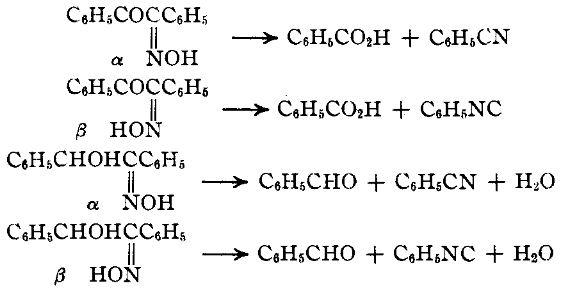
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HOWARD UNIVERSITY]

The Second Order Beckmann Rearrangement

BY A. H. BLATT AND R. P. BARNES

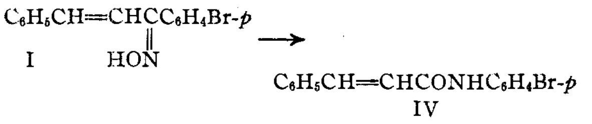
In 1891 Wege[1] showed that the Beckmann rearrangement would take place in an alkaline solution if benzene sulfonyl chloride was used as the rearranging agent. Later Werner and his collaborators[2] examined the action of benzene sulfonyl chloride together with aqueous alkali or pyridine on the monoximes of a variety of ketones. In the majority of cases the customary rearrangement to an amide took place. The oximes of benzoin and the monoximes of benzil, however, reacted in the fashion shown in the equations[3]



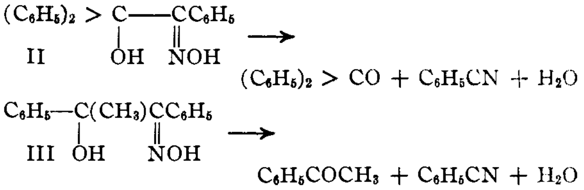
$$\begin{array}{ll}
C_6H_5CO\underset{\underset{\alpha\ \ NOH}{\|}}{C}C_6H_5 & \longrightarrow C_6H_5CO_2H + C_6H_5CN \\
C_6H_5CO\underset{\underset{\beta\ \ HON}{\|}}{C}C_6H_5 & \longrightarrow C_6H_5CO_2H + C_6H_5NC \\
C_6H_5CHOH\underset{\underset{\alpha\ \ NOH}{\|}}{C}C_6H_5 & \longrightarrow C_6H_5CHO + C_6H_5CN + H_2O \\
C_6H_5CHOH\underset{\underset{\beta\ \ HON}{\|}}{C}C_6H_5 & \longrightarrow C_6H_5CHO + C_6H_5NC + H_2O
\end{array}$$

Werner suggested for these cleavage reactions the designation of Beckmann rearrangements of the second order (literally, "second type").

We have examined the behavior toward benzene sulfonyl chloride of the oximes I, II and III. Oxime I, in which the carbon–oxygen double bond of a benzil monoxime has been replaced by a carbon–carbon double bond, undergoes normal rearrangement to the amide IV. Oximes II and III, however, in which the α-hydrogen atom of a benzoin oxime has been replaced by a phenyl and a methyl group, respectively, undergo second order rearrangements.



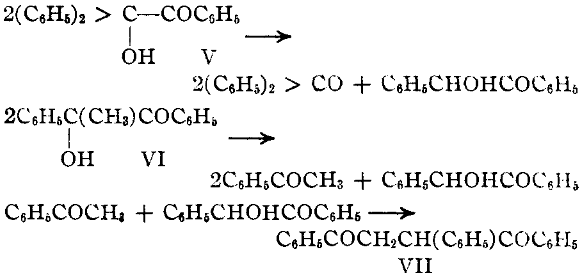
$$\underset{\text{I}}{C_6H_5CH{=}CH\underset{\underset{HON}{\|}}{C}C_6H_4Br\text{-}p} \longrightarrow \underset{\text{IV}}{C_6H_5CH{=}CHCONHC_6H_4Br\text{-}p}$$



$$\underset{\text{II}}{(C_6H_5)_2>\underset{\underset{OH}{|}}{C}-\underset{\underset{NOH}{\|}}{C}C_6H_5} \longrightarrow (C_6H_5)_2>CO + C_6H_5CN + H_2O$$

$$\underset{\text{III}}{C_6H_5-\underset{\underset{OH}{|}}{C}(CH_3)\underset{\underset{NOH}{\|}}{C}C_6H_5} \longrightarrow C_6H_5COCH_3 + C_6H_5CN + H_2O$$

It is our opinion that the second order rearrangement of an oxime is primarily a cleavage process. It is a manifestation in an oxime of a structural weakness already present in the ketone from which the oxime is prepared, for all of the oximes which have been mentioned as undergoing the second order rearrangement are obtained from ketones which are themselves easily cleaved. Thus it has long been known that benzil on treatment with potassium cyanide is cleaved to benzaldehyde and benzoic acid,[4] while recently it has been shown that benzoin is to a very slight extent cleaved to benzaldehyde by the same reagent.[5] We have found that phenyl benzoin and methyl benzoin—the ketones from which oximes II and III are obtained—are also readily cleaved. On treatment with potassium cyanide phenyl benzoin (V) furnishes benzophenone and benzaldehyde which, of course, immediately condenses to benzoin. Methyl benzoin (VI) upon similar treatment furnishes acetophenone and benzoin and, as a result of the condensation of these two products, desylacetophenone (VII).



$$2\underset{\text{V}}{(C_6H_5)_2>\underset{\underset{OH}{|}}{C}-COC_6H_5} \longrightarrow 2(C_6H_5)_2>CO + C_6H_5CHOHCOC_6H_5$$

$$2\underset{\text{VI}}{C_6H_5\underset{\underset{OH}{|}}{C}(CH_3)COC_6H_5} \longrightarrow 2C_6H_5COCH_3 + C_6H_5CHOHCOC_6H_5$$

$$C_6H_5COCH_3 + C_6H_5CHOHCOC_6H_5 \longrightarrow \underset{\text{VII}}{C_6H_5COCH_2CH(C_6H_5)COC_6H_5}$$

Not only is the second order rearrangement confined to oximes derived from ketones which are themselves subject to cleavage, but in certain cases the same reagent, potassium cyanide, which effects cleavage of a ketone will bring about a second order rearrangement of its oxime.

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[1] Wege, *Ber.*, **24**, 3537 (1891).

[2] (a) Werner and Piguet, *ibid.*, **37**, 4295 (1904); (b) Werner and Detscheff, *ibid.*, **38**, 69 (1905).

[3] The configurations assigned the benzil monoximes are those established by Meisenheimer, *ibid.*, **54**, 3206 (1921). Configurations are assigned the benzoin oximes on the basis of the observation of Werner and Detscheff, Ref. 2b, that the acetate of the β-oxime of benzoin furnishes on oxidation the acetate of β-benzil monoxime. Additional evidence for these configurations for the benzoin oximes is advanced later in the present article. It will be noticed that α-oximes yield nitriles on rearrangement while β-oximes yield isonitriles.

[4] Jourdan, *Ber.*, **16**, 659 (1883).

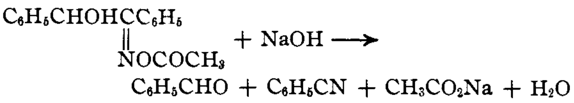
[5] Buck and Ide, THIS JOURNAL, **53**, 2350, 2784 (1931).

Thus α-benzil monoxime, α-benzoin oxime and methyl benzoin oxime when heated in alcoholic solution with potassium cyanide undergo second order rearrangements. β-Benzil monoxime and β-benzoin oxime, however, on treatment with potassium cyanide, react differently. These oximes are destroyed, no isocyanide is formed and the only product which has been identified is benzonitrile in the case of the β-benzil monoxime.

In the case of the α-oximes—those which furnish nitriles on rearrangement—the evidence is sufficient, we feel, to show that the second order rearrangement is essentially a cleavage reaction. In the case of the β-oximes—those which furnish isonitriles on rearrangement—there must be an actual rearrangement at some stage of the process, for a group attached to carbon at the start of the reaction is found attached to nitrogen at its close. Even with these β-oximes, however, cleavage is a primary process; the second order rearrangement does not proceed through normal rearrangement followed by cleavage of the rearrangement product. This can be shown most easily with the β-oxime of benzoin whose normal rearrangement product, mandelic anilide (VIII), is known. The behavior of mandelic anilide on treatment with phosphorus pentachloride—*i. e.*, the conditions under which β-benzoin oxime undergoes the second order rearrangement—has been reported by Bischoff and Walden[6] and by Buck and Ide.[7] The former workers found that mandelic anilide with phosphorus pentachloride gave the anilide of phenylchloroacetic acid (IX); the latter workers observed the formation of phenyl isocyanide. We have repeated the treatment of mandelic anilide with phosphorus pentachloride and have confirmed the results of Bischoff and Walden. The failure to form phenyl isocyanide from mandelic anilide upon the same treatment whereby β-benzoin oxime is cleaved to phenyl isocyanide makes it clear that even the second order rearrangement of β-oximes is primarily a cleavage process and is not normal rearrangement followed by cleavage.

$C_6H_5CHOHCONHC_6H_5$ VIII $\qquad$ $C_6H_5CHClCONHC_6H_5$ IX

We have also examined the behavior of the acetates of the benzoin oximes toward alkali. When the acetate of α-benzoin oxime is shaken with cold 5% sodium hydroxide solution, it is smoothly cleaved according to the equation



$$C_6H_5CHOH\underset{\underset{NOCOCH_3}{\|}}{C}C_6H_5 + NaOH \longrightarrow C_6H_5CHO + C_6H_5CN + CH_3CO_2Na + H_2O$$

The principal products are the same as those formed in the second order rearrangement of α-benzoin oxime. The process, however, does not go through α-benzoin oxime, for that oxime on treatment with 5% sodium hydroxide goes into solution as the sodium salt and from such a solution is regenerated by acidification. When the acetate of β-benzoin oxime is treated with cold 5% sodium hydroxide, it is hydrolyzed to sodium acetate and the sodium salt of the β-oxime; there is no indication of cleavage.

This behavior of the acetates of α-benzoin oxime and β-benzoin oxime on treatment with alkali is paralleled by the behavior of the acetates of α-benzil monoxime and β-benzil monoxime.[8] In both series the acetates of the α-oximes are cleaved, while the acetates of the β-oximes are hydrolyzed. The parallel behavior of the acetate of α-benzoin monoxime and the acetate of α-benzil monoxime is, we feel, excellent evidence for assigning similar configurations to these two acetates and hence to the two oximes from which they are derived. Likewise, the parallel behavior of the acetate of β-benzoin oxime and the acetate of β-benzil monoxime is comparable evidence for assigning to β-benzoin oxime acetate and to β-benzoin oxime configurations corresponding to those of β-benzil monoxime acetate and β-benzil monoxime. This links the configurations of the benzoin oximes to the very well established configurations of the benzil monoximes. Whether the behavior of benzoin oxime acetates on attempted alkaline hydrolysis can generally be used as a diagnostic reaction for oxime configurations as well as for the structures of the benzoins themselves, we are not as yet prepared to say. Similarly, we prefer to postpone until additional facts are available any discussion of

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(6) Bischoff and Walden, *Ann.*, **279**, 123 (1894).

(7) Buck and Ide, THIS JOURNAL, **53**, 1913 (1931).

(8) In the case of the benzil monoximes the difference in the behavior of the acetates and benzoates of the α-monoxime and those of the β-monoxime was long unrecognized and has caused considerable confusion. Auwers and V. Meyer, *Ber.*, **22**, 545 (1889), reported that the acetates of both the α- and the β-benzil monoximes were hydrolyzed by alkali to regenerate the corresponding monoximes. Meisenheimer, *Ann.*, **446**, 212 (1926), however, found that the acetate of α-benzil monoxime was cleaved by cold alkali. We have verified the observations that alkali cleaves the α-monoxime acetate and hydrolyzes the β-monoxime acetate.

the significance, for an understanding of the second order rearrangement, of this difference in behavior of isomeric oxime acetates.

Finally we have to mention the behavior on heating of α-benzoin oxime acetate and β-benzoin oxime acetate—behavior that is of interest in connection with Kuhara's[9] contention that acyl derivatives of oximes rather than oximes themselves undergo rearrangement. α-Benzoin oxime acetate undergoes a smooth second order cleavage to furnish benzaldehyde, benzonitrile and acetic acid at about 145°, while α-benzoin oxime itself only undergoes cleavage at a much higher temperature (240°).[10] β-Benzoin oxime acetate is pyrolyzed at about 165° and yields the same products as does the α-oxime acetate. For comparison with the acetates of the benzoin oximes the benzil monoxime acetates were subjected to pyrolysis. The acetate of α-benzil monoxime cleaves smoothly at 140° to furnish, after treatment with water, acetic and benzoic acids and benzonitrile. The acetate of β-benzil monoxime, however, is not affected by heating at 190°.

Experimental

Preparation of Methyl Benzoin Oxime (III).—To a solution of 3.0 g. of methyl benzoin[11] in 15 cc. of hot methyl alcohol we added a solution of 1.5 g. of hydroxylamine hydrochloride and 1.8 g. of sodium acetate in 8 cc. of hot water. The reaction mixture was boiled for four hours, then diluted with hot water. On cooling it deposited 3.0 g. of oxime which was purified by crystallization from alcohol; m. p. 125°.

Anal. Calcd. for $C_{15}H_{15}O_2N$: C, 74.7; H, 6.2. Found: C, 74.4; H, 6.45.

Rearrangements with Benzene Sulfonyl Chloride

In each experiment 0.01 mole of oxime dissolved in 10–15 cc. of pyridine was treated at the ordinary temperature with a slight excess of benzene sulfonyl chloride. After four hours the reaction mixture was decomposed with ice and dilute hydrochloric acid. The products of the reaction were extracted with ether and identified, after conversion into solid derivatives when necessary, by mixed melting points.

From 3.0 g. of benzal-*p*-bromoacetophenone oxime (I),[12] there was obtained 2.6 g. of the *p*-bromoanilide of cinnamic acid (IV). There was no indication of cleavage. From 3.0 g. of phenyl benzoin oxime (II) there was obtained, on evaporation of the ether extract and separation of the remaining liquid by steam distillation, a residue of 1.6 g. of benzophenone and a distillate which, on treatment with alkaline hydrogen peroxide, gave 0.3 g. of benzamide.[13] From 2.4 g. of methyl benzoin oxime (III), on evaporation of the ether extract there was obtained 2.2 g. of residual oil. This residue was shown to consist in part of acetophenone by the formation of *p*-chlorobenzalacetophenone,[14] and in part of benzonitrile by hydrolysis to ammonia and benzoic acid.

Cleavages with Potassium Cyanide

A solution of 5.0 g. of phenyl benzoin (V) in 50 cc. of alcohol and 2.0 g. of potassium cyanide in 10 cc. of water was boiled for two hours, cooled and extracted with ether. The aqueous layer on acidification yielded nothing. The ether layer on concentration and addition of alcohol furnished 0.8 g. of benzoin and, after a brief steam distillation to remove organic solvents, left a residue of 2.8 g. of benzophenone which was identified as the oxime.

A solution of 4.5 g. of methyl benzoin (VI) in 25 cc. of alcohol and 2.0 g. of potassium cyanide in 5 cc. of water was boiled for one-half hour, during which time it turned orange in color, a yellow precipitate formed and an odor of acetophenone developed. After standing overnight the precipitate, which weighed 1.5 g., was identified as desylacetophenone.[15] From the filtrate acetophenone was identified as *p*-chlorobenzalacetophenone, 0.9 g. of the unsaturated ketone being obtained.

A solution of 6.2 g. of α-benzil monoxime in 40 cc. of alcohol and 3.0 g. of potassium cyanide in 10 cc. of water was boiled for three hours, then cooled and extracted with ether. The alkaline aqueous layer on acidification evolved hydrogen cyanide and furnished a small amount of benzoin. From the ether layer benzaldehyde was removed with sodium bisulfite solution and identified as benzal-*p*-bromoacetophenone. The residual oil left by complete evaporation of the ether was identified as benzonitrile by conversion to benzamide.[13]

When β-benzoin oxime was treated with alcoholic potassium cyanide, the reaction being carried out exactly as with the α-oxime, no definite products could be identified although the oxime was destroyed.

A solution of 4.5 g. of α-benzil monoxime in 40 cc. of alcohol and 3 g. of potassium cyanide in 8 cc. of water was boiled for three hours, then cooled and extracted with ether. From the alkaline layer on acidification benzoic acid was obtained. From the ethereal layer, after evaporation and subsequent treatment with alkaline hydrogen peroxide, benzonitrile was identified as benzamide.

When a solution of 6.75 g. of β-benzil monoxime in 40 cc. of hot alcohol was mixed with a solution of 3.0 g. of potassium cyanide in 10 cc. of water, there was a brisk exothermic reaction and ammonia was evolved. At the close of the spontaneous reaction, the solution was cooled and extracted with ether. From the aqueous layer a low melting solid, whose identity has not been established, was obtained in very small amounts. No benzoic acid was found. From the ether layer benzonitrile was identified by conversion to benzamide.[13]

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(9) Kuhara, "On the Beckmann Rearrangement," Imp. Univ. Kyoto, Tokio, 1926.

(10) Kotz and Wunstorf, *J. prakt. Chem.*, [2] **88**, 527 (1913).

(11) Rogers, *J. Chem. Soc.*, **127**, 523 (1925).

(12) Blatt and Stone, THIS JOURNAL, **53**, 4142 (1931).

(13) McMaster and Langreck, *ibid.*, **39**, 104 (1917).

(14) V. Walther and Rätze, *J. prakt. Chem.*, [2] **65**, 280 (1902). The melting point given here for *p*-chlorobenzalacetophenone is 103–104°. Our material from the rearrangement as well as a synthetic sample of this unsaturated ketone melted at 113–114°.

(15) Smith, *J. Chem. Soc.*, **57**, 644 (1890).

Treatment of Mandelic Anilide with Phosphorus Pentachloride.—A suspension of 2.3 g. of the anilide (VIII), m. p. 149°, in 150 cc. of absolute ether was shaken with 2.1 g. of phosphorus pentachloride until the anilide dissolved (seven hours), then the solution was poured on ice. Evaporation of the ether furnished the anilide of phenylchloroacetic acid (IX), m. p. 147°. A mixture of this material and mandelic anilide melted at 120–135°. The only indication of isonitrile formation was the presence of a faint isonitrile odor observed on washing the flask in which the reaction was performed.

Action of Aqueous Sodium Hydroxide on the Oxime Acetates

When 5.4 g. of α-benzoin oxime acetate was shaken with 25 cc. of 5% sodium hydroxide solution, the acetate soon liquefied, while an odor of benzaldehyde and benzonitrile developed and considerable heat was evolved. After thirty minutes the reaction mixture was extracted with ether. In the aqueous layer on acidification the odor of acetic acid was apparent and a small amount of benzoin separated. From the ether layer benzaldehyde was removed as the bisulfite compound and identified as benzal-*p*-bromoacetophenone, while benzonitrile, after treatment with alkaline hydrogen peroxide, was identified as benzamide.

When 5.0 g. of β-benzoin oxime acetate was shaken with 50 cc. of 5% sodium hydroxide solution, it dissolved slowly to furnish a colorless, odorless solution from which ether extracted nothing, and which on acidification gave an almost quantitative yield of β-benzoin oxime. When α-benzoin oxime was shaken with 5% sodium hydroxide, most of the material dissolved to furnish a clear, odorless solution. This solution, filtered from a small amount of undissolved α-oxime and acidified, yielded nothing but unchanged α-benzoin oxime.

Pyrolysis of the Oxime Acetates

The acetates were decomposed by heating in a Pyrex test-tube. A small thermometer recorded the temperature of the melt, and a second thermometer recorded the temperature of the heating bath, which was about 10° higher than the melt. The temperatures recorded are those at which a vigorous decomposition set in. When the pyrolysis was complete, sodium carbonate solution and ether were added, and the products were isolated and identified in suitable fashion. In each decomposition the presence of acetic acid was evidenced by its odor.

When 2.7 g. of α-benzoin oxime acetate was heated, decomposition took place at 145°. On working up the reaction products benzaldehyde was identified as benzal-*p*-bromoacetophenone (1.5 g.) and benzonitrile as benzamide (0.6 g.). When 2.5 g. of β-benzoin oxime acetate was heated, decomposition set in at 165°, and the temperature of the melt rose rapidly to 195°. There was a slight odor of isonitrile but no indication of its presence in any quantity could be obtained. Benzaldehyde and benzonitrile were identified as benzal-*p*-bromoacetophenone and benzamide, respectively.

When 2.7 g. of α-benzil monoxime acetate was heated, decomposition took place at 135–140° and benzoic acid and benzonitrile were identified as the products, the former by its melting point and the latter by conversion to benzamide. When 2.7 g. of β-benzil monoxime acetate was heated to 190° no decomposition took place and, on cooling the melt, the acetate was recovered unchanged.

Summary

1. The second order Beckmann rearrangement in open chain compounds is undergone by the monoximes of ketones which are themselves cleaved by potassium cyanide and, in certain cases, this rearrangement of an oxime can be brought about by the same reagent which cleaves the parent ketone. It is suggested that the second order rearrangement is essentially a cleavage reaction.

2. The acetate of α-benzoin oxime, like the acetate of α-benzil monoxime, undergoes a second order rearrangement on treatment with cold alkali. The acetate of β-benzoin oxime, like the acetate of β-benzil monoxime, is hydrolyzed without cleavage by this treatment. These reactions are suggested as a basis for relating the configurations of the benzoin oximes to those of the benzil monoximes.

3. The acetates of α-benzoin oxime and β-benzil monoxime on thermal decomposition give the same products which they furnish on a second order rearrangement. The acetate of β-benzoin oxime on thermal decomposition gives the same products as does the α-acetate. The acetate of β-benzil monoxime resists thermal decomposition.

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