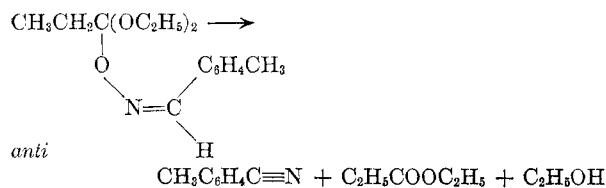
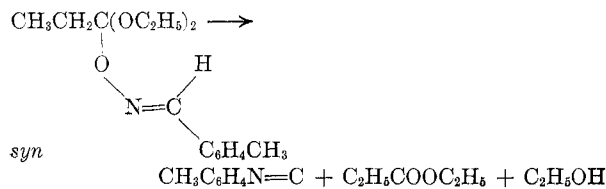


TABLE I

THE YIELDS, PHYSICAL PROPERTIES AND ANALYSES FOR ADDUCTS OF ALDOXIMES AND METHYLKETENE DIETHYLACETAL

Aldoxime	Yield, %	M.P.	B.P. (mm.)	n_D^{25}	Formula of Adduct	Analyses, %	
						Calcd.	Found
Benz- <i>syn</i> -	83		123 (4.8)	1.4890	C ₁₄ H ₂₁ NO ₃	C, 66.90 H, 8.42 N, 5.57	C, 66.75 H, 8.25 N, 5.75
<i>p</i> -Tolu- <i>syn</i> -	95		122-123 (0.55)	1.4825	C ₁₅ H ₂₃ NO ₃	C, 67.89 H, 8.74 N, 5.28	C, 68.29 H, 8.69 N, 5.49
<i>p</i> -Nitro- <i>syn</i> -	52	89-90.5			C ₁₄ H ₂₀ N ₂ O ₅	C, 56.74 H, 6.80 N, 9.45	C, 56.78 H, 6.81 N, 9.63
Benz- <i>anti</i> -	61		117-118 (2)	1.4850	C ₁₄ H ₂₁ NO ₃	C, 66.90 H, 8.42	C, 66.89 H, 8.33
<i>p</i> -Tolu- <i>anti</i> -	61		113 (0.4)	1.4865	C ₁₅ H ₂₃ NO ₃	C, 67.89 H, 8.74 N, 5.28	C, 68.18 H, 8.71 N, 5.40
Heptan-	74		107-108 (4)	1.4338	C ₁₄ H ₂₉ NO ₃	C, 64.82 H, 11.27 N, 5.40	C, 65.06 H, 11.37 N, 5.69

doximes and methylketene diethylacetal. The yields, physical properties, analyses, and infrared absorption bands for these adducts are listed in Tables I and II. The adducts were subjected to decomposition in the presence of a catalytic amount of boron trifluoride and mercuric oxide in dry ether. It was observed that adducts of *syn*-aldoximes decomposed into the corresponding isonitriles in yields ranging from 50 to 75% (see Table III). On the other hand, adducts of *anti*-aldoximes decomposed to yield only the corresponding nitriles under the same conditions but no isonitriles were obtained. Nitriles and isonitriles thus obtained were identified by their boiling points and the characteristic infrared absorption bands of benzonitrile and benzisonitrile at 4.48 μ and 4.72 μ , *p*-tolunitrile and *p*-toluisonitrile at 4.48 μ and 4.71 μ , respectively.



The formation of nitriles along with isonitriles by the decomposition of adducts of *syn*-aldoximes as shown in Table III is regarded as resulting from the rearrangement of the initially formed isonitriles during distillation. This is confirmed by the fact that, whereas only *p*-toluisonitrile was obtained by decomposing an adduct of *p*-tolualdoxime and distilling it at a lower temperature, *p*-tolunitrile

TABLE II

RECURRING BANDS IN INFRARED SPECTRA OF ADDUCTS OF ALDOXIMES AND METHYLKETENE DIETHYLACETAL

Aldoxime	8 μ (S) ^a	8 μ (MS)	9 μ (S)	10 μ (M) ^b
Benz- <i>syn</i> -	8.12	8.69	9.41	9.99
<i>p</i> -Tolu- <i>syn</i> -	8.11	8.69	9.40	9.76
<i>p</i> -Nitro- <i>syn</i> -	8.21 ^c	8.68 ^c	9.40 ^c	9.92 ^c
Benz- <i>anti</i> -	8.11	8.70	9.42	9.85 ^d
<i>p</i> -Tolu- <i>anti</i> -	8.10	8.71	9.40	9.76
Heptan-	8.10	8.68	9.40	9.78

^a Strong. ^b Medium. ^c Weak. ^d Broad.

was obtained in addition if the same decomposition products were distilled at an elevated temperature.

Further, it was observed that the decomposition of an adduct of an aliphatic aldoxime, heptanaldoxime, and methylketene diethylacetal gave heptanenitrile alone under the same conditions but no isonitrile was obtained. Accordingly, the formation of isonitrile by the present type of rearrangement seems to be characteristic of aromatic-*syn*-aldoximes in which *trans* migration of the phenyl group is involved in the process. The adducts of *anti*-aldoximes undergo decomposition by *trans* elimination of proton to yield nitriles.

In general, an aromatic-*syn*-aldoxime reacts with methylketene diethylacetal to form an initial adduct, which in turn decomposes to give an isonitrile. However, *p*-anis-*syn*-aldoxime did not react as readily with methylketene diethylacetal as the other aromatic aldoximes and, on prolonged heating, gave monoethyl di-*p*-anisaldimino ortho-propionate instead of the expected adduct. No dehydrated product was obtained.

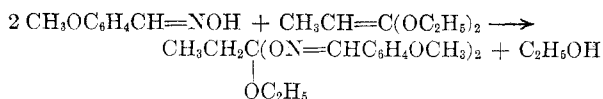


TABLE III

THE DECOMPOSITION OF ADDUCTS OF *syn*- AND *anti*-ALDOXIMES AND METHYLKETENE DIETHYLACETAL IN THE PRESENCE OF A CATALYTIC AMOUNT OF BORON TRIFLUORIDE AND MERCURIC OXIDE IN DRY ETHER

Aldoxime	Isonitrile			Nitrile		
	Yield, %	M.P.	B.P. mm.	Yield, %	M.P.	B.P. (mm.)
Benz- <i>syn</i> -	50		64 (22) ^a	45		70 (9) ^b
<i>p</i> -Tolu- <i>syn</i> -	73	20-21	62 (6) ^c	23	27-28	52 (4) ^d
<i>p</i> -Nitro- <i>syn</i> -	70	119-120				
Benz- <i>anti</i> -				60		95-96 (35)
<i>p</i> -Tolu- <i>anti</i> -				80	27-28	60 (2)
Heptan-				67		59-60 (21)

^a The infrared spectrum showed a characteristic absorption peak¹³ at 4.72 μ . ^b The infrared spectrum showed an absorption peak at 4.48 μ . ^c The infrared spectrum showed an absorption peak at 4.71 μ . ^d The infrared spectrum showed an absorption peak at 4.48 μ .

TABLE IV

THE DECOMPOSITION OF AN ADDUCT OF *p*-TOLU-*syn*-ALDOXIME AND METHYLKETENE DIETHYLACETAL IN THE PRESENCE OF VARIOUS ACID CATALYSTS

Catalyst	Amount	Reaction Time, Hr.	Yield, %		Recovered Adduct, %
			Isonitrile	Nitrile	
Mercuric acetate	0.01 g.	3	—	—	55
Mercuric chloride	0.01 g.	3	—	—	47
Mercuric sulfate	0.01 g.	3	—	—	57
Mercuric oxide	0.02 g.	3	—	—	88
Titanium tetrachloride	5 drops	3	—	75	—
Zinc chloride	0.01 g.	3	Trace	—	53
Zinc chloride	0.05 g.	14	Trace	60	—
Zinc chloride	1.55 g.	3	20	38	—
Ferric chloride	0.05 g.	3	Trace	—	33
Aluminum chloride	0.05 g.	3	—	15	40
Boron trifluoride	3 drops	1	48	38	—
Boron trifluoride and mercuric oxide	3 drops	3	70	25	—
<i>p</i> -Toluenesulfonic acid	0.01 g.	3	—	—	50 ^a
<i>p</i> -Toluenesulfonic acid	0.05 g.	3	—	—	50 ^a
Hydrogen chloride	5 bubbles	3	—	15	40
Hydrogen chloride	Saturated	—	—	40	— ^c
Hydrogen bromide	5 bubbles	3	—	23	33
Boric acid	0.01 g.	3	—	—	57 ^b

^a A crystalline product, monoethyl dialdoximino orthopropionate, m.p. 111.5-113° was obtained. ^b Monoethyl dialdoximino orthopropionate was obtained in 30% yield. ^c *p*-Tolualdoxime hydrochloride, m.p. 146-150° dec. was obtained in 60% yield.

As shown above, isonitriles were obtained in high yields when the adducts of aromatic-*syn*-aldoximes were decomposed in the presence of a catalytic amount of boron trifluoride and mercuric oxide. However, only a 30% yield of isonitrile was obtained when the adduct of *p*-tolualdoxime was decomposed in the presence of a catalytic amount of boron trifluoride and mercuric acetate. In addition, it was found that the decomposition of the adduct of *p*-tolu-*syn*-aldoxime in the presence of a catalytic amount of boron trifluoride alone gave *p*-toluisonitrile in 38% yield along with tarry products. On the other hand, when the adduct was refluxed in the presence of a catalytic amount of mercuric oxide in dry ether, no reaction occurred and the adduct was recovered quantitatively.

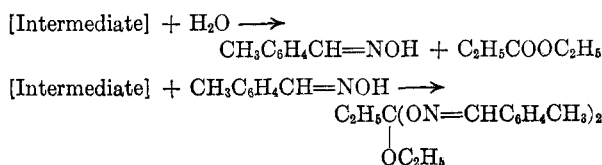
In order to examine the possibility of using some other catalysts than those utilized in the above

experiment, the decomposition of the adduct of *p*-tolu-*syn*-aldoxime in the presence of similar Lewis acids, such as aluminum chloride, titanium tetrachloride, zinc chloride and ferric chloride, and of mercuric salts, such as mercuric acetate and mercuric chloride, has been investigated. The results are summarized in Table IV. In view of these results, it is concluded that a mixed catalyst of boron trifluoride and mercuric oxide is the most effective for decomposition of the adduct to form *p*-toluisonitrile.

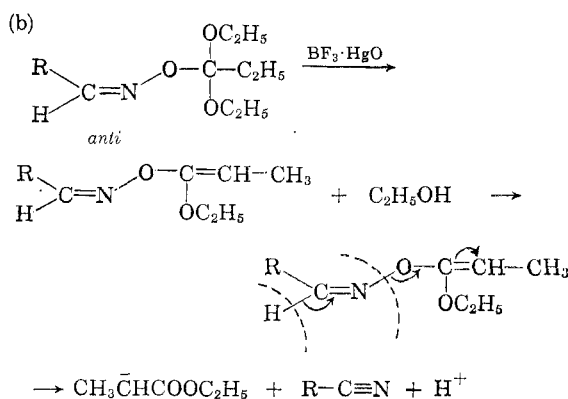
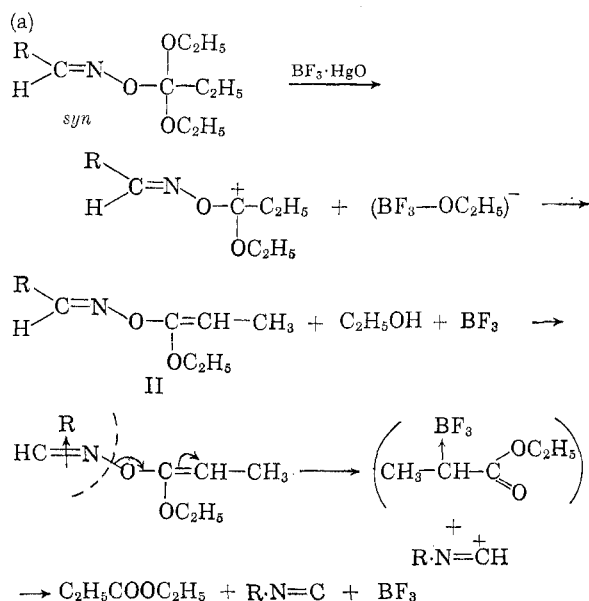
Besides, it was found that a hygroscopic crystalline product which readily decomposes on heating to give isonitrile was obtained when the adduct of *p*-tolu-*syn*-aldoxime was treated in the presence of a catalytic amount of boron trifluoride in dry ether at 10° for three hours. This crystalline product decomposed, when refluxed in the presence of a

catalytic amount of boron trifluoride and mercuric oxide in dry ether, to give a 60% yield of *p*-toluisonitrile, but only a 30% of *p*-toluisonitrile was obtained if the same product was refluxed in dry ether with boron trifluoride alone as the catalyst. It is noteworthy that these results are similar to those obtained when the adduct of *p*-tolu-*syn*-aldoxime and methylketene diethylacetal was decomposed under the same conditions as in the above mentioned experiments. Accordingly, it is reasonable to consider the compound as an intermediate in the dehydration reaction. Since this was hydrolyzed readily to give oxime, however, this compound cannot be analyzed.

It is now established that the intermediate was hydrolyzed to give *p*-tolu-*syn*-aldoxime in 80% yield along with ethyl propionate, and that it reacted with *p*-tolu-*syn*-aldoxime to give monoethyl dialdoximino orthopropionate in 95% yield.



[Adduct]



It may accordingly be said that the intermediate is methylketene monoaldoximino monoethylacetal (II) which has been formed by eliminating one mole of ethanol from the adduct. The course of this rearrangement can therefore be shown by the following scheme.

The intermediate (II) shown in the above scheme is considered to be an unstable enol derivative of ethyl propionate, which readily decomposes with oxygen-nitrogen bond fission to form stable ethyl propionate by the shift of an electron pair. It has two pathways of decomposition, namely (a) the formation of isonitrile cation by the migration of the phenyl group and (b) the formation of nitrile by the direct deprotonation of (II), both of which take place along with the formation of the stable ester. Isonitrile cation produced in the first way loses its proton and becomes isonitrile.

The course of the decomposition through the two pathways mentioned above seems to be determined either by the migratory aptitude of the substituents of aldoximino groups or by the kind of the catalysts used.

EXPERIMENTAL

Materials. Methylketene diethylacetal was prepared by the method of Walters and McElvain.⁵ Aldoximes used in this experiment were prepared from corresponding aldehydes and hydroxylamine hydrochloride.⁶⁻¹¹

*Preparation of the addition compound of benz-*syn*-aldoxime and methylketene diethylacetal.* A solution of 4.7 g. (0.038 mole) of benz-*syn*-aldoxime⁶ and 5.0 g. (0.038 mole) of methylketene diethylacetal in 20 ml. of dry ether was refluxed for 4 hr., and the solvent was then distilled. The residue was further distilled under reduced pressure and 8.0 g. (83% of theoretical), b.p. 123° (4.8 mm), *n*_D²⁵ 1.4890, of an addition compound was obtained. The infrared spectrum of the adduct showed bands similar to those of an orthoester¹² at 8.12 μ, 8.69 μ, 9.41 μ, and 9.99 μ.

When benz-*anti*-aldoxime⁷ *p*-tolu-*syn*-aldoxime,⁸ *p*-tolu-*anti*-aldoxime,⁹ and heptanaldoxime¹¹ were used in the place of benz-*syn*-aldoxime in the above experiment, adducts corresponding to each of them were obtained. The yield, physical properties, analyses, and infrared absorption bands for these adducts are listed in Table I and Table II.

When *p*-nitro-benz-*syn*-aldoxime¹⁰ was used in the place of benz-*syn*-aldoxime in the above experiment, a crystalline product was obtained after the solvent was distilled. It was recrystallized from ligroin and 2.2 g. (52%) m.p. 89-90.5°, of adduct was obtained.

When *p*-anis-*syn*-aldoxime was used in the place of benz-*syn*-aldoxime in the above experiment, *p*-anis-*syn*-aldoxime was recovered quantitatively. When a solution of 2.5 g. (0.016 mole) of *p*-anis-*syn*-aldoxime and 1.96 g.

(5) P. M. Walters and S. M. McElvain, *J. Am. Chem. Soc.*, **62**, 1482 (1940).

(6) E. Beckmann, *Ber.*, **23**, 1684 (1890).

(7) E. Beckmann, *Ber.*, **23**, 1685 (1890); *Ann.*, **365**, 202 (1909).

(8, 9) A. Hantzsch, *Z. Physik. Chem.*, **13**, 510, 523 (1894).

(10) S. Gabriel and M. Herzberg, *Ber.*, **16**, 2000 (1883).

(11) E. W. Bousquest, *Org. Syntheses*, Coll. Vol. **II**, 313 (1943).

(12) S. M. McElvain and R. E. Starn, Jr., *J. Am. Chem. Soc.*, **77**, 4571 (1955).

(0.016 mole) of methylketene diethylacetal in 20 ml. of dry ether was refluxed for 15 hr., and treated in the same manner, 2.2 g. of monoethyl di-*p*-anisaldoximino orthopropionate, b.p. 122–125° (1 mm.) was obtained.

Anal. Calcd. for $C_{21}H_{26}N_2O_8$: C, 65.27; H, 6.78; N, 7.25. Found: C, 67.91; H, 7.07; N, 7.51.

Decomposition of the adducts. A solution of 8.0 g. (0.03 mole) of the adduct of *p*-tolu-*syn*-aldoxime and methylketene diethylacetal in 20 ml. of dry ether was refluxed in the presence of a mixed catalyst of 2 drops of boron trifluoride (40% ether solution) and 0.01 g. of mercuric oxide for 3 hr. and the solvent was then distilled. The residue was distilled further under reduced pressure, and ethanol, 0.5 g. of ethyl propionate, 2.5 g. (73%) of *p*-toluisonitrile, b.p. 52° (4 mm.), and 0.8 g. (23%) of *p*-tolunitrile, b.p. 79–80° (6 mm.), were obtained. The infrared spectra of *p*-toluisonitrile and *p*-tolunitrile showed the characteristic bands¹³ at 4.71 μ and 4.48 μ , respectively.

The same reaction mixture, when distilled below 100° under reduced pressure, yielded ethanol, ethyl propionate, and 1.7 g. (57%) of *p*-toluisonitrile, b.p. 42–43° (2 mm.).

When adducts of benz-*syn*-aldoxime and *p*-nitro-benz-*syn*-aldoxime with methylketene diethylacetal were used in the place of the adduct of *p*-tolu-*syn*-aldoxime and methylketene diethylacetal in the above experiment, corresponding isonitriles and nitriles were obtained. The yields and boiling points are listed in Table III.

When adducts of benz-*anti*-aldoxime, *p*-tolu-*anti*-aldoxime, and heptanaldoxime with methylketene diethylacetal were used in the place of the adduct of *p*-tolu-*syn*-aldoxime and methylketene diethylacetal in the above experiment, ethanol, ethyl propionate, and corresponding nitriles were obtained. The yields and boiling points are listed in Table III.

Decomposition of the adduct of p-tolu-syn-aldoxime and methylketene diethylacetal with the other catalysts. A solution of 3 g. (0.011 mole) of the adduct in 3 ml. of dry ether was refluxed in the presence of 0.05 g. of aluminum chloride for 3 hr., and the solvent was then distilled. The residue was further distilled under reduced pressure and ethanol, ethyl propionate, 0.2 g. (15%) of *p*-tolunitrile, b.p. 79–80° (6 mm.), were obtained, and 1.2 g. (40%) of the adduct was recovered.

When other Lewis acids, such as 5 drops of titanium tetrachloride, 0.01 g. of zinc chloride, or 0.05 g. of ferric chloride, protonic acids, such as 5 bubbles of hydrogen chloride, hydrogen bromide, 0.01 g. of boric acids, or 0.05 g. of *p*-toluenesulfonic acid, and mercuric salts, such as 0.01 g. of mercuric acetate, 0.01 g. of mercuric chloride, or 0.01 g. of mercuric sulfate, were used in the place of aluminum chlo-

ride in the above experiment, ethanol, ethyl propionate, and the corresponding nitriles were obtained, or the adduct was recovered. The yields are summarized in Table IV.

When one equivalent of zinc chloride (1.55 g.) was used in the place of the above catalysts in the above experiments, ethanol, ethyl propionate, 0.26 g. (20%) of *p*-toluisonitrile, b.p. 53–54° (4 mm.), and 0.5 g. (38%) of *p*-tolunitrile, b.p. 58–59° (2 mm.), were obtained.

When a solution of 5 g. (0.019 mole) of the adduct of *p*-tolu-*syn*-aldoxime and methylketene diethylacetal in dry ether was saturated with hydrogen chloride, at room temperature, 0.8 g. (40%) of *p*-tolunitrile, b.p. 86° (8 mm.), and 2.0 g. (60%) of *p*-tolu-aldoxime hydrochloride, 146–150° dec., were obtained.

Isolation of the intermediate (II). A solution of 5.0 g. (0.019 mole) of the adduct of *p*-tolu-*syn*-aldoxime and methylketene diethylacetal in 5 ml. of dry ether was stirred in an ice bath in the presence of 1 drop of boron trifluoride (40% ether solution) for 3 hr., and the solvent was then distilled under reduced pressure at room temperature to yield 4.5 g. of a crystalline product.

Thermal decomposition of the intermediate (II). A crystal of 4.5 g. of the intermediate (II) was heated at 120° for 5 min. or 95° for 30 min. and distilled under reduced pressure. Ethyl propionate 1.0 g. (45%), 0.9 g. (41%) of *p*-toluisonitrile, b.p. 53–54° (4 mm.), 1.0 g. (40%) of *p*-tolu-*syn*-aldoxime, b.p. 89–90° (0.4 mm.), m.p. 78°, 1.0 g. were obtained.

Reactions of the intermediate (II). A 0.9-g. sample of the intermediate (II) and 0.3 g. of water were mixed and the reaction mixture was left standing at room temperature for 12 hr. A crystalline product was obtained after water and ethyl propionate were distilled under reduced pressure. When it was recrystallized from ligroin, 0.65 g. (80%) of *p*-tolu-*syn*-aldoxime, m.p. 78°, was obtained.

Reaction of the intermediate (II), with p-tolu-syn-aldoxime. A solution of 4.6 g. (0.019 mole) of the intermediate (II) and 2.5 g. (0.019 mole) of *p*-tolu-*syn*-aldoxime in 3 ml. of dry ether was left standing at room temperature for 5 hr. A crystalline product was obtained after the solvent was distilled under reduced pressure. It was recrystallized from ligroin, and 6.4 g. (95%) of monoethyl di-*p*-tolu-aldoximino orthopropionate, m.p. 111.5–113°, was obtained.

Anal. Calcd. for $C_{21}H_{26}N_2O_8$: C, 71.16; H, 7.39; N, 7.90. Found: C, 71.00; H, 7.53; N, 7.70.

Acknowledgment. The authors wish to express their hearty thanks to Mr. Asaji Kondo for the microanalyses.

OOKAYAMA, MEGURO-KU
TOKYO, JAPAN

(13) I. Ugi and R. Meyr, *Ber.*, **93**, 239 (1960).