

ethanol-hexane (charcoal) yielded clusters of colorless prisms (negative Liebermann test), mp 175–177° dec. An additional recrystallization yielded pure **2c**: mp 176–178° dec; uv max (dioxane) 232 and 300 m μ (ϵ 15,000 and 6300); ir (Nujol) 3155 (sydnone CH), 1728 (sydnone C=O), 1714 (carboxyl or acetamido C=O), 1703 (carboxyl or acetamido C=O), 1355 and 1165 cm⁻¹ (SO₂); ir (dioxane) 1765 (sydnone C=O), 1750 (carboxyl C=O), and 1715 cm⁻¹ (acetamido C=O).

Anal. Calcd for C₁₄H₁₅N₃O₇S: C, 45.53; H, 4.09; N, 11.38; S, 8.66. Found: C, 45.06; H, 4.06; N, 11.27; S, 8.65.

2-[N-Acetyl(tosylamino)]acrylic Acid (3). A. From **2c** and Acetic Anhydride.—A suspension of 500 mg (1.4 mmol) of **2c** and 2.5 ml of acetic anhydride was heated on the steam bath with protection from moisture. The solid gradually dissolved with moderate evolution of gas; after 30 min the orange solution was cooled (ice bath) and 8.5 ml of ice-cold water was added. Stirring was continued for several hours during which the initially formed oil became a semisolid. On being warmed to room temperature the solid dissolved, and the solution was evaporated to dryness *in vacuo*. Drying *in vacuo* over KOH produced a semisolid which on trituration and washing with several portions of anhydrous ether left 110 mg (29%) of **3** as a light tan powder, mp 140–144° dec. Two recrystallizations from ethyl acetate-hexane (charcoal) yielded clusters of small colorless needles: mp 143–145° dec; ir (Nujol) 1720 (acetamido C=O), 1690 (conjugated carboxyl C=O), 1635 (conjugated olefin C=C), 1350 and 1165 (SO₂), and 915 cm⁻¹ (olefin CH deformation).¹²

Anal. Calcd for C₁₂H₁₃NO₅S: C, 50.88; H, 4.63; N, 4.95; S, 11.30. Found: C, 50.81, 50.69; H, 4.64, 4.53; N, 4.80; S, 11.34.

B. From **1e** and Acetic Anhydride.—A stoppered suspension of 1.00 g (2.9 mmol) of once-recrystallized **1e** and 5 ml of acetic anhydride was allowed to stand in the dark at room temperature with occasional swirling. Within 12 hr complete solution occurred; after 2 weeks the clear, orange solution was added with stirring to 20 ml of cold water (ice bath). The ice bath was removed after several hours, but vigorous stirring was continued overnight until the amorphous semisolid was converted into a uniform suspension of flocculent solid. After cooling, the product which was filtered, washed thoroughly with ice water, and dried gave 0.44 g (54%) of cream-colored powder, mp 141–143° dec. Its ir was identical with that obtained for the product in part A above.

N-Acetyl-N-tosylalanine (5b). A. From **5a** and Acetic Anhydride.—A stoppered suspension of 7.29 g (0.0300 mol) of powdered N-tosyl-DL-alanine (**5a**)¹³ and 30 ml of acetic anhydride was stirred at room temperature. Within 12 hr solution occurred, and after 26 hr this was cooled (ice bath) and 100 ml of ice-cold water added with stirring. The ice bath was removed after 3 hr but stirring was continued for 1 hr during which the initially formed colorless oil dissolved. A small sample of this solution was removed, diluted with excess water, and scratched to initiate crystallization. The reaction mixture then was seeded, and after standing 2 hr (ice bath) the solid was filtered, washed with cold water, and air-dried: yield, 6.30 g (74%) of a snow-white solid; mp 122–123°. Recrystallization from 2:1 carbon tetrachloride-benzene gave colorless prisms: mp 122.5–123.5°; uv max (dioxane) 232 m μ (ϵ 14,500); ir (Nujol) 1713 (carboxyl or acetamido C=O), 1700 (carboxyl or acetamido C=O), 1350 and 1170 cm⁻¹ (SO₂); ir (dioxane) 1755 (carboxyl C=O) and 1707 cm⁻¹ (acetamido C=O).

Anal. Calcd for C₁₂H₁₅NO₅S: C, 50.52; H, 5.30; N, 4.91; S, 11.22. Found: C, 50.57; H, 5.19; N, 4.80; S, 11.48.

The acetyl group of **5b** was readily cleaved to regenerate **5a**.¹⁴ Thus, when a solution of 2.00 g (7 mmol) of **5b** and 5 ml concentrated NH₄OH, which had been allowed to stand at room temperature for 1 hr, was diluted with water (5 ml) and acidified (pH 1–2) with concentrated HCl, a colorless oil separated which readily solidified. Filtration, washing, and drying gave a 92% yield of **5a**: mp 140–142°, no melting point depression with authentic¹³ **5a** and identical ir.

B. By Catalytic Reduction of **3**.—PtO₂ (40 mg), 280 mg (0.99 mmol) of **3**, and 20 ml of glacial HOAc was hydrogenated (Parr apparatus) for 12 hr at 40 psig. The catalyst was washed with a little glacial HOAc the combined filtrates were evaporated

in vacuo almost to dryness. Addition of 15 ml of water to the residual oil and scratching initiated solidification. After cooling (ice bath), the solid was filtered, washed with cold water, and dried: yield 210 mg (75%) of cream powder; mp 122–124°, mmp 122–124° with sample prepared as in A. The ir was identical with that obtained for the product in A.

Registry No. —**1b**, 24571-53-7; **1c**, 24627-11-0; **1d**, 24599-14-2; **1e**, 24627-12-1; **2c**, 24627-13-2; **3**, 24571-54-8; **5b**, 24627-13-4.

Dehydration of Amidoximes with and without Rearrangement¹

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Carbodiimides **4** and amidines **5** have been obtained for the first time from the reaction between an N-aryl or N-alkyl amidoxime **1** and benzenesulfonyl chloride in pyridine.^{2,3} As expected, a 2-substituted benzimidazole is the major product from an N-aryl amidoxime,³ but similar dehydration of an N-alkyl amidoxime, previously unexplored, does not give an intramolecular cyclization.

Dehydration of an amidoxime without rearrangement leaves an azomethine nitrene **6**. Presumably as a triplet, the nitrene abstracts hydrogen from solvent to bring about the formation of an amidine **5**. Ring closure by intramolecular insertion into an appropriate aromatic CH bond may proceed from a nitrene such as **6a** and **6d**.⁴ However, the formation of benzimidazoles in the dehydration of N-aryl amidoximes **1a** and **1d** does not depend on nitrene intermediacy insofar as ring closure from a corresponding nitrenium cation may occur.⁵ The formation of a carbodiimide has been found to be concerted with the elimination of carbon dioxide from an oxadiazolone rather than by rearrangement of an azomethine nitrene which is also produced.⁴ We now suggest that carbodiimide formation proceeds from an O-benzenesulfonyl ester **2** of an amidoxime simultaneously with α or 1,3 elimination.

(1) Financial assistance was received from NASA Grant No. NGR 14-012-004.

(2) M. W. Partridge and H. A. Turner, *J. Pharm. Pharmacol.*, **5**, 103 (1959), established the initial product as a carbodiimide (RN=C=NH) which rearranged into a cyanamide (RNHCN) in the similar dehydration of a primary amidoxime.

(3) M. W. Partridge and H. A. Turner, *J. Chem. Soc.*, 2086 (1958), produced 2-substituted benzimidazoles from similar treatment of N-aryl amidoximes. When carried out in aqueous sodium hydroxide, carbodiimides, but not benzimidazoles, were obtained from C₆H₅NHC(R)=NOH and benzenesulfonyl chloride.

(4) J. H. Boyer and P. J. A. Frints, *in press*.

(5) Cyclization into a 2-substituted benzimidazole from azomethine nitrenium cations, produced by dissociation of the ester,² has been proposed. A discrepancy between product yields for **3a**,⁶ **4a**, and **3d**⁷ and the corresponding yields previously obtained³ (Table I) has not been accounted for.

(6) F. C. Cooper and M. W. Partridge, *J. Chem. Soc.*, 225 (1953). An authentic sample was prepared by mixing equivalent amounts of 2-benzylbenzimidazole and benzenesulfonic acid in chloroform.

(7) K. Hoffmann in "The Chemistry of Heterocyclic Compounds," A. Weissberger, Ed., John Wiley & Sons, Inc., New York, N. Y., 1953, p 380; **3d** hydrochloride mp 90–92°; **3d** picrate mp 212–213°.

(12) L. J. Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen and Co., London, 1960, p 34.

(13) A. F. Beecham, *J. Amer. Chem. Soc.*, **79**, 3257 (1957).

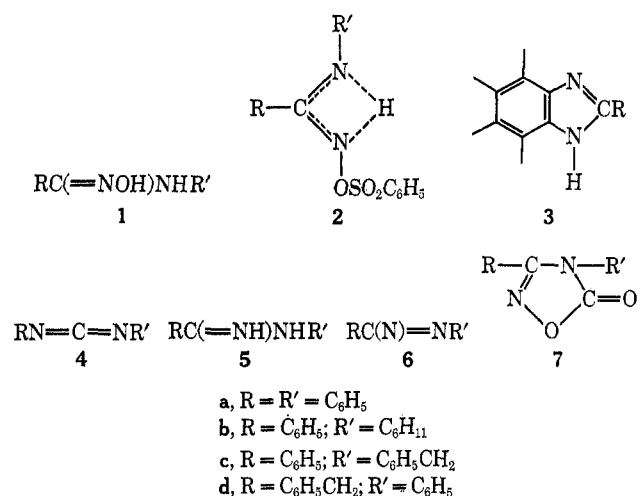
(14) J. M. Swan and V. du Vigneaud, *ibid.*, **76**, 3110 (1954).

TABLE I
 PRODUCTS FROM AMIDOXIMES 1 AND BENZENESULFONYL CHLORIDE IN ANHYDROUS PYRIDINE^a

1	Solvent ^a	Products ^b							
		3 ^c		4			5		
		Mp, °C	Yield, %	Bp, °C (mm)	Yield, %	Derivative, ^d mp, °C	Mp, °C	Yield, %	Derivative, ^e mp, °C
a	Benzene	290–291 ^h	72 ^f		18 ^g	236–237 ^h		0	
b	Benzene			116–118 ^h (0.7)	64	180–182 ^h	114–115 ^h	Trace	278–280 ⁱ
c	Dioxane Benzene			138–140 ^h (0.25)	83 ⁱ 88 ⁱ	168–169 ^h		1.5 Trace	222–225 ^h
d	Dioxane	187–188 ^h	72 ^f		0		137–139 ^h	10	

^a Benzene was dried over sodium wire. Dioxane was refluxed over lithium aluminum hydride for 3 hr and distilled from the hydride immediately before use. Pyridine was stored over potassium hydroxide pellets for at least 1 week before use. ^b Each product identification consisted of identical comparison of ir and/or nmr spectra with authentic spectra and mixture melting point. ^c 3a picrate mp 270–272°; ^d 3d benzenesulfonate mp 183–184°, ^e 3d hydrochloride mp 90–92°, ^f 3d picrate mp 212–213°. ^g Each carbodiimide 4a–c was converted into the corresponding urea by stirring with 6 N hydrochloric acid for a few minutes. The melting point of each urea is recorded. ^h 5b hydrochloride and 5c hydrochloride precipitated from aqueous acid solution. The melting point of each hydrochloride is recorded. ⁱ A 98% yield was reported. ^j A 69% yield was reported for the reaction in aqueous sodium hydroxide. ^k J. H. Boyer and P. J. A. Frints, submitted for publication. ^l Yield based on assumed quantitative conversion into the corresponding urea. ^m P. Oxley and W. F. Short, *J. Chem. Soc.*, 499 (1949). ⁿ P. Oxley and W. F. Short, *ibid.*, 1114 (1947). ^o A 63% yield was previously reported.³

In agreement with earlier observations on the azomethine nitrenes 6a–d⁴ cyclization accompanying dehydration of amidoximes has not been observed when an



N–C bond formation required (1) attack at an aliphatic carbon atom, (2) indole rather than benzimidazole ring closure, and (3) ring closure to a six-membered ring. In contrast to results from oxadiazolones **8**⁴ fragmentation of an amidoxime into a nitrile (RCN) and a nitrene (R'N) was not detected.

Experimental Section

Each amidoxime 1a–d was previously prepared as an intermediate for conversion into an oxadiazolone 7a–d.⁴

Except for product isolation the general procedure described by Partridge and Turner^{2,3} was followed for treating each amidoxime with benzenesulfonyl chloride in pyridine. A solution of 0.01 mol of the amidoxime dissolved in 10 ml of benzene and 5 ml of pyridine, protected from moisture, was cooled to 0–5° in an ice bath. A solution of 1.76 g (0.01 mol) of benzenesulfonyl chloride in 5 ml of benzene was added dropwise with stirring. The addition was completed in 30 min during which time a colorless solid separated and a light yellow color developed. The mixture was kept overnight at 0–5°.

Products from N-Cyclohexylbenzamidoxime.—Removal of the solvent from the reaction mixture obtained from N-cyclohexylbenzamidoxime left a light brown oil and a solid residue. Extraction with 25 ml of hexane left 3.3 g of an insoluble colorless solid, mp 107–115°. Its aqueous solution was made basic by adding solid potassium hydroxide and was then extracted with chloroform in which 8 mg of light brown solid, mp 105–110°, did not dissolve and gave an ir spectrum which resembled that of N-cyclohexylbenzamidine. Removal of hexane from the first extraction left 1.85 g of an oil from which N-cyclohexyl-N'-phenylcarbodiimide distilled at 116–118° (0.7 mm),⁴ 1.27 g (64%), and left a dark black residue. Both ir and nmr spectra of the distillate were identical with the respective spectra for an authentic sample of N-cyclohexyl-N'-phenylcarbodiimide.⁴ Quantitative hydrolysis with 2 N hydrochloric acid gave N-cyclohexyl-N'-phenylurea, mp and mmp 180–182°, with both ir and nmr spectra identical with the respective spectra for an authentic sample of the urea.⁴

When anhydrous dioxane was substituted for benzene, the reaction mixture was stirred with 10 ml of 6 N hydrochloric acid. Almost immediately, a precipitate of colorless N-cyclohexyl-N'-phenylurea appeared. After 30 min it was isolated, 1.65 g (7.5 mmol), 75%, mp 181–182.5°. A chloroform extract of the filtrate was dried over magnesium sulfate, filtered, and concentrated to give a light brown solid, mp 150–160°, which recrystallized from acetone as 170 mg (0.7 mmol), 7.8%, mp and mmp 180–181.5° of N-cyclohexyl-N'-phenylurea, ir and nmr spectra identical with those of authentic material. The acid solution was treated with potassium hydroxide pellets while cooling in an ice bath and was extracted with chloroform. After drying, filtering, and evaporating, the chloroform extracts a brown solid, which became colorless N-cyclohexylbenzamidine hydrochloride after washing with ether, mp 278–280°, 42 mg (0.17 mmol), 1.7%, identical with those of an authentic sample. After treating the hydrochloride with potassium hydroxide pellets with stirring for 15 min, the solution was extracted with ether. Evaporation of the dried ether extracts gave 30 mg (0.15 mmol), 1.5%, of colorless N-cyclohexylbenzamidine, mp and mmp 112–114°, ir and nmr spectra identical with those for an authentic sample.⁴

Isolation of 2-Phenylbenzimidazole.—In working up the reaction mixture from N-phenylbenzamidoxime, hexane extraction left an insoluble solid. After washing with 10% potassium hydroxide, the solid recrystallized from ethanol as colorless 2-phenylbenzimidazole, mp 290–291°, 1.39 g (72%).

Other products are isolated by similar procedures and are described in Table I.

Registry No.—1a, 3488-57-1; 1b, 24706-91-0; 1c, 3488-55-9; 1d, 24711-18-0; benzenesulfonyl chloride, 98-09-9.