	k_1	ϵ_4	ϵ_6	k_4	k_6
At $\mu = 0.09$	5200 ± 500	0.018 ± 0.002	20 ± 1	0.009 ± 0.001	0.0145 ± 0.001
At $\mu = 0$	48,500	0.028	75	0.009	0.035

	k_1'	ϵ'	k_4'	K
At $\mu = 0.09$	0.70 ± 0.05	1/(700 ± 50)	$(10.0 \pm 0.5)(10^{-8})$	10,000 ± 1000
At $\mu = 0$	2.7	1/290	$6.4\ (10^{-8})$	148,000 ± 20,000

Concentrations are expressed in moles per liter and time intervals in minutes.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF DUKE UNIVERSITY]

The Use of Certain Amines for Distinguishing Geometrically Isomeric Aldoximes and their Acyl Derivatives

BY CHARLES R. HAUSER AND EARL JORDAN

A pair of geometrically isomeric aldoximes was originally distinguished by Hantzsch[1] by the reactions of their acetyl derivatives with cold sodium carbonate solution; with this reagent the derivative prepared from the β-aldoxime gave mainly nitrile,[2] whereas the one obtained from the α-isomer was unaffected. In an extensive investigation of this field, Brady and co-workers have found that three acetyl-β-aldoximes,[3] similar to their α-isomers, are unaffected by cold sodium carbonate.[4] These three acetyl-β-aldoximes, however, are readily decomposed by 2 *N* sodium hydroxide to give nitrile, but, as was shown recently, this reagent decomposes acetyl-β-aldoximes to form oxime in addition to nitrile, the relative yields of these products being dependent upon the temperature of the reaction.[5] The use of sodium hydroxide for distinguishing acylaldoximes is further complicated by the fact that certain acetyl-α-aldoximes are decomposed by hot alkali to give some nitrile (or corresponding acid) in addition to oxime;[5] moreover, certain carbethoxy-α-aldoximes, with this reagent, give even more nitrile than oxime.[6]

Obviously, it would be desirable to find a reagent or a combination of reagents which would react with acyl-β-aldoximes to give only nitrile, but which would either not react with the corresponding α-isomers, or form only aldoxime; pyridine, especially when used in connection with *n*-butylamine, apparently meets these requirements.

In a previous paper[7] it has been shown that the acetyl-β-3,4-methylenedioxybenzaldoxime is readily decomposed by pyridine to form only nitrile, whereas the corresponding α-isomer is stable in pyridine solution even at 100°. These isomers are distinguished, also, by their reactions with *n*-butylamine;[8] with this reagent the α-isomer dissolves without noticeable rise of temperature to give only the corresponding aldoxime, but the β-isomer reacts vigorously with this amine to form both β-aldoxime[9] and nitrile, the yield of the latter being almost quantitative when *n*-butylamine[8] is added, in one cubic centimeter portions, to a gram sample of the acetyl-β-aldoxime.

These reactions have now been carried out with a series of representative acetyl-α- and acetyl-β-aldoximes. In Table I are given the yields of

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[1] Hantzsch, *Ber.*, **24**, 21 (1891).

[2] Recently, it has been found that at least certain acetyl-β-aldoximes with sodium carbonate give small amounts of aldoxime in addition to nitrile. See Hauser and Jordan, THIS JOURNAL, **57**, 2450 (1935).

[3] Acetyl-3,4-dimethoxy-5-bromobenzaldoxime, Wentworth and Brady, *J. Chem. Soc.*, **117**, 1045 (1920); acetyl-3,4-dimethoxybenzaldoxime, Brady and Dunn, *ibid.*, **123**, 1800 (1923); acetyl-2-methoxycinnamaldoxime, Brady and Grayson, *ibid.*, **125**, 1419 (1924). See also Brady, *Science Progress*, **29**, 485 (1935).

[4] Whether or not these particular acetyl-β-aldoximes would give nitrile with hot sodium carbonate apparently has not been determined.

[5] Nevertheless, it is possible to distinguish geometrically isomeric acetyl-aldoximes by means of alkali, since, at the same temperature, the β-isomers give much higher yields of nitrile than the corresponding α-isomers; at 30°, the latter generally give only traces of nitrile or corresponding acid. See especially the reference in Note 2.

[6] Hauser, Jordan and O'Connor, THIS JOURNAL, **57**, 2456 (1935).

[7] See Hauser and Jordan, *ibid.*, **58**, 1419 (1936).

[8] Piperidine and diethylamine react in a similar manner; see ref. 7.

[9] It should be pointed out that when the acetyl-β-aldoxime was added in small portions to *n*-butylamine kept at room temperature or below, mainly β-oxime was obtained, but when the reaction was carried out at the boiling point of the amine (78°), only nitrile could be isolated; see ref. 7.

TABLE I

PERCENTAGE YIELDS OF PRODUCTS FROM THE ACETYL DERIVATIVES OF SUBSTITUTED BENZALDOXIMES WITH PYRIDINE

		Nitrile			Recovered acetate		
Substituent	Isomer	Yield, %	M. p., °C. Crude prod.[a]	Literature m. p., °C.	Yield, %	M. p., °C. Crude prod.[a]	Literature m. p., °C.
Benzal-	α				96	Oil	14–15
Benzal-	β	87	Oil	−13			
3-Nitro-	α				99	126–127	128
3-Nitro-	β	96	114–115	117–118			
4-Methoxy-	α				99	48	48
4-Methoxy-	β	96	56–57	60			
3,4-Methylenedioxy-	α				92	105	105
3,4-Methylenedioxy-	β	99	92–94	94–95			
2-Chloro-[b]	α				94	85–87	88
2-Nitro-[b]	α				86	66	66
4-Dimethylamino-	α				87	108	108

[a] The melting points of these products were raised by recrystallization to those reported in the literature. [b] This reaction was carried out at 97–100°.

TABLE II

PERCENTAGE YIELDS OF PRODUCTS OBTAINED BY ADDING 5 CC. OF *n*-BUTYLAMINE IN 1-CC. PORTIONS TO 1–2 G. SAMPLES OF ACETYL DERIVATIVES OF SUBSTITUTED BENZALDOXIMES

		Corresponding oxime			Nitrile		
Substituent	Isomer	Yield, %	M. p., °C. Crude prod.[a]	Literature m. p., °C.	Yield, %	M. p., °C. Crude prod.[a]	Literature m. p., °C.
Benzal-	α	95	Oil	35			
Benzal-	β				86	Oil	−13
3-Nitro-	α	99	123	123			
3-Nitro-	β				89	115	117–118
4-Methoxy-	α	91	63–64	64			
4-Methoxy-	β				84	52–55	60
3,4-Methylenedioxy-	α	91	108–110	110			
3,4-Methylenedioxy-	β				99	91–93	94–95
2-Chloro-	α	97	72–74	75–76			
2-Nitro-	α	99	102–103	102–103			
4-Dimethylamino-	α	86	143–144	144			

[a] The melting points of these products were raised by recrystallization to those reported in the literature.

nitrile and recovered acetyl-α-aldoxime from the reactions with pyridine, and in Table II, those of nitrile and α-aldoxime from the reactions with *n*-butylamine. The reactions with pyridine were carried out at room temperatures unless otherwise stated; in these cases the yields of products presumably are not affected by a variation of temperature from 0 to 100°. The reactions with *n*-butylamine were carried out by adding the amine, which was at room temperature, to the acetyl-aldoximes as indicated in Table II. In the case of the acetyl-β-aldoximes, the mixtures became hot immediately, producing high yields of nitrile, no aldoxime being found. On the other hand, the α-isomers merely dissolved in the amine without noticeable rise of temperature, giving only α-aldoxime.[10] It should be pointed out that the products of these reactions are readily isolated from the amine solutions; the addition of crushed ice precipitates nitrile, unchanged acetyl-α-aldoxime, or part of the α-oxime, the remainder of the latter being obtained from the filtrate in the usual manner.

These reactions with pyridine and *n*-butylamine may thus be used to distinguish the pairs of geometrically isomeric acetyl-aldoximes listed in Tables I and II; in the cases in which only one geometrical isomer has been studied, their reactions with amines indicate that they have the α- or *syn*-configuration.[11] Since these acetyl derivatives are readily prepared from the corresponding aldoximes, the latter also may be distinguished by this method, but whether or not this method is applicable in all cases remains to be determined by experiment. On this basis α-aldoximes[12] would be those whose acetyl derivatives are stable in pyridine, but react with

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(10) It should be mentioned that even when acetyl-α-3,4-methylenedioxybenzaldoxime was added to *n*-butylamine at 97–100°, only oxime was obtained; see ref. 7.

(11) Contrary to the older view, α-aldoximes are now considered to have the "*syn*" configuration, and the β-aldoximes, the "*anti*" configuration. For references see Hauser and Jordan.[3]

(12) In this connection see note of paper by Brady and McHugh, *J. Chem. Soc.*, 2415 (1925).

TABLE III

PERCENTAGE YIELDS OF PRODUCTS FROM CARBANILINO DERIVATIVES OF SUBSTITUTED BENZALDOXIMES WITH PYRIDINE

Substituent	Isomer	Nitrile Yield, %	M. p., °C. Crude prod.[a]	Literature m. p., °C.	Recovered product Yield, %	M. p., °C. Crude prod.[a]	Literature m. p., °C.
3,4-Methylenedioxy-	α				91	103–104	104
3,4-Methylenedioxy-	β	98	94–95	94–95			
3-Nitro-	α				99	145–147	148
3-Nitro-	β	97	112–114	117–118			

[a] The melting points of these products were raised by recrystallization to those reported in the literature.

TABLE IV

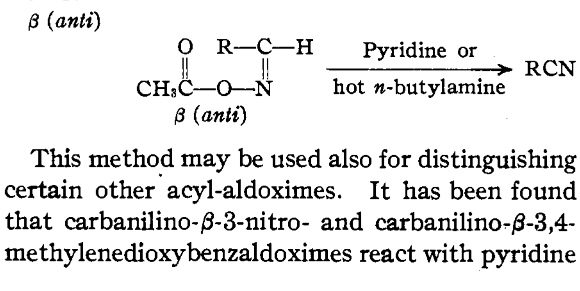
PERCENTAGE YIELDS OF PRODUCTS OBTAINED BY ADDING 5 CC. OF *n*-BUTYLAMINE IN 1-CC. PORTIONS TO 1–2 G. SAMPLES OF CARBANILINO DERIVATIVES OF SUBSTITUTED BENZALDOXIMES

Substituent	Isomer	Corresponding oxime Yield, %	M. p., °C. Crude prod.[a]	Literature m. p., °C.	Nitrile Yield, %	M. p., °C. Crude prod.[a]	Literature m. p., °C.
3,4-Methylenedioxy-	α[b,c]	81	109–110	110			
3,4-Methylenedioxy-	β				90	94–95	94–95
3-Nitro-	α[c]	89	120–121	123			
3-Nitro-	β				99	110–112	117–118

[a] The melting points of these products were raised by recrystallization to those reported in the literature. [b] In this case the carbanilino derivative was added to boiling *n*-butylamine. [c] N-Phenyl-N′-*n*-butylurea was obtained in a yield of 98%.

n-butylamine to regenerate the original aldoxime, whereas the β-aldoximes[12] would be those whose acetyl derivatives are decomposed by pyridine or by hot *n*-butylamine to form the corresponding nitrile. Although pure acetyl-aldoximes have generally been used in this work, similar results have been obtained when α-, and β-3,4-methylenedioxybenzaldoximes were treated with acetic anhydride, and, without isolating the acetyl derivatives, the mixtures treated with pyridine or *n*-butylamine.

Using the newer configurations[11] for aldoximes and their acetyl derivatives, these reactions may be represented as follows



This method may be used also for distinguishing certain other acyl-aldoximes. It has been found that carbanilino-β-3-nitro- and carbanilino-β-3,4-methylenedioxybenzaldoximes react with pyridine to give only nitrile whereas the corresponding α-isomers are stable in pyridine solution. Moreover, when *n*-butylamine is added to the β-isomers vigorous reactions occur giving high yields of nitrile, whereas the corresponding α-isomers with this amine give only α-aldoxime. The yields of these products are given in Tables III and IV. It should be pointed out that from the α-isomers with *n*-butylamine high yields of N-phenyl-N′-*n*-butylurea were obtained.

For comparison with these results the yields of products obtained from the reactions of the carbanilino-aldoximes with alkali are given in Table V. It can be seen that, similar to the acetyl-β-aldoximes, these carbanilino-β-aldoximes with alkali give both nitrile and β-aldoxime, although the yield of the latter from the 3-nitro derivative at 25–30° is very small. Alcoholic alkali was used in these cases since these carbanilino derivatives are relatively insoluble in cold aqueous alkali. The reactions with the carbanilino-α-aldoximes give the corresponding oxime as previously reported by others.[13]

It has been shown also that the carbethoxy and benzoyl derivatives of α-aldoximes are stable in pyridine, but are decomposed readily by *n*-butylamine to regenerate the original aldoxime. The yields of recovered acyl-aldoxime and of α-aldoxime obtained in these cases are given in Tables VI and VII.

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[13] See especially Brady and Dunn, *J. Chem. Soc.*, **109**, 650 (1916).

TABLE V

PERCENTAGE YIELDS OF PRODUCTS FROM CERTAIN CARBANILINO DERIVATIVES OF SUBSTITUTED BENZALDOXIMES WITH 2 *N* SODIUM HYDROXIDE

				Corresponding oxime			Nitrile			Acid		
Substituent	Isomer	Base	Temp., °C.	Yield, %	M. p., °C. Crude prod.[a]	Lit. m. p., °C.	Yield, %	M. p., °C. Crude prod.[a]	Lit. m. p., °C.	Yield, %	M. p., °C. Crude prod.[a]	Lit. m. p., °C.
3,4-Methylenedioxy-	α	Aq. NaOH	97–100	83	110	110				3	210–212	228
3,4-Methylenedioxy-	β	Alc. NaOH	0	45	145–146	146	46	94–95	94–95			
3,4-Methylenedioxy-	β	Alc. NaOH	25–30	29	145–146	146	21	158–160	166[b]	30	220–221	228
3,4-Methylenedioxy-	β	Aq. NaOH	97–100	Trace						96	225	228
3-Nitro-	α	Aq. NaOH	97–100	94	121–122	123				Trace		
3-Nitro-	α	Alc. NaOH	25–30	95	121–122	123				3	134–136	140
3-Nitro-	β	Aq. NaOH	97–100				54	114–115	117–118	38	134–136	140
3-Nitro-	β	Alc. NaOH	25–30	5	118–120	123				93	138–139	140

[a] The melting points of these products were raised by recrystallization to those reported in the literature. [b] This is the melting point of the corresponding amide.

TABLE VI

PERCENTAGE YIELDS OF PRODUCTS FROM CARBETHOXY DERIVATIVES OF SUBSTITUTED α-BENZALDOXIMES WITH *n*-BUTYLAMINE AND PYRIDINE

			Oxime			Recovered derivatives		
Substituent	Amine	Temp., °C.	Yield, %	M. p., °C. Crude prod.[a]	Literature m. p., °C.	Yield, %	M. p., °C. Crude prod.[a]	Literature m. p., °C.
4-Methoxy-	*n*-Butylamine	25–30	90	64	64			
4-Methoxy-	Pyridine	97–100				87	72–74	74
2-Chloro-	*n*-Butylamine	25–30	85	75–76	75–76			
2-Chloro-	Pyridine	97–100				72	46–47	47
3-Nitro-	*n*-Butylamine	25-30	94	118–120	123			
3-Nitro-	Pyridine	97–100				70	96–97	97–98
3,4-Methylenedioxy-	*n*-Butylamine	25–30	99	104–106	110			
3,4-Methylenedioxy-	Pyridine	25–30				94	78	78
3,4-Methylenedioxy-	Pyridine	97–100				95	73–75	78

[a] The melting points of these products were raised by recrystallization to those reported in the literature.

TABLE VII

PERCENTAGE YIELDS OF PRODUCTS FROM BENZOYL DERIVATIVES OF SUBSTITUTED α-BENZALDOXIMES WITH *n*-BUTYLAMINE AND PYRIDINE

			Oxime			Recovered derivatives		
Substituent	Amine	Temp., °C.	Yield, %	M. p., °C. Crude prod.[a]	Literature m. p., °C.	Yield, %	M. p., °C. Crude prod.[a]	Literature m. p., °C.
3-Nitro-	*n*-Butylamine	25–30	98	119–120	123			
3-Nitro-	Pyridine	97–100				99	162–163	164
3,4-Methylenedioxy-	*n*-Butylamine	25–30	90	109–110	110			
3,4-Methylenedioxy-	Pyridine	97–100				99	167–168	168

[a] The melting points of these products were raised by recrystallization to those reported in the literature.

These results are of especial significance in connection with the configuration of the carbethoxy-aldoximes which have been isolated in only one geometrical form. Certain of these compounds, although prepared from the corresponding α-aldoximes, were originally assigned the β-configuration by Brady and McHugh,[14] because with hot alkali, nitrile or the corresponding acid was obtained. Recently, however, it has been shown that these carbethoxy-aldoximes react with alkali to give both nitrile and α-aldoximes,[6] the yields of the latter predominating in most cases at 30° or below. Since the aldoximes obtained had been assigned previously the α-configuration as determined by the reactions of their acetyl derivatives with alkali, it was concluded that these carbethoxy derivatives should likewise be assigned the α-configuration; this conclusion is now supported by the fact that, like the acetyl-α-aldoximes, these carbethoxy derivatives are stable in pyridine solution, but are readily decomposed by *n*-butylamine to give the corresponding α-aldoxime.

In conclusion, it should be pointed out that, although the method for distinguishing geometri-

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[14] Brady and McHugh, *J. Chem. Soc.*, **123**, 1190 (1923). These workers assigned the α-configuration to certain other carbethoxy-aldoximes because with alkali the original aldoxime was obtained. At the time of their work the effect of temperature on the relative yields of nitrile and oxime produced by these reactions was presumably not known; see ref. 6.

cally isomeric acyl-aldoximes described in this paper is very satisfactory for the compounds studied, it is possible that certain types of acyl-α-aldoximes, as well as their β-isomers, might be decomposed by pyridine or *n*-butylamine to give nitrile, especially if there is present in these compounds an activated aldehydic hydrogen atom, or groups that would hinder the aminolysis[7] to aldoxime. Even in these cases, however, it should be possible to distinguish the α- and β-isomers, since the latter would probably form nitrile more readily.[15]

Experimental

Preparation of Acyl-aldoximes.—The acetyl-α- and acetyl-β-aldoximes were prepared according to methods previously described.[2]

The carbanilino-α- and carbanilino-β-aldoximes were prepared by treating the corresponding aldoximes in ether solution with phenyl isocyanate according to the methods described by Brady and others.[13] Crystals of the β-derivatives formed almost immediately; these were purified by recrystallization from alcohol and water. Crystals of the α-derivatives formed on standing several hours; these were purified by boiling them in alcohol solution for an hour, followed by recrystallization from alcohol and water as described by Brady and co-workers.[13] The melting points of these derivatives agreed with those reported by the earlier workers.

The carbethoxy-α-aldoximes[14] and benzoyl-α-aldoximes[16] were prepared from α-aldoximes according to methods previously described.

Reactions of Acyl-aldoximes with Pyridine and *n*-Butylamine.—These amines (4–6 cc.) were added, in 1-cc. portions, to 1–2 g. samples of the acyl-aldoximes. The reactions of *n*-butylamine with the acetyl-β- and carbanilino-β-aldoximes were vigorous, generating considerable heat; in the other reactions the acyl-aldoximes dissolved without appreciable rise of temperature. After standing several hours, crushed ice was added to the amine solutions, and the products isolated as described previously for the case of the acetyl-3,4-methylenedioxybenzaldoximes.[7] In the reactions of *n*-butylamine with the carbanilino-α-aldoximes a solid was obtained which was insoluble in alkali; it melted at 130°, and was shown to be identical with N-phenyl-N′-*n*-butylurea[17] synthesized from phenyl isocyanate and *n*-butylamine.

In order to show that α- and β-3,4-methylenedioxybenzaldoximes may be distinguished without isolating the corresponding acetyl derivatives, 1-g. samples of these aldoximes were dissolved in minimum quantities of acetic anhydride (about 1 cc.) at room temperature and the solutions cooled in an ice-bath. The mixtures were then treated with approximately 6 cc. of pyridine or *n*-butylamine; when the latter was added the mixture became very hot. After standing for an hour, ice water was added and the products isolated in the usual manner. The yields of products obtained were as follows: from the β-aldoxime with pyridine, 97% nitrile, and with *n*-butylamine, 84% nitrile; from the α-aldoxime with pyridine, 80% of the corresponding acetyl-α-aldoxime, and with *n*-butylamine, 72% of the original α-aldoxime.

Reactions of Carbanilino-aldoximes with 2 *N* Sodium Hydroxide.—These reactions were carried out and the products isolated as described previously for the reactions of the acetyl-aldoximes with alkali.[2] In the reactions with the carbanilino-α-aldoximes, diphenylurea was obtained as previously reported.[13]

Summary

A method for distinguishing geometrically isomeric aldoximes and their acyl derivatives is described; it is based on the reactions of the latter with pyridine and *n*-butylamine.

Acetyl-β- and carbanilino-β-aldoximes are decomposed by pyridine to form nitrile, while the corresponding α-isomers are stable in pyridine solution.

Acetyl-β- and carbanilino-β-aldoximes react vigorously with *n*-butylamine, the hot mixture giving mainly nitrile, whereas the corresponding α-isomers dissolve in *n*-butylamine without noticeable rise of temperature, giving aldoxime.

α- and β-aldoximes are readily converted into their corresponding acetyl derivatives; consequently, the method may be used to distinguish geometrically isomeric aldoximes.

The carbethoxy and benzoyl derivatives of α-aldoximes are stable in pyridine solution, but are decomposed by *n*-butylamine to regenerate the original aldoxime.

DURHAM, N. C.

RECEIVED JUNE 27, 1936

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(15) It might be mentioned in this connection that often it is not possible to isolate the β-isomers, especially when the β-aldoximes are treated with the acylating agent in a basic medium; however, the presence of the β-isomers is indicated by the formation of nitrile directly; see ref. 6.

(16) See Brady and McHugh, *J. Chem. Soc.*, 2414 (1925).

(17) Recently, this compound (m. p. 130°) has been synthesized from *n*-butyl isocyanate and aniline by Boehmer, *Rec. trav. chim.*, **55**, 379 (1936).