachon, Gagnon and Kane, *Can. J. Res.*, **11**, 644 (1934).

(11) Allen and Overbaugh, THIS JOURNAL, **57**, 740 (1935).



layer quickly gave off hydrogen chloride (four to five minutes) and after a further five to ten minutes solidified; longer heating gave the cyclic ketone. The reddish solid was triturated with water, boiled with 25 cc. of methanol, filtered hot and washed with the same solvent. It was dissolved in a minimum of boiling benzene; on cooling to 40° the trimolecular product (I) separated, was filtered and recrystallized from benzene (3 cc. per g.). The yield was 4 g. (15%). It formed colorless plates, m. p. 187–188°. It is slightly soluble in benzene, acetic acid and chloroform, but insoluble in alcohol; it gives a yellow solution with concentrated sulfuric acid.

The original filtrate deposited 12 g. (63%) of the bimolecular product (II) on standing; it was best recrystallized from acetic acid, but the melting point was never sharp; the analytical sample melted over the range 141–144°. On warming with 70% sulfuric acid and an equivalent of β-chloropropiophenone for five to ten minutes, it gave the trimolecular product.

Anal. Calcd. for $C_{23}H_{18}O$: C, 84.6; H, 5.5. Found: C, 84.5; H, 5.8. Calcd. for $C_{32}H_{26}O$: C, 83.8; H, 5.7. Found: C, 84.1; H, 5.8.

When 0.25 g. of II in 15 cc. of methanol containing 2 drops of 20% aqueous sodium hydroxide was allowed to stand a solid slowly separated; this was found to be the trimolecular product.

Oxidation.—To a boiling solution of 0.5 g. of the substance in 7 cc. of acetic acid was added, in small portions, a slight excess of a solution of chromium trioxide in 50% acetic acid; after five minutes of further refluxing the anthraquinone was precipitated by the addition of water. It was identified by melting point, mixed melting point, and the formation of a red vat with alkali and zinc dust. Sulfuric acid (2 cc.) was added to the filtrate, and the benzoic acid extracted with ether and identified in the usual manner. The oxidation products are the same with the bi- and trimolecular products.

Dioxime.—The trimolecular product was treated with hydroxylamine acetate in the usual manner; colorless rods separated on cooling after twenty minutes of refluxing. They were recrystallized from alcohol; m. p. 244–245°.

Anal. Calcd. for $C_{32}H_{29}O_3N_2$: N, 5.7. Found: N, 5.8.[12]

The bimolecular product gave an oil from which the same dioxime was separated.

Action of Bromine.—A chloroform solution of II decolorized bromine rapidly, and a gum was left on evaporation. On warming with alcohol, yellow crystals of anthraquinone separated and were identified as above. A similar behavior was exhibited by the homolog formed by the addition of anthrone to benzalacetophenone.[13]

Ring Closure.—A mixture of 10 g. of the bimolecular product and 100 g. of 80% sulfuric acid was heated, with stirring, in a boiling water bath for twenty-five minutes. The resulting thick oil was chilled, washed by decantation, and triturated with water; the solid was filtered, boiled with 25 cc. of methanol, filtered, and the insoluble substance dissolved in the minimum of acetic acid. On cooling, the Bz-1-phenylbenzanthrone separated in rosets of yellow needles, which, after recrystallization, melted at 182–183°. The yield was 4.2 g. (50%). *Anal.* Calcd. for $C_{23}H_{14}O$: C, 90.2; H, 4.6. Found: C, 89.9; H, 4.4.

(**Second Method.**)—Equal weights (50 g. each) of cinnamic aldehyde and anthrone and 25 g. of α-chloronaphthalene were heated in an oil-bath to 250° over a period of twenty minutes; at about 185° steam was evolved. The mixture was heated a further one and a third hours at 250–260°, transferred to a flask fitted for steam distillation, and the solvent removed by steam. The water was decanted from the cooled residue and the solid dissolved in 100 cc. of boiling butyl alcohol. As soon as the solution was sufficiently cool, 25 cc. of acetone was added, and after several hours the crystalline product was filtered, washing 5 or 6 times with 25-cc. portions of acetone to remove the dark color. The yield of product, m. p. 178–180°, from several runs was 30–38 g. It was used directly in most reactions; it recrystallized well from chlorobenzene (5 cc. per g.) or *p*-cymene (3 cc. per g.). On long standing, the filtrate deposited a solid, largely dianthrone (10 g. from a typical run, on recrystallization). The yield of Bz-1-phenylbenzanthrone, based on anthrone not recovered as dianthrone, was 50–60%.

The structure was shown by the production of α-benzoylanthraquinone on oxidation by chromic acid in acetic acid in the usual manner. After refluxing for a half

(12) A dioxime of the bimolecular product would have contained 7.9% nitrogen.

(13) The last reaction was investigated by Dr. F. B. Wells in this Laboratory in 1931.

TABLE I

PROPERTIES OF SUBSTITUTED Bz-1-PHENYLBENZANTHRONES

No.	VII, R =	Yield, %	Solvent for purification	M. p., °C.	Formula	Calcd., % C	Calcd., % H	Found, % C	Found, % H
XI	C_2H_5	35	Alcohol[b]	120–122	$C_{25}H_{18}O$	89.8	5.4	89.6	5.7
XII	n-C_4H_9	53	Acetone, 2 pts.	81–82	$C_{27}H_{22}O$	89.5	6.1	89.4	6.0
XIII	n-C_6H_{13}	47	Methanol, 3 pts.[c]	88	$C_{29}H_{26}O$	89.2	6.7	89.2	6.6
XIV	Cyclohexyl	22	Acetic acid[b]	190–191	$C_{29}H_{24}O$	89.7	6.2	89.5	6.2
XV	C_6H_5	45	Acetic acid[b]	223–224	$C_{29}H_{18}O$	91.1	4.7	91.4	4.8
XVI	$C_6H_5CH_2$	19	Acetic acid[b]	179–180	$C_{30}H_{20}O$	90.9	5.1	91.1	5.1
XVII	$C_6H_5CH_2CH_2$	51	Acetic acid[b]	154–155	$C_{31}H_{22}O$	90.7	5.4	90.9	5.4
XVIII	$C_6H_5CH{=}CH$[a]	6	Acetic acid[b]	186–187	$C_{31}H_{20}O$	91.2	4.8	90.9	4.9
X	t-C_4H_9	10	Acetic acid[b]	159–160	$C_{27}H_{24}O$	89.0	6.6	88.6	6.4

[a] Decolorized bromine instantly. [b] Plates. [c] Needles.

TABLE II

PROPERTIES OF 4-SUBSTITUTED α-BENZOYLANTHRAQUINONES

No.	VIII, R =	M. p., °C.	Crystal form	Formula	Calcd., % C	Calcd., % H	Found, % C	Found, % H
XIX	C_2H_5	198	Needles	$C_{23}H_{16}O_3$	81.2	4.7	81.2	5.0
XX	n-C_4H_9	123–124	Needles	$C_{25}H_{20}O_3$	81.5	5.4	81.0	5.5
XXI	n-C_6H_{13}	128	Rods	$C_{27}H_{24}O$	81.8	6.1	81.8	6.4

hour, the solution was diluted with five volumes of water and allowed to stand. The product (0.8 g. from 0.9 g. of the cyclic compound) was filtered, recrystallized, and identified by comparison with an authentic specimen.[14]

Reactions of the Grignard Reagents with Bz-1-phenylbenzanthrone.—These reactions were carried out essentially as described in the first paper,[15] using Grignard reagents containing the following radicals: ethyl, n-butyl, n-hexyl, benzyl, phenyl, cyclohexyl, β-styryl, β-phenylethyl, t-butyl. The t-butyl gave a carbinol as before; all the others gave ketones, the properties of which are summarized in Table I. Oils only resulted with methyl, n-heptyl, and i-propylmagnesium halides. The carbinol gave a deep green color with concentrated sulfuric acid, but all the ketones gave deep red solutions. In the Grignard machine, the ketones showed one addition and no active hydrogen, but the carbinol, the reverse; unfortunately, the reaction products were amorphous as in the previous paper.

The benzanthrones do not give 4-phenylbenzanthrones when treated by Fuson's[16] method, only halochromic salts being obtained.

Oxidation of the Disubstituted Benzanthrones.—This reaction was carried out as described in the previous paper for 4-benzylbenzanthrone. On dilution after a half hour, 4-benzyl-Bz-1-phenylbenzanthrone (XVI) gave 1,4-dibenzoylanthraquinone, identified by mixed melting point, β-styryl (XVIII) gave the acid IX, while the other ketones gave 4-alkyl-1-benzoylanthraquinones. The latter were again oxidized by refluxing for two hours a mixture of 0.15 g. of the substance, 0.75 g. of chromium trioxide, 8 cc. of acetic acid and 2 cc. of water, and isolated by diluting and allowing to stand. The precipitate was filtered, dissolved in dilute ammonium hydroxide and converted into the silver salt. The latter was then refluxed with 4 cc. of methyl iodide for two hours, and the residue, after evaporation of the excess iodide, warmed with 2 cc. of chloroform; the solution was decanted, evaporated nearly to dryness, and methanol added. In each case, the same methyl ester of 4-benzoylanthraquinone-1-carboxylic acid was obtained, and on comparison with an authentic sample, m. p. 184–185°, the mixed melting point was not depressed. The properties of the substituted ketones are given in Table II; all were recrystallized from acetic acid. They all gave yellow solutions in concentrated sulfuric acid, which turned green on the addition of copper powder, the color changing to violet on dilution.

The 4-phenyl-Bz-1-phenylbenzanthrone (XV) was very resistant to oxidation. It was not attacked by alkaline permanganate; chromium trioxide or nitric acid (sp. gr. 1.1) in a sealed tube at 180° for five hours, gave dark, amorphous products.

This work has been assisted by a generous grant from the Cyrus M. Warren Fund of the American Academy of Arts and Sciences.

Summary

Bz-1-phenylbenzanthrone is obtained either by ring closure of the bimolecular product resulting from the addition of anthrone to vinyl phenyl ketone, or directly by interaction of anthrone and cinnamic aldehyde.

The different mechanisms involved are discussed, with reference to the Skraup synthesis as applied to benzanthrone formation.

The action of Grignard reagents is similar to that of benzanthrone, ketones resulting with all except t-butylmagnesium chloride, which again gave an alcohol.

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(14) This was kindly prepared by Miss Margaret R. Gilbert.

(15) Although both benzanthrone and Bz-1-phenylbenzanthrone add but one equivalent of Grignard reagent, as shown by quantitative measurements in the machine, the best yields result when a large excess is used. This is to be expected by analogy with similar cases involving open chain conjugated systems. Kohler and Peterson [THIS JOURNAL, **55**, 1073 (1933)].

(16) R. C. Fuson, D. B. Black, and J. T. Eaton, THIS JOURNAL, **56**, 687 (1934).