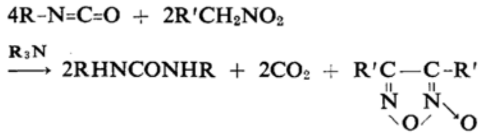
The Dehydration Reactions of Nitroparaffins and Aldoximes

By Teruaki MUKAIYAMA and Tsujiaki HATA

(Received May 4, 1960)

The preceding paper¹⁾ describes the reaction of primary nitroparaffin with isocyanate which gives *sym*-disubstituted urea, furoxane and carbon dioxide in excellent yields in the presence of a catalytic amount of tertiary amine.

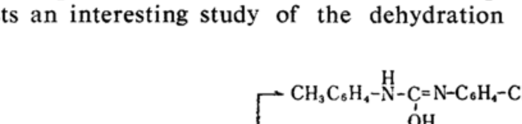


$$4R\text{-}N{=}C{=}O + 2R'CH_2NO_2 \xrightarrow{R_3N} 2RHNCONHR + 2CO_2 + R'C\text{—}C\text{-}R'$$

(1)

This reaction proceeds to the formation of disubstituted urea and furoxane through intermediates or amine and nitrile oxide which are formed by the decomposition of the addition compound of isocyanate and *aci*-nitroparaffin with spontaneous evolution of carbon dioxide. The reaction of the amine with isocyanate yields di-substituted urea and furoxane is formed by the dimerization of nitrile oxide.

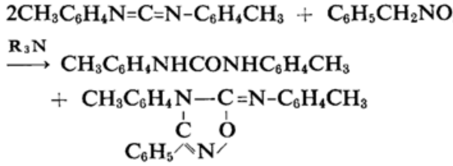
Nitrile oxide, one of the two intermediates, was confirmed by the formation of isoxazoline when isocyanate, nitroparaffin and tertiary amine are reacted in the presence of unsaturated compound as shown in the following equation.



$$RCH_2NO_2 + CH_2{=}CH\text{-}OAc + 2R'\text{-}N{=}C{=}O \xrightarrow{R_3N} CO_2 + R'HNCONHR' + CH_2\text{-}CH\text{-}OAc$$

(2)

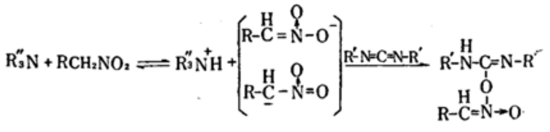
These two reactions 1 and 2 involve initial formation of nitrile oxide by the dehydration of nitroparaffiin with isocyanate and this suggests an interesting study of the dehydration of nitroparaffin with the other organic reagents. Three organic reagents were used to check the dehydration process of nitroparaffins. Firstly, the reaction of primary nitroparaffin with carbodiimide²⁾ is studied because of its similar behavior to isocyanate. When di-*p*-tolyl carbodiimide and phenylnitromethane are reacted in the presence of tertiary alkyl amine, *sym*-di-*p*-tolylurea and 3-phenyl-4-*p*-tolyl-5-*p*-tolylimino-oxadiazole are obtained (Eq. 3).



$$2CH_3C_6H_4N{=}C{=}N\text{-}C_6H_4CH_3 + C_6H_5CH_2NO_2 \xrightarrow{R_3N} CH_3C_6H_4NHCONHC_6H_4CH_3 + CH_3C_6H_4N\text{—}C{=}N\text{-}C_6H_4CH_3$$

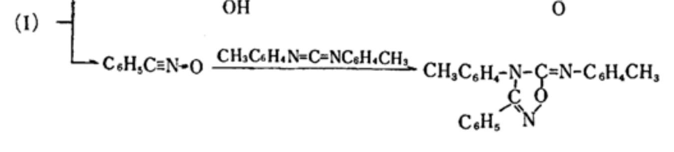
(3)

The reaction is satisfactorily explained by the same consideration described in the case of isocyanate which involves the initial formation of nitronate ion by the interaction of nitroparaffin with tertiary amine. One of the oxygen atoms of the nitro group combines in turn with the positively charged carbon of carbodiimide, forming the addition compound I shown in the next scheme.



(I)

By transferring the hydrogen atom attached to the carbon as a proton, the adduct I decomposes to nitrile oxide and isourea. The latter readily isomerizes to urea and the nitrile oxide adds to carbodiimide, forming oxadiazolone-anil.

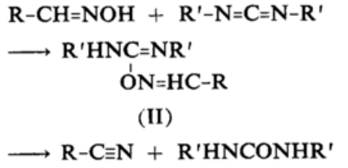


---

[1] T. Mukaiyama and T. Hoshino, *J. Am. Chem. Soc.*, in press.

[2] H. G. Khorana, *Chem. Revs.*, 53, 145 (1953).

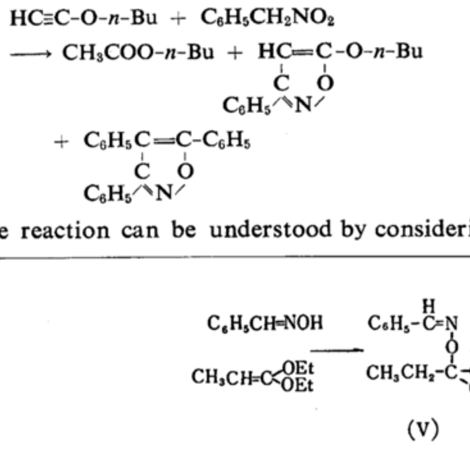
From the above result it appears interesting to extend the dehydration reaction to aldoxime which has a structure similar to that of *aci*-nitroparaffin. When aldoximes and carbodiimide react with each other, *sym*-disubstituted urea and corresponding nitriles result in high yields either in the absence or the presence of tertiary amine according to the Eq. 4.



$$\begin{aligned}&R\text{-}CH{=}NOH + R'\text{-}N{=}C{=}N\text{-}R'\\ &\longrightarrow R'HN\underset{\displaystyle ON{=}HC\text{-}R}{\underset{|}{C}}{=}NR' \quad (\text{II})\\ &\longrightarrow R\text{-}C{\equiv}N + R'HNCONHR' \qquad (4)\end{aligned}$$

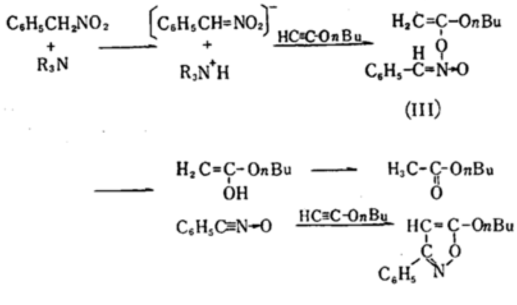
Unlike the case of nitroparaffin, the dehydration of aldoxime is carried out even in the absence of catalyst. This would be rationalized if the intermediate II is considered to be formed by the addition of aldoxime, which contains a reactive hydroxyl group in itself, to carbodiimide.

Secondly, the reactions of nitroparaffin and aldoxime with acetylenic ether which is known as a strong dehydrating agent were tested, and the similar results were obtained[3,4]. When *n*-butyl acetylenic ether and phenylnitromethane are reacted in the presence of tertiary alkyl amine, *n*-butyl acetate and 3-phenyl-5-*n*-butoxyisoxazole are obtained along with by-product, i. e. 3, 4, 5-triphenylisoxazole, formed by the self-condensation of phenylnitromethane[5].



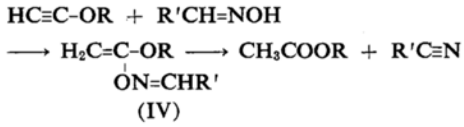
(5)

The reaction can be understood by considering the addition compound III formed by the addition of the nitronate ion of nitroparaffin to acetylenic ether. By transferring a hydrogen atom, this decomposes to nitrile oxide and enolic derivative of ester. The latter readily isomerizes to ester, and the nitrile oxide adds to acetylenic ether to form isoxazole.



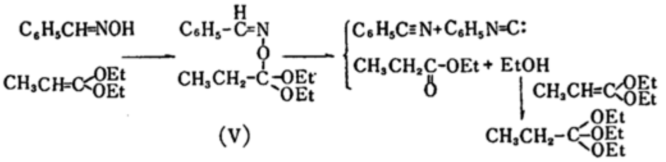
(III)

Aldoxime reacts with acetylenic ether to give ester and nitrile in high yields at room temperature in the absence of tertiary amine probably through intermediate IV.



$$\begin{aligned}&HC{\equiv}C\text{-}OR + R'CH{=}NOH\\ &\longrightarrow H_2C{=}\underset{\displaystyle ON{=}CHR'}{\underset{|}{C}}\text{-}OR \longrightarrow CH_3COOR + R'C{\equiv}N \qquad (6)\\ &\quad (\text{IV})\end{aligned}$$

Thirdly, further study on the dehydration of aldoxime with ketene acetal[6] which reacts with water to form ester and alcohol was tested. In the presence of a catalytic amount of boron trifluoride and yellow mercuric oxide, the reaction of benzaldoxime and methyl ketene diethyl acetal gives two dehydrated products, benzonitrile and benzoisonitrile, in nearly the same amount, along with ethyl propionate and ethyl orthopropionate. The unexpected formation of benzoisonitrile is of much interesting and this rearrangement found in this reaction is considered to be the simplest model of the Beckmann rearrangement.



(V)

Although the addition compound V can not be isolated when benzaldoxime and the ketene acetal are reacted in the presence of the said catalysts, it can be produced in good yield by reacting them either in the presence of triethylamine or in the absence of a catalyst. When the addition compound thus obtained is decomposed in the presence of boron trifluoride and mercuric oxide, both benzoisonitrile and benzonitrile are obtained. But when the adduct is decomposed in the presence of boron trifluoride alone, benzoisonitrile is not obtained

---

[3] J. F. Arens and T. Doornbos, *Rec. trav. chim.* **74**, 79 (1955).

[4] T. L. Jacobs, R. Cramer and J. E. Hanson, *J. Am. Chem. Soc.*, **64**, 223 (1942).

[5] W. R. Dunstan and T. S. Dymond, *J. Chem. Soc.*, **59**, 410 (1891); S. B. Lippincott, *J. Am. Chem. Soc.*, **62**, 2604 (1940).

[6] S. M. McElvain, *Chem. Revs.*, **45**, 453 (1949).

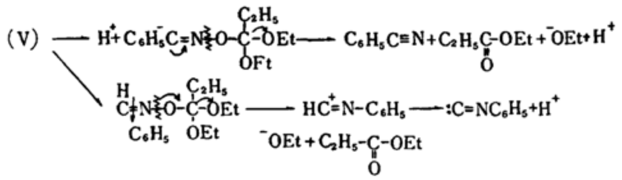
and benzonitrile is exclusively obtained. And no reaction is observed when only mercuric oxide is used. This gives the conclusion that the coexistence of boron trifluoride and mercuric oxide is a necessary condition for the formation of isonitrile.

$$V \xrightarrow{BF_3} C_6H_5C{\equiv}N + CH_3CH_2COOC_2H_5$$

$$V \xrightarrow{HgO} \text{no reaction}$$

Since it has been confirmed that the reaction of aliphatic aldoxime or *n*-heptanaldoxime and ketene acetal gives only nitrile under the same condition, the above-mentioned rearrangement is surely one of the characteristics of aromatic aldoximes.

The course of the rearrangement can be shown by the following scheme.



The addition compound V containing three oxygen atoms attached to one carbon atom has two pathways of decomposition, namely the decomposition with oxygen-carbon bond fission and that with nitrogen-carbon bond fission. The analogous reaction is already known in the decomposition of orthoester[4] to form ester and ether. In the compound V, the decomposition with oxygen-carbon bond fission to form alkyl cation is considered to be more difficult than that with nitrogen-carbon bond to form nitrile or isonitrile cations shown in the above scheme. By direct deprotonation from V, nitrile and orthoester anions are formed. On the other hand, with the migration of phenyl group, the isonitrile cation is formed along with simultaneous formation of the orthoester anion. The former deprotonates to form isonitrile and the orthoester anion loses the alkoxyl anion by the shift of an electron pair and forms ethyl propionate. Further work on this rearrangement of aldoximes and ketoximes is now in progress and will be reported in a later paper.

It is worth while reconsider the above-discussed dehydration reactions carried out with carbodiimide, acetylenic ether and ketene acetal. It is known that these compounds react readily with water to form urea, ester, and ester and alcohol according to the Eqs. 7, 8 and 9, respectively.

$$R{-}N{=}C{=}N{-}R + H_2O \longrightarrow R{-}NH\underset{\displaystyle OH}{C}{=}N{-}R \longrightarrow RHNCONHR \qquad (7)$$

$$HC{\equiv}C{-}OR + H_2O \longrightarrow CH_2{=}\underset{\displaystyle OH}{C}{-}OR \longrightarrow CH_3COOR \qquad (8)$$

$$CH_2{=}C(OR)_2 + H_2O \longrightarrow CH_3\underset{\displaystyle OH}{C}{-}(OR)_2 \longrightarrow CH_3COOR + R{-}OH \qquad (9)$$

Finding a compound reactive with water would accordingly provide a method of looking for a dehydrating agent. If compounds with carbon-carbon or carbon-nitrogen bond are considered, allene with a twinned double bond and nitrile with a triple bond may also be used as an effective dehydrating agent.

$$R{-}CH{=}C{=}CH{-}R + H_2O \longrightarrow RCH_2\underset{\displaystyle OH}{C}{=}CH{-}R \longrightarrow RCH_2COCH_2R \qquad (10)$$

$$R{-}C{\equiv}N + H_2O \longrightarrow R{-}\underset{\displaystyle OH}{C}{=}NH \longrightarrow RCONH_2 \qquad (11)$$

The hydration reactions of Eqs. 10 and 11 have already been studied[7,8]. These compounds may be added to the agents of the intramolecular dehydration reactions of the here-discussed type.

Experimental

Reaction of Phenylnitromethane with Di-*p*-tolylcarbodiimide.—To a solution of phenylnitromethane (6.1 g., 0.045 mol.) and di-*p*-tolylcarbodiimide (10 g., 0.045 mol.) in 25 ml. dry benzene were added 10 drops of triethylamine. Then the mixture was heated under reflux for 2.5 hr. and *sym*-di-*p*-tolylurea precipitated. It was filtered and washed with benzene and weighed 5.2 g., (48% of theoretical), m. p. 257~9°C. 3-Phenyl-4-*p*-tolyl-5-*p*-tolylimino-oxadiazole was separated as a white crystal on standing the filtrate overnight at room temperature. It was recrystallized from 95% ethanol, 1.5 g., (10% of theoretical), m. p. 171~2°C.

Found: C, 77.42; H, 5.57; N, 12.30. Calcd. for $C_{22}H_{19}ON_3$: C, 77.75; H, 5.56; N, 12.24%.

---

[7] G. Gustavson and N. Demjanow, *J. prak. Chem.*, [2], 38, 202 (1888).

[8] J. J. Sudborough, *J. Chem. Soc.*, 67, 601 (1895).

Reactions of Aldoximes with Di-*p*-tolylcarbodiimide.—A solution of α-benzaldoxime (4.4 g., 0.036 mol.) and di-*p*-tolylcarbodiimide (8 g., 0.036 mol.) in 35 ml. dry ether was heated under reflux for 11 hr. and *sym*-di-*p*-tolylurea precipitated. It was filtered and washed with ether and weighed 5.5 g., (63% of theoretical), m. p. 258~259°C. The filtrate was evaporated and distilled. Benzonitrile, b. p. 70~2°C (21 mmHg), 2.4 g., (65% of theoretical) was obtained. The same result was obtained when α-benzaldoxime and di-*p*-tolylcarbodiimide were reacted in the presence of tertiary alkyl amine.

When *n*-heptanaldoxime (4.7 g., 0.036 mol.) in place of α-benzaldoxime in the above experiment was used, di-*p*-tolylurea, 7.3 g., (67% of theoretical) and *n*-heptanneitrile, 2.3 g., (57% of theoretical) were obtained.

Reactions of Aldoximes with Dicyclohexylcarbodiimide.—To a solution of dicyclohexylcarbodiimide (10 g., 0.049 mol.) in 50 ml. dry benzene was added α-benzaldoxime (5.9 g., 0.049 mol.). Then the reaction started soon with the liberation of heat and *sym*-dicyclohexylurea began to precipitate. After the mixture was refluxed for 7 hr., it was cooled and filtered. The precipitate of *sym*-dicyclohexylurea was weighed 11 g., (92% of theoretical), m. p. 226~228°C. The filtrate was worked up in the usual manner, benzonitrile 5.1 g., (77% of theoretical), b. p. 83~84°C (21 mmHg), was obtained.

With *n*-heptanaldoxime (6.3 g., 0.049 mol.) in place of α-benzaldoxime in the above experiment, dicyclohexylurea 8.9 g., (81% of theoretical) and *n*-heptaennitrile 3.3 g., (62% of theoretical) were obtained.

Reaction of Phenylnitromethane with *n*-Butyl Acetylenic Ether. — To a solution of phenylnitromethane (2.8 g., 0.02 mol.) and *n*-butyl acetylenic ether (4.0 g., 0.04 mol.) in 10 ml. dry benzene were added 20 drops of triethylamine and the mixture was refluxed for 10 hr. After removing benzene and triethylamine in vacuo, *n*-butyl acetate 1.5 g., (32% of theoretical), b.p. 123~126°C and 3-phenyl-5-*n*-butoxyisoxazole 0.8 g., (18% of theoretical), b. p. 120~125°C (0.1 mmHg) were obtained. The latter solidified on cooling and melted at 59~61°C (recrystallized from ethanol-water).

Found: C, 71.8; H, 6.94; N, 6.63. Calcd. for $C_{13}H_{15}NO_2$: C, 71.8; H, 6.93; N, 6.46%.

The residual oil crystallized by the addition of 95% ethanol and melted at 209~210°C (recrystallized from 95% ethanol), (0.2 g.). It was 3,4,5-triphenylisoxazole.

Reaction of Benzaldoxime with Methyl Acetylenic Ether. — To a solution of α-benzaldoxime (6.1 g., 0.05 mol.) and methyl acetylenic ether (2.8 g., 0.05 mol.) in 10 ml. dry ether were added 20 drops of triethylamine and the mixture was allowed to stand for 43 hr. at room temperature. Then it was worked up in the usual manner, methyl acetate 1.5 g., (41% of theoretical), b. p. 57°C and benzonitrile 3.6 g., (69% of theoretical), b. p. 187~189°C, were obtained.

Reaction of α-Benzaldoxime with Methyl Ketene Diethyl Acetal in the Presence of Boron Trifluoride and Mercuric Oxide. — To a solution of methyl ketene diethyl acetal (3 g., 0.023 mol.) and α-benzaldoxime (2.8 g., 0.023 mol.) in 10 ml. dry ether were added 2 drops of boron trifluoride (40% ether solution) and 0.1 g. of mercuric oxide. After the mixture was refluxed for 6 hr., ether was removed and distilled. Ethyl propionate 0.8 g., (68% of theoretical), b. p. 45°C (108 mmHg), benzonitrile 0.9 g., (38% of theoretical), b.p. 57~59°C (4 mmHg), benzoisonitrile 0.5 g., (21% of theoretical), b. p. 38~42°C (3 mmHg), and ethyl orthopropionate 0.6 g., (30% of theoretical), b. p. 89°C (75 mmHg) were obtained.

Reaction of α-Benzaldoxime with Methyl Ketene Diethyl Acetal in the Presence of Triethylamine. —To a solution of methyl ketene diethyl acetal (3 g., 0.023 mol.) and α-benzaldoxime (2.8 g., 0.023 mol.) in 10 ml. dry ether was added 2 drops of triethylamine. After refluxing the mixture for 7 hr., it was worked up in the usual manner, the addition compound of α-benzaldoxime and methyl ketene diethyl acetal 4.8 g., (83% of theoretical), b. p. 157~158°C (18 mmHg), was obtained.

Found: C, 66.75; H, 8.25; N, 5.57. Calcd. for $C_{14}H_{21}NO_3$: C, 66.90; H, 8.42; N, 5.57%.

The same result was observed when α-benzaldoxime and methyl ketene diethyl acetal were reacted in the absence of catalyst.

Decomposition of the Addition Compound in the Presence of Boron Trifluoride and Mercuric Oxide.—To a solution of the above addition compound (2.5 g., 0.01 mol.) in 5 ml. dry ether were added 2 drops of boron trifluoride (40% ether solution) and 0.1 g. of mercuric oxide. After refluxing the mixture for 6 hr., it was treated in the usual manner and ethanol 0.1 g. (22% of theoretical), ethyl propionate 0.6 g. (59% of theoretical), b.p. 38°C (120 mmHg), benzonitrile 0.5 g. (40% of theoretical), b. p. 52°C (2 mmHg), and benzoisonitrile 0.6 g. (50%. of theoretical), b. p. 54°C (12 mmHg) were obtained.

Decomposition of the Addition Compound in the Presence of Boron Trifluoride.—With 2 drops of boron trifluoride (40% ether solution) in place of the said two catalysts in the above experiment, ethanol 0.1 g. (22% of theoretical), ethyl propionate 0.5 g. (49% of theoretical), b. p. 42°C (96 mmHg) and benzonitrile 0.5 g. (41% of theoretical), b. p. 68.5°C (10 mmHg) were obtained.

Decomposition reaction of the addition compound in the presence of mercuric oxide could not be observed and the starting material was recovered.

Reaction of *n*-Heptanaldoxime with Methyl Ketene Diethyl Acetal in the Presence of Boron Trifluoride and Mercuric Oxide.—To a solution of *n*-heptanaldoxime (2.8 g., 0.022 mol.) and methyl ketene diethyl acetal (2.8 g., 0.022 mol.) in 10 ml. dry ether were added 2 drops of boron trifluoride (40% ether solution) and 0.1 g. of mercuric oxide. After the mixture was refluxed for 7 hr., it was treated in the usual manner and ethanol 0.7 g. (78% of theoretical), ethyl propionate 0.2 g. (10% of theoretical), b. p. 44~47°C (89 mmHg) and *n*-heptanitrile 1.3 g. (54% of theoretical), b. p. 67~67.5°C (13 mmHg) were obtained.

The authors wish to express their hearty thanks to Professor Toshio Hoshino for his encouragement and to Mr. Norio Shibata for his help throughout the course of this experiment. Thanks are also due to Mr. Asaji Kondo for the microanalyses.

Department of Chemistry
Tokyo Institute Technology
Meguro-ku, Tokyo