ture for 70 hours. A sample was withdrawn, and the reaction mixture was heated again for an additional 50-hour period. Analysis of the reaction mixture after 70 hours showed 71.8% of the usual carboxylic acids, 16.3% of II, and 10.8% of unreacted I. Material balance 98.9%. Analysis after 120 hours showed 87.6% of oxidized material, 10.5% of II, and 4.1% of unreacted I. Material balance 102.2%.

Isolation of 5-(1,1-Dinitroethyl)-2-picoline, II. A 200-ml. aliquot of the reactor effluent was stirred with 200 grams of ice, and the pH was adjusted exactly to a phenolphthalein end point using sodium hydroxide. The resulting solution was distilled, and the turbid azeotropic fraction was isolated and exhaustively extracted with methylene chloride. The methylene chloride was removed using a steam bath and the residue distilled in vacuo. Compound II had a boiling point of 112° C. at 1 mm. Hg and a boiling point of 138° C. at 4 mm. Hg. In an alternate method of isolation, an aliquot of the glassware reaction mixture was exhaustively extracted with methylene chloride after the pH was adjusted to 8.0. The methylene chloride layer was treated then as above.

Anal. Calcd. for $C_8H_9N_3O_4$: C, 45.50; H, 4.30; N, 19.90; Found: C, 45.92; H, 4.08; N, 19.73.

Infrared Determinations. A weighed sample of purified II was dissolved in methylene chloride, and solutions of concentrations of 0.02 gram per 25 ml. to 0.25 gram per ml. were scanned—Perkin-Elmer Infracord, Model 137—from 4 to 8 microns using 0.2 mm. fixed thickness sodium chloride liquid cells. The absorbance of these solutions, determined at 6.4 microns, adhered to the Beer-Lambert law. In practice, if I is present, a compensating blank containing a known amount of I in methylene chloride based on vapor phase assay, is used in the determination.

Reduction of II. A 2-gram sample of II was reduced using an aqueous solution of tin and hydrochloric acid. The reduction product was extracted with methylene chloride and recrystallized from methylene chloride–hexane giving 0.95 gram of 5(1-oximinoethyl)-2-picoline as a white solid. Melting point 183–185° C. uncorrected; literature (*11*) 182° C. The infrared and NMR spectra of this material was consistent with III.

Anal. Calcd for $C_8H_{10}N_2O$: C, 64.0; H, 5.66; N, 18.66. Found: C, 64.16; H, 6.47; N, 18.95.

ACKNOWLEDGMENT

The authors are indebted to Nelson J. Trenner of Merck & Co., Inc., Rahway, N. J., and his staff for carrying out the NMR and analytical work and their helpful interpretation of these data. The authors also express gratitude to Ronald Harmetz of Merck & Co., Danville, Pa., for his aid in supplying some of the experimental data.

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Reactions of Oximes with Diketene

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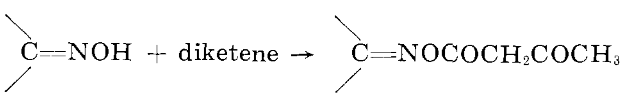
The reaction of diketene with oximes in the presence of 1,4-diazabicyclo[2.2.2]octane gave good yields of new derivatives of oximes, the O-acetoacetyl derivatives. Attempted O-acetoacetylation of *N*-phenylpyruvamidoxime led to 4-acetyl-3-methyl-1-phenyl-3-pyrroline-2,5-dione 2-oxime, and the O-acetoacetylation of the oxime of dehydroacetic acid gave 3,6-dimethyl-4*H*-pyrano[3,4-*d*]isoxazol-4-one.

THE present paper describes the reaction of diketene with oximes leading to novel *O*-acetoacetyl derivatives.



$$>C{=}NOH + \text{diketene} \rightarrow >C{=}NOCOCH_2COCH_3$$

The reaction proceeded in an inert solvent without catalyst but was accelerated by tertiary amines. For benzaldoxime, under identical conditions an uncatalyzed reaction gave 56% yield, while trimethylamine and 1,4-diazabicyclo[2.2.2]octane (DABCO) in a concentration of 1% by weight with respect to diketene gave 86 and 90%, respectively. The general scheme for the reaction was to add diketene slowly to a mixture of the oxime and the catalyst in the presence

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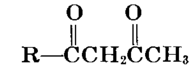
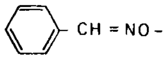
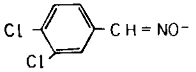
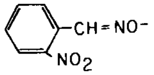
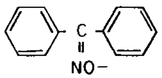
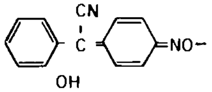
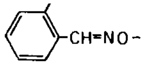
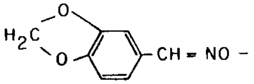
Table I. O-Acetoacetyl Derivatives of Oximes



$$R{-}\overset{O}{\overset{\|}{C}}CH_2\overset{O}{\overset{\|}{C}}CH_3$$

R	Yield, %	React. Solvent[b]	Cryst. Solvent[b]	M.P., ° C.[c]	Formula	Calcd. and Found[d] C	H	N	Cl	Oxime Source	M.P., ° C.[c]
CH=NO— | CH=NO—	95	E	C	128–130	$C_{10}H_{12}N_2O_6$	46.87 47.34	4.72 4.75	10.94 10.67		[e]	172–174
	90	B	B + C	60–61	$C_{11}H_{11}NO_3$	64.38 64.52	5.40 5.44	6.83 6.78		[e]	B.p. 85°/3 mm.
	76	B	M	84–86	$C_{11}H_9Cl_2NO_3$	48.20 48.61	3.31 3.56	5.11 5.14	25.87 25.78	[e]	116–118
	47	E	B + C	63–66	$C_{11}H_{10}N_2O_5$	52.80 52.83	4.03 3.95	11.20 11.28		[f]	95–97
	58	E	B + C	68–70	$C_{17}H_{15}NO_3$	72.58 72.45	5.38 5.35	4.98 5.10		[g]	137–141
	74	B	D	114–115 (decomp.)	$C_{18}H_{14}N_2O_3$	70.58 70.34	4.58 4.52	9.15 9.17		[f]	158–160
 [a]	38	B	T	86–87	$C_{11}H_{11}NO_4$	59.60 59.95	5.42 5.14	6.33 6.30		[g]	53–56
	68	E	B + C	98–101	$C_{12}H_{11}NO_5$	57.80 57.37	4.42 4.33	5.62 5.58		[e]	106–108
$Cl_3CCH{=}NO{-}$	17	B	B + C	50–53	$C_6H_6Cl_3NO_3$	29.23 29.46	2.45 2.47	5.68 5.58	43.15 43.18	[e]	B.p. 76/14 mm.
Cpd. III[h]	34	E	T	146–148	$C_{13}H_{12}N_2O_3$	63.93 63.80	4.92 5.00	11.47 11.22		(*6*)	110–112
Cpd. V	18	B[i]	T	121–123[j]	$C_8H_7NO_3$	58.18 58.48	4.24 4.28	9.03 9.06		(*5*)	. . .

[a] Infrared spectrum indicated no acetoacetylation occurred at the phenolic hydroxyl group in the material isolated.

[b] B = benzene, C = cyclohexane, D = chloroform, E = ether, M = methanol, T = toluene.

[c] All melting points uncorrected.

[d] Upper figures, calculated values; lower figures, found values.

[e] Oxime prepared from the carbonyl compound and hydroxylamine.

[f] Aldrich Chem. Co.

[g] Eastman Org. Chem. Co.

[h] 0.05 mole, 100 cc., E, 0.1 gram DABCO.

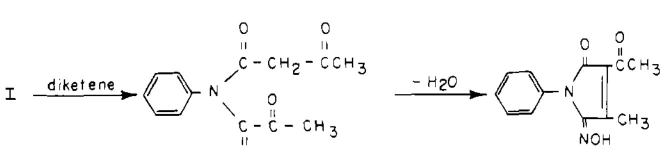
[i] 150 cc.

[j] M.p. 124–125°C, reference (*4*).

of an inert solvent. The product formed, after isolation from the reaction mixture and recrystallization, was characterized by spectral and elemental analyses.

Attempted purification by distillation of *O*-acetoacetyl derivatives of some simple oximes resulted in decomposition. The derivative of acetone oxime, which was water soluble and could not be purified by the usual method, decomposed to acetone oxime and dehydroacetic acid. *O*-Acetoacetylbenzaldoxime decomposed to benzonitrile and unidentified resinous material. This behavior is similar to that reported for the pyrolysis of the *O*-acetyl derivatives of these two oximes (*2*, *3*). In general, the stability of the *O*-acetoacetyl derivatives is about the same as that of the other *O*-acyl derivatives of oximes. They are easily hydrolyzed by acids and bases (*1*), and are thermally unstable.

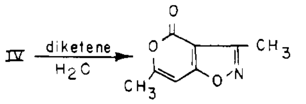
In an attempt to prepare the *O*-acetoacetyl derivative of *N*-phenylpyruvamidoxime (I) (*6*), the main product formed was dehydroacetic acid. A new compound, identified as 4-acetyl-3-methyl-1-phenyl-3-pyrroline-2,5-dione 2-oxime (III), was isolated in 34% yield. The formation of III from I and diketene might be explained by the following reactions:



II III

The structure of III was confirmed by infrared and NMR spectroscopy and elemental analyses.

Attempted *O*-acetoacetylation of the oxime IV (*5*) of dehydroacetic acid failed. The products isolated were dehydroacetic acid and 3,6-dimethyl-4*H*-pyrano-[3,4-*d*]isoxazol-4-one (V). The latter compound, which was identified by elemental and spectral analyses, was obtained in 18% yield.



V

A compound with a molecular formula $C_8H_7NO_3$ was obtained also by Minunni (*4*) from the reaction of IV with acetic anhydride; however, no structure was presented. In the authors' investigation, the reaction with acetic anhydride produced the same compound in 42% yield, which was identical in all respects with the product obtained from oxime IV and diketene.

EXPERIMENTAL

All melting and boiling points are uncorrected. Infrared spectra were taken on Baird-Atomic Models 4-55 and AB-2. NMR spectra were taken on a Varian A 60 instrument; the line positions are quoted in parts per million from tetramethylsilane as internal reference. Microanalyses were performed by Union Carbide European Research Associates, Brussels, Belgium.

Reagents. The oximes used in these reactions were either obtained from commercial sources or prepared by the interaction of an aldehyde or ketone with hydroxylamine. The catalyst used in each experiment was DABCO (Houdry Process Corp.). For benzaldoxime, the use of trimethylamine (Matheson Co., Inc.) was investigated also. Diketene was the commercial product of Union Carbide Corp.

Procedure. Generally, a slight excess of diketene was added dropwise at 20° to 30° C., with external cooling if necessary, to a stirred solution or suspension in a flask that contained 100 ml. of solvent and 0.1 gram of DABCO per 0.1 mole of oxime. The solvent was benzene or ether. Stirring was maintained at 20° to 30° C. for an hour after addition was completed. Dehydroacetic acid was usually formed also. Then the reaction mixture was extracted repeatedly with equal volumes of aqueous 5% sodium bicarbonate solution until no dehydroacetic acid precipitated from the extracts after acidification. The reaction mixture was finally washed with water and dried over magnesium sulfate. The solvent was then removed on a rotatory evaporator. The residual product was generally of high purity (>95%) and contained at most only a few per cent of unchanged oxime. The solid residue was purified further by recrystallization from a suitable solvent and identified by infrared and NMR spectroscopy and elemental analyses.

No attempt was made to separate the syn- and anti-isomers of either the starting oximes or the products. The geometry of the products was undetermined also.

The preparations of *O*-acetoacetyl oxime derivatives and other pertinent data are summarized in Table I.

4-Acetyl-3-methyl-1-phenyl-3-pyrroline-2,5-dione 2-oxime (III). In the NMR spectrum, using acetone-d_6 as solvent, singlets at 2.37 and 2.46 p.p.m. confirmed the presence of three protons each for an allylic methyl and an acetyl group. A slightly broadened peak at 7.28 p.p.m. was assigned to the five aromatic protons. A broad resonance signal at 10.8 p.p.m. indicated the presence of one proton in the oxime group.

The infrared spectrum (KBr pellet) showed intense broad bands at 3.0 (O—H) and 5.9 μ (C=O), peaks at 6.12 (C=N), 6.27 (stronger than normal for aromatic C=C, probably also conjugated C=C in five-membered ring), 10.55 μ (N—O), and a strong anomalous band at 8.85 μ.

3,6-Dimethyl-4*H*-pyrano[3,4-*d*]isoxazol-4-one (V). In the NMR spectrum, using chloroform as solvent, a doublet at 2.40 p.p.m. (J~0.9 c.p.s.) was assigned to the three protons of the methyl group in the 6-position. The doublet was caused by long-range coupling with the olefinic hydrogen. A singlet at 2.60 p.p.m. was in agreement with the presence of the three protons of the methyl group in the 3-position. A quartet at 6.60 p.p.m. (J~0.9 c.p.s.) confirmed the presence of one olefinic hydrogen.

The infrared spectrum (KBr pellet) showed characteristic absorption bands for a delta lactone at 5.74, 7.96, and 8.15 μ, peaks at 6.15 (C=N), 6.32 (conjugated C=C), and 10.35 μ (N—O).

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