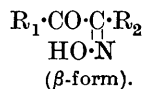
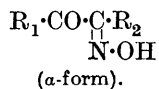


CCLXXII.—*The Configurations of the  $\alpha$ -Oximinoketones.*

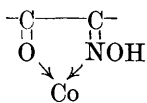
By THOMAS WESTON JOHNS TAYLOR.

AN oximinoketone of the general formula  $\text{COR}_1\cdot\text{CR}_2\text{:}(\text{NOH})$  should exist in two geometrically isomeric forms; these, from analogy with the best known case, that of the benzilmonoximes, will be designated in this paper as the  $\alpha$ - and  $\beta$ -forms, the configurations being



The most general method of deciding whether a given compound of this class is an  $\alpha$ - or a  $\beta$ -oxime is by means of the Beckmann transformation, interpreted in accordance with Meisenheimer's view that the groups involved in that transformation are those in the *anti*-position to one another. In addition to this, however, there are three properties of these oximes which give an indication of their configuration, and these indications are consistent with the result deduced from the Beckmann transformation in all cases where the necessary experimental evidence exists. These three sets of properties are as follows :

(1) The formation of co-ordination complexes with certain metals, notably copper and cobalt, is typical of the  $\alpha$ -configuration. This was established for the benzilmonoximes by Tschugaev (*J. pr. Chem.*, 1907, **76**, 88), and results given in this paper and others shortly to be published show that it is true generally. This property finds a reasonable explanation in the views of Pfeiffer and Richarz (*Ber.*, 1928, **61**, 103) as to the structure of the complexes, since the first stage of the reaction is the formation of the appended complex.



(2) Comparison of the reactivity of the carbonyl group and of the solubility relationships of the oximes gives an indication of the configurations. As was pointed out by Taylor and Ewbank (*J.*, 1926, 2818), the observations of von Auwers and V. Meyer (*Ber.*, 1889, **22**, 540) on the relative ease of formation of the anils and hydrazones of the benzilmonoximes are consistent with their configurations as deduced from the Beckmann transformation. Further, the different types of solubility of the benzilmonoximes in benzene (Taylor and Marks, *J.*, 1930, 2302) can be explained most easily if the same configurations are assumed true.

(3) In the case of compounds which contain the group  $\text{---CO}\cdot\text{CH}\cdot\text{NOH}$ , the observations of Borsche (*Ber.*, 1907, **40**, 742) on their coupling with aromatic diazo-compounds give an indication of configuration. For example, oximinoacetophenone couples with diazotised aniline to give  $\alpha$ -benzilmonoxime. This is evidence for the  $\alpha$ -structure of oximinoacetophenone, especially since  $\alpha$ -benzilmonoxime is the less stable of the two benzilmonoximes. The result is in agreement with that deduced from the ready metallic complex formation of oximinoacetophenone.

This body of consistent evidence leads to the conclusion that it is possible to allot configurations to oximinoketones with a reasonable degree of certainty. The methods have been applied to a series of compounds of this class; the results obtained are always consistent amongst themselves and are given in Table I. They are

not in every case in agreement with the configurations which have been proposed formerly; the validity of the evidence in these cases is discussed in the experimental section.

TABLE I.

Substance, $R_1 \cdot CO \cdot C(\cdot NOH)R_2$ .		Configur- ation.	Beck- mann transf.	Metallic com- plexes.	Pro- perties.	Borsche reaction.
Two forms known, $\beta$ -form more stable.						
$R_1 =$	$R_2 =$					
1. $C_6H_5$	$C_6H_5$	$\alpha$ and $\beta$	$a$	$b, c$	$c, d$	—
2. $CH_3O \cdot C_6H_4$	$C_6H_5$	$\alpha$ and $\beta$	$e, f$	Ex.	—	—
3. $C_6H_5$	$C_6H_4 \cdot OCH_3$	$\alpha$ and $\beta$	$e$	—	—	—
4. $CH_3 \cdot C_6H_4$	$C_6H_5$	$\alpha$ and $\beta$	Ex.	Ex.	Ex.	—
One form only known.						
5. $C_6H_5$	$CH_3$	$a$	—	$h$	—	—
6. $CH_3$	$C_6H_5$	$a$	Ex.	Ex.	Ex.	—
7. $CH_3$	$C_6H_4 \cdot OCH_3$	$a$	Ex.	Ex.	—	—
8. $C_6H_5$	H	$a$	—	$c$	—	$g$
9. $CH_3$	H	$a$	—	$c$	—	$g$
10. $CH_3$	$CH_3$	$a$	—	$c$	—	—
11. $CH_3O \cdot C_6H_4$	$\begin{cases} CH_3 \\ C_6H_5 \end{cases}$	$a$	—	Ex.	—	—
12. $C_6H_5 \cdot CH_2$	$C_6H_5$	$a$	Ex.	Ex.	—	—

The letters in the columns indicate that the method has been applied, and they relate to the references below; Ex. is a reference to the experimental section of this paper.

$a$ , Beckmann and Sandal, *Annalen*, 1897, **296**, 280; Beckmann and Koster, *ibid.*, 1893, **274**, 7.

$b$ , Tschugaev, *loc. cit.*

$c$ , Taylor and Ewbank, *loc. cit.*

$d$ , Taylor and Marks, *loc. cit.*

$e$ , Meisenheimer, Lange, and Lamparter, *Annalen*, 1925, **444**, 94.

$f$ , Meisenheimer and Lange, *Ber.*, 1924, **57**, 282.

$g$ , Borsche, *Ber.*, 1907, **40**, 742.

$h$ , Hey, J., 1930, 20.

The results can be expressed in one generalisation, but this generalisation raises a difficulty which seems quite inexplicable. The table shows that oximes of a  $\beta$ -configuration are found only when both the groups  $R_1$  and  $R_2$  are aromatic. There are, however, two other substances of the class, indications of whose configurations exist, and the following discussion of these shows that a truer form of the generalisation is that two oximes exist, of which the  $\beta$  is the more stable if  $R_1$  is an aromatic group and  $R_2$  is attached to the rest of the molecule by a tertiary carbon atom.

Now, in oximes of this class the  $\alpha$ -form always passes over into the  $\beta$ -form with ease. The change takes place on melting the substance or heating its solution; it is catalysed by hydrogen chloride (Meisenheimer and Heim, *Annalen*, 1907, **355**, 281) and is very rapid in the presence of certain charcoals (Taylor and Marks, *Nature*, 1930, **125**, 636). In those cases in Table I where only one oxime is known, that oxime has the  $\alpha$ -structure and is completely

stable. None of the methods which produce such ready conversion of  $\alpha$ -oximes into the  $\beta$ -forms with members of the first class is found to have any effect at all on the  $\alpha$ -oximes of the second class. The difficulty is the more pronounced because the greater stability of the  $\beta$ -oximes finds a plausible explanation in the suggestion (Taylor and Ewbank, *loc. cit.*) that in such oximes the stereochemical arrangement enables co-ordination to take place between the hydrogen atom of the oxime group and the carbonyl group.

The most surprising cases are those of oximinophenylacetone (I) and oximinodibenzylketone (II).

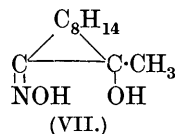
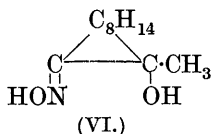
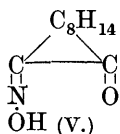


Here the groups immediately attached to the carbon atom carrying the oximino-group are identical with those in the benzilmonoximes, and yet these compounds undoubtedly have the  $\alpha$ -configuration and no  $\beta$ -oximes can be obtained.

Of the two cases not included in the table which have been mentioned, the first is ethyl oximinobenzoylacetate. It was found earlier (Taylor and Ewbank, *loc. cit.*) that, whereas ethyl oximinobenzoylacetate gives a series of metallic co-ordination complexes, ethyl oximinobenzoylacetate forms none at all. No explanation could be offered at the time, but it is clear now that the acetyl compound has the  $\alpha$ -configuration (III) and the benzoyl compound the  $\beta$  (IV), a conclusion which is in agreement with the generalisation given above. The benzoyl compound seems to be the only case where there is only one oxime known and it is a  $\beta$ -oxime.



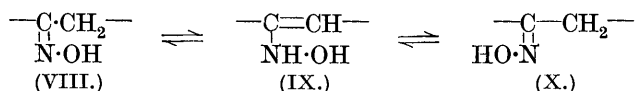
The second case is that of the isomeric oximinocamphors (V). The configurations which were allotted to these by Forster (J., 1905, **87**, 232) were based on the anhydride formation of the derivatives of them shown in (VI) and (VII).



The derivative of the stable oxime (m. p. 152°) gives an anhydride with ease and hence Forster allotted to it the  $\beta$ -configuration (VII). In view of work such as that of Meisenheimer and Lamparter (*Ber.*, 1924, **57**, 276) on the relative ease of anhydride formation of the benzildioximes, this assumption would seem very doubtful, and

that it is indeed erroneous is shown by the fact that this stable oxime forms metallic co-ordination complexes and thus has the  $\alpha$ -configuration, so that its derivative is (VI). This, therefore, is a case of two isomeric oximes of which that with the  $\alpha$ -configuration is the more stable. It conforms with the generalisation given above, since  $R_1$ , though united to the carbonyl group by a tertiary carbon atom, is not an aromatic group.

Substances 5, 10, and 11 of Table I contain the grouping (VIII), which Raikowa (*Ber.*, 1929, **62**, 1626, 3142) has suggested can pass easily into the geometrically isomeric form (X) through the intermediate tautomeric form (IX).



If these tautomeric equilibria are really established in solution, the allotment of configurations to these three oximes by the test applied is valueless. No objection of this kind, however, is possible with the remaining five oximes of this group; these must possess the  $\alpha$ -configuration. Hence it would appear probable that the three oximes 5, 10, and 11 also possess that configuration.

It does not seem possible at the moment to advance any satisfactory explanation of the remarkable difference between the two classes of oximinoketone, those giving a stable  $\beta$ -form and those giving a stable  $\alpha$ -form. The facts, however, are so clear that it seems desirable to put them on record.

#### EXPERIMENTAL.

(The numbers are those used in Table I.)

6. Oximinophenylacetone (Kolb, *Annalen*, 1896, **291**, 280) was obtained as colourless plates, m. p. 169—170° after several recrystallisations from benzene. An alcoholic solution gives with aqueous copper acetate the deep grass-green colour characteristic of an  $\alpha$ -oxime. In alcoholic solution with cobalt acetate, ammonium acetate, and a few drops of ammonia, deep red crystals of the *cobalt* complex  $R_3Co$  are slowly formed; this can be recrystallised by dissolution in hot benzene, followed by addition of absolute alcohol (Found: Co, 10.6.  $C_{27}H_{24}O_6N_3Co$  requires Co, 10.8%). The oxime was recovered unchanged after being suspended in concentrated hydrochloric acid for 10 days; another sample was unchanged after being boiled in benzene solution with animal charcoal for 2 hours. When the oxime in dry ethereal solution was treated with phosphorus pentachloride, the mixture poured into water, and the ether removed, a brown oil remained which refused to solidify. It

was rapidly hydrolysed by dilute sodium hydroxide solution, and from the resulting liquid benzoic acid was obtained in 85% yield; no aniline could be detected among the hydrolysis products.

An alcoholic solution of the oxime containing the equivalent of phenylhydrazine and a little glacial acetic acid was heated to 40° for 4 hours. Yellow needles of the *phenylhydrazone* separated, which after recrystallisation from alcohol, in which it is readily soluble, formed very pale yellow needles, m. p. 146—147° (Found : C, 71.1; H, 5.8.  $C_{15}H_{15}ON_3$  requires C, 71.5; H, 5.9%). These were the conditions used by von Auwers and V. Meyer (*loc. cit.*) in the case of the benzilmonoximes, and the hydrazone formation supports the  $\alpha$ -configuration which can be deduced from the above observations.

A  $\beta$ -configuration has been allotted to this substance by Orékhov and Tiffeneau (*Bull. Soc. chim.*, 1927, **41**, 839) on the ground that with phenylmagnesium bromide it gives the compound  $CH_3 \cdot CPh(OH) \cdot CPh \cdot NOH$ , which is identical with the product obtained by the action of methylmagnesium iodide on  $\beta$ -benzilmonoxime. This conclusion is in disagreement with the above observations, but the argument used has no stereochemical value, since it was found that  $\alpha$ -benzilmonoxime (6 g.) in dry ether reacted with methylmagnesium iodide (obtained from 15.2 g. of methyl iodide) to give a product (4 g.), m. p. 124° after two recrystallisations from benzene (Found : C, 74.4; H, 6.4.  $C_{15}H_{15}O_2N$  requires C, 74.7; H, 6.2%), which is identical (m. p. and mixed m. p.) with the product obtained from  $\beta$ -benzilmonoxime. This *methylbenzoinoxime* gives with solutions of copper salts a pale green amorphous precipitate similar to that given by  $\alpha$ -benzoinoxime (Feigl, *Ber.*, 1923, **56**, 2083; 1925, **58**, 2294). Hence it is probable that its configuration is similar to that of  $\alpha$ -benzoinoxime. If this is so, the stereochemical inversion, which, since the products are identical, must have occurred in the action of the Grignard reagent on one of the benzilmonoximes, has taken place in the reaction with the  $\beta$ -oxime.

7. Oximino-*p*-methoxyphenylacetone was prepared partly according to Borsche (*loc. cit.*), but, since the yield was very low, mainly by the action of amyl nitrite and sodium ethoxide on an absolute-alcoholic solution of *p*-methoxyphenylacetone which had been obtained from anethole dibromide (Hoering, *Ber.*, 1905, **38**, 3469). It formed short colourless needles, m. p. 151°. Neither treatment in the cold for 4 days with concentrated hydrochloric acid nor boiling in benzene solution with animal charcoal caused any change. The compound gives the characteristic blue coloration with alkaline ferrous sulphate and green coloration with copper acetate. Its

*cobalt* complex, prepared as above, is  $R_3Co$  (Found : Co, 9.4.  $C_{30}H_{30}O_9N_3Co$  requires Co, 9.3%). The Beckmann transformation, carried out as above, gave an 80% yield of anisic acid, and no anisidine could be detected.

Borsche (*loc. cit.*), by the action of dilute sulphuric acid on this compound, obtained the diketone  $CH_3O \cdot C_6H_4 \cdot CO \cdot CH_3$ , and a substance melting at  $128^\circ$  which he considered to be the product of a Beckmann transformation. On the ground of his analyses and the solubility in dilute alkali, he deduced that this compound was pyruvylanisidine,  $CH_3 \cdot CO \cdot CO \cdot NH \cdot C_6H_4 \cdot OCH_3$ . If this conclusion is correct, the oxime must have a  $\beta$ -configuration, a result in contradiction to that deduced from the above observations.

Borsche's compound was obtained in the manner described by him. It could be boiled for long periods with aqueous alkali without any hydrolysis taking place, so the amide structure seemed unlikely. The yellow colour of the solution in alkalis suggested that it was an  $\alpha$ -oximinoketone. It was proved to be the oxime,  $p\text{-}CH_3 \cdot O \cdot C_6H_4 \cdot CO \cdot CMe : NOH$ , isomeric with the original oxime, by synthesising this oxime and by the m. p.'s and mixed m. p.'s of the two samples. The compound obtained by Borsche is not the product of a Beckmann change; its formation is due to hydrolysis of the original oxime to hydroxylamine and the diketone, followed by recombination of the two to give the structurally isomeric oxime. This mechanism is confirmed by the fact that the diketone was found to combine with hydroxylamine to give this second monoxime even in the presence of 25% sulphuric acid. The same compound was obtained by Wieland (*Ber.*, 1903, **36**, 3020), though he did not prove its structure, as the first stage in the hydrolysis of the dioxime of the diketone; a sample prepared by Wieland's method was identical with the synthetic sample and with Borsche's product.

11. *Oximino-p-methoxypropiophenone* was prepared in small yield by the action of amyl nitrite and sodium ethoxide (or preferably, hydrochloric acid) on an absolute-alcoholic solution of *p*-methoxypropiophenone obtained from anethole dibromide (Wallach and Pond, *Ber.*, 1895, **28**, 2714). The substance was recrystallised from benzene; m. p.  $128^\circ$  (Found : C, 62.2; H, 5.9.  $C_{10}H_{11}O_3N$  requires C, 62.2; H, 5.7%). It was unaffected by treatment for 3 days with cold concentrated hydrochloric acid or by boiling in benzene solution with animal charcoal. It gave the characteristic colours with copper and ferrous solutions, and formed a *cobalt* complex  $R_3Co$  (Found : Co, 9.0.  $C_{30}H_{30}O_9N_3Co$  requires Co, 9.3%).

12. *Oximinodibenzylketone* was obtained by the action of amyl nitrite and sodium ethoxide on dibenzylketone in absolute alcohol;

it forms shining plates from benzene, m. p.  $114^{\circ}$  (Found: C, 75.2; H, 5.4.  $C_{14}H_{11}O_2N$  requires C, 75.3; H, 5.4%). Its alcoholic solution gives with copper acetate a green colour which is distinctly yellower than that given by the other  $\alpha$ -oximes; the solution slowly deposits a green insoluble *complex* which, for analysis, was well washed with alcohol and water; it is probably  $RCuOH$  (Found: Cu, 20.1.  $C_{14}H_{11}O_3NCu$  requires Cu, 20.0%). With aqueous cobalt acetate and ammonium acetate, together with a little ammonia, a chocolate-brown *cobalt* complex separates from the alcoholic solution. This is freely soluble in benzene, but separates from this solution on the addition of light petroleum. Its constitution,  $R_2Co$  (Found: Co, 11.7.  $C_{28}H_{20}O_4N_2Co$  requires Co, 11.6%), is different from that of the cobalt complexes formed by the other  $\alpha$ -oximes described here, but is analogous to that of the complexes obtained by Ponzio (*Gazzetta*, 1922, **52**, i, 285) from oximinoacetylacetone and oximino-benzoylacetone, which Taylor and Ewbank (*loc. cit.*) were unable to obtain.

The oxime is unaffected by treatment with cold concentrated hydrochloric acid or by boiling in benzene solution with animal charcoal. The product of the Beckmann transformation carried out as above was a mixture of benzoic and phenylacetic acids; no aniline could be detected.

2. *The 4'-Methoxybenzil- $\alpha$ -oximes.* (With NORMAN J. MAWBY.)—The  $\alpha$ -oxime has been described by Meisenheimer and Lange (*loc. cit.*) as melting at  $87.5$ — $89^{\circ}$ . Our observations indicate that their sample was contaminated with the  $\beta$ -oxime.

Methoxydeoxybenzoin (7 g.) was suspended in absolute alcohol (150 c.c.), and sodium (0.72 g.) dissolved in alcohol (30 c.c.) added. The mixture was cooled in ice, and amyl nitrite (3.6 g.) added with stirring during 2 hours; the whole was then left for 12 hours. One litre of water was added together with 5 c.c. of 2*N*-sodium hydroxide solution, and the mixture was extracted twice with ether. The passage of carbon dioxide through the aqueous layer, which had been freed from ether, precipitated a solid which was extracted with ether. The solid obtained from the dried ethereal solution melted sharply after two recrystallisations from carbon disulphide at  $95.5^{\circ}$  (yield 3.5 g.). The extraction after dilution with water removed considerable quantities of the  $\beta$ -oxime, which seems to be a distinctly weaker acid than the  $\alpha$ -oxime; if it were omitted, the resulting mixture of  $\alpha$ - and  $\beta$ -oximes could not be separated completely by recrystallisation; our best samples of the  $\alpha$ -oxime so obtained melted somewhat indistinctly at  $87^{\circ}$ .

The  $\alpha$ -oxime in alcohol gives the characteristic colour with alkaline ferrous solution and a green precipitate with copper acetate solution.



Its *cobalt* complex, obtained under the conditions described above, is  $R_3Co$  (Found: Co, 7.4.  $C_{45}H_{36}O_9N_3Co$  requires Co, 7.2%); it is freely soluble in benzene and sparingly soluble in alcohol. The oxime resembles  $\alpha$ -benzilmonoxime in being rapidly converted into the  $\beta$ -form in the presence of animal charcoal.

The  $\beta$ -oxime was obtained partly from the pure  $\alpha$ -oxime by boiling it in benzene solution with animal charcoal, and mainly from the ethereal extract mentioned above; this was heated under reduced pressure to remove ether, etc., and the residue was boiled in benzene with animal charcoal and then recrystallised twice from carbon disulphide (m. p. 130°). The  $\beta$ -oxime gives no coloration with ferrous or copper solutions, and treatment with cobalt acetate for 2 days, as described above, gave no complex.

4. *The 4-Methylbenzil- $\alpha$ -oximes.* (With NORMAN J. MAWBY and GWENYTH M. PRICE.)—4-Methyldeoxybenzoin (Mann, *Ber.*, 1881, 14, 1646) was treated with amyl nitrite as described in the foregoing section. The  $\alpha$ -oxime was recrystallised from carbon disulphide or from benzene-light petroleum; m. p. 111.5° (Found: C, 75.3; H, 5.4; N, 5.7.  $C_{15}H_{13}O_2N$  requires C, 75.3; H, 5.4; N, 5.9%). This oxime does change into its  $\beta$ -form as readily as does the corresponding methoxy-compound, though here again the change is rapid in hot benzene solution in the presence of animal charcoal. It behaves as an  $\alpha$ -oxime towards ferrous and cupric solutions; its *cobalt* complex, obtained as described above, is  $R_3Co$  (Found: Co, 7.3.  $C_{45}H_{36}O_6N_3Co$  requires Co, 7.6%).

When the oxime (1 g.) was warmed to 40° with the equivalent of phenylhydrazine and five drops of glacial acetic acid in alcoholic solution, the *phenylhydrazone* separated; it was sparingly soluble in alcohol; m. p. 183° (Found: C, 76.4; H, 5.9.  $C_{21}H_{19}ON_3$  requires C, 76.6; H, 5.8%).

The anil was formed when the oxime was warmed with excess of aniline on the water-bath for 10 hours; it was recrystallised from alcohol; m. p. 215–216°.

When submitted to the action of phosphorus pentachloride, the oxime afforded a product which on hydrolysis gave a mixture of benzoic and *p*-toluic acids; no aromatic amine could be detected.

The  $\beta$ -oxime was obtained as described in the case of the corresponding methoxy-compound. After recrystallisation from benzene and drying in the steam-oven, it melted at 123.5° (Found: C, 75.2; H, 5.5; N, 6.1%). It resembles  $\beta$ -benzilmonoxime in forming a *compound* with benzene, but the composition,  $C_{15}H_{13}O_2N.C_6H_6$ , is different (Found: loss on heating, 24.6.  $C_{21}H_{19}O_2N$  requires loss, 24.6%); the compound, which begins to melt at 90°, loses its benzene on standing, or very readily at 100°. The oxime gives no coloration

with either ferrous or cupric solutions and no cobalt complex could be obtained. There was no formation of an anil or a phenylhydrazone under the conditions which sufficed for the  $\alpha$ -oxime.

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