Reaction of Arylamidoximes with Dimethyl Acetylenedicarboxylate and Diethyl Chlorofumarate. Stereochemistry of the Adducts and the Derived 1,2,4-Oxadiazines (1).

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It was shown that the addition of benzamidoxime to dimethyl acetylenedicarboxylate was predominantly *cis*-oid in methanol or acetonitrile solution and mainly *trans*-oid when benzene was the solvent. The stereochemistry of the *cis*-oid (**4a**) and *trans*-oid (**5**) adducts was deduced by transformation into the oxadiazinones (**7a** and **8a**) which, upon hydrolysis and subsequent reaction with acetic anhydride, gave the furo-[2,3-*c*]-1,2,4-oxadiazine (**9**) and the symmetrical anhydride (**10**), respectively.

The reaction of diethyl chlorofumarate with the sodium salt of benzamidoxime produced the oxadiazinone (**8c**).

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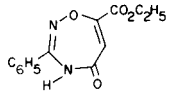
In 1898, Wolf (2) reported that warming an ethanolic solution of equimolar amounts of the sodium salt of benzamidoxime and diethyl chlorofumarate, gave a crystalline solid, m.p. 154°, which was considered to possess a structure represented by either formula **1** or **2a**. An analogous product was obtained from phenylacetamidoxime. On the basis that the oxadiazinone (**2a**) represented the correct structure of Wolf's compound (3) it occurred to us that substances of the general type **2** ought to be preparable from amidoximes and acetylene dicarboxylic acid esters. Indeed, it has recently been reported (4-6) that dimethyl acetylenedicarboxylate and amidoximes gave 1:1 adducts (**3**) which underwent cyclization (5) to the oxadiazinones (**2b**) under alkaline conditions. In no case, however, was Wolf's publication cited and only in one instance was reference (6) made to the stereochemistry of the adducts (**3**). No mention was made of the double bond stereochemistry of the oxadiazinones (**2b**). This paper contains experimental data which establishes the stereochemistry of the benzamidoxime-dimethyl acetylenedicarboxylate adducts and the derived oxadiazinones, as well as the structure and stereochemistry of Wolf's compound, m.p. 154°.



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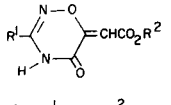
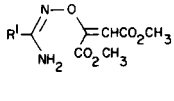


2a, $R^1=C_6H_5$, $R^2=C_2H_5$

2b, $R^2=CH_3$



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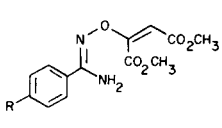
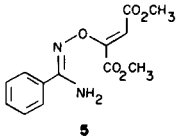
When a methanolic solution of benzamidoxime and dimethyl acetylenedicarboxylate was heated at reflux temperature, a high yield of a mixture (5.5:1) of isomeric adducts, separable by thin layer chromatography (tlc) on silica gel [hexane-ethyl acetate (7:3)], was obtained. Initially, the less polar, more abundant isomer was considered to have the (*E*)-geometry (**4a**) on the expectation that, as for alcohols (7), the uncatalysed addition of the amidoxime would occur in a *cis* manner. This assignment was taken to be mainly of heuristic value when it was found that the composition of the mixture was strongly solvent dependent. Thus, the isomer ratio varied from 2:1 in favor of the less polar isomer, when acetonitrile was the solvent, to 1:6.5 in benzene solution. Further discussion of this phenomenon is deferred to a later stage of the paper.



4a, R=H
4b, R=CH_3
4c, R=Cl
4d, R=OCH_3
4e, R=NO_2



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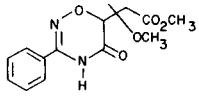

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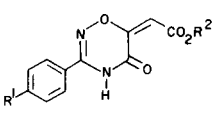
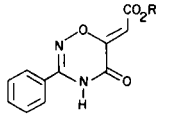
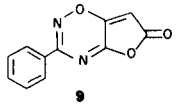


7a, $R^1=H$, $R^2=CH_3$
7b, $R^1=R^2=H$
7c, $R^1=H$, $R^2=C_2H_5$
7d, $R^1=R^2=CH_3$
7e, $R^1=Cl$, $R^2=CH_3$
7f, $R^1=CH_3O$, $R^2=CH_3$
7g, $R^1=NO_2$, $R^2=CH_3$



8a, R=CH_3
8b, R=H
8c, R=C_2H_5



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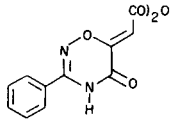

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The cyclization of the "so-called" (*E*)-adduct **4a** to the carbomethoxymethylenoxadiazinone **7a** was first attempted with sodium methoxide in methanol solution at reflux temperature. The principle product formed under these

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conditions was, however, the oxadiazinone (6) derived from the base catalysed addition of methanol to the activated olefinic system of **7a** (direction of addition not determined). This difficulty was obviated by effecting the cyclization with 1,4-diazabicyclo[4.3.0]non-4-ene (DBN) in acetonitrile solution, at reflux temperature, in which case **7a** was obtained in satisfactory yield. Under the same conditions, the isomeric adduct (5) gave a compound (**8a**) which was very similar, but not identical, to **7a**. Because of the sensitivity of **7a** and **8a** to the addition of nucleophiles, hydrolysis thereof was carried out in acidic solution (acetic acid-dilute sulfuric acid) at 40-50°. Sulfuric acid catalysed esterification with methanol reconverted the carboxylic acids (**7b** and **8b**) into the esters (**7a** and **8a**), respectively, confirming that no isomerization had taken place during the hydrolysis. Whereas the carboxylic acid (**7b**) was converted into the furo[2,3-*c*]-1,2,4-oxadiazine (**9**) [ir (chloroform): 1827, 1720 (w), 1676, 1620 cm^{-1}] on warming with acetic anhydride at 50°, the isomeric acid (**8b**) produced the symmetrical anhydride (**10**) [ir (chloroform): 3450, 3116, 1808, 1670, 1620 cm^{-1}] when heated at reflux temperature with the same reagent. Methanolysis of the bicyclic anhydro compound (**9**) at room temperature gave back the ester **7a** thus establishing that this compound and the precursor thereof (**4a**), did indeed possess the (*E*)-geometry. Ethanolysis of the symmetrical anhydride (**10**) gave the carboxylic acid (**8b**) and the corresponding ethyl ester (**8c**). The latter substance was identical to the compound, m.p. 154°, synthesized in the manner described by Wolf, and the physical properties thereof were considerably different from the product (**7c**) obtained by the acid catalysed esterification of the (*E*)-acid (**7b**).

The *para* substituted adducts (**4b-4e**), assumed to be of the (*E*)-series (8), were also synthesized by heating a methanol solution of the requisite amidoxime and dimethyl acetylenedicarboxylate. Compounds (**4a-4c**) have been described previously (4,5), as crystalline solids, but in our hands, adducts **4a** and **4b** were obtained as oils (Culbertson) (6) also described **4a** as an oil). Nevertheless, the nmr spectra of the literature compounds were identical (9) to those measured by us (Table II).

The cyclization of the adducts (**4b-4c**) to the oxadiazinones (**7d-7g**) (Tables I and II) was accomplished by the method described above for the synthesis of the parent system (**7a**). The ir and nmr spectra of the *p*-chloro compound (**7e**) were identical to those observed by Santilli and Scotese (9).

Heindel and Chun (10) have shown that aryl amidoximes add to propiolate esters, in methanol solution, to give the (*Z*)-adduct. This is in contrast to the results described herein for the reaction of benzamidoxime with dimethyl acetylenedicarboxylate which, under the same reaction conditions, gave the (*E*)-adduct (*cis*-oid addition) as the main product. Although a detailed study was not undertaken, the nature of the additon was strongly dependent on the dielectric constant of the solvent. Thus, predomi-

Table I

Yields, Physical Constants, *etc.*, of Amidoxime-Dimethyl Acetylenedicarboxylate Adducts and Derived 1,2,4-Oxadiazinones

Compound No.	Yield (%)	Crystallization Solvent	M.p. °C	Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
4a	76 (a)		oil (b)	56.10	5.07	10.06	55.78	5.09	10.07
4b	92		oil (c)						
4c	93	ether-hexane	65-66 (d)	49.92	4.18	8.96	49.98	4.16	9.15 (e)
4d	91	ether-hexane	67-68	54.53	5.23	9.08	54.39	5.32	9.23
4e	90	ether-hexane	114	48.30	4.05	12.99	48.17	4.09	13.00
5	78 (f)	ether-hexane	91	56.10	5.07	10.06	55.89	4.86	10.07
7a	51	ethyl acetate	176-178	58.53	4.09	11.38	58.37	4.01	11.46
7b	27	methanol	214-215	56.89	3.47	12.06	56.97	3.44	12.26
7c	39	dichloromethane-hexane	138	59.99	4.64	10.76	59.91	4.63	10.45
7d	70	ethyl acetate-hexane	240	59.99	4.64	10.76	60.03	4.70	10.82
7e	56	ethyl acetate-hexane	229 (g)	51.34	3.23	9.98	51.51	3.26	9.99 (h)
7f	58	ethyl acetate-hexane	232	56.51	4.38	10.14	56.42	4.25	10.04
7g	60	ethyl acetate-hexane	238	49.49	3.11	14.42	49.51	3.15	14.49
8a	56	ethyl acetate-hexane	182-183	58.53	4.09	11.38	58.35	4.04	11.59
8b	25	tetrahydrofuran-hexane	219-220	56.89	3.47	12.06	56.60	3.44	11.93
8c	53	ethanol	154-156 (i)	59.99	4.64	10.76	59.89	4.71	10.82

(a) A 14% yield of **5** was also obtained. (b) Heindel and Chun (4) report m.p. 78-79°. The nmr spectrum of **4a** was identical to that recorded by these authors (see reference 9). (c) Heindel and Chun (4) report m.p. 69-70°. The nmr spectrum of **4b** was identical to that recorded by these authors (see reference 9). Satisfactory analysis not obtained, but mass spectrum consistent with structure. (d) Literature m.p. 57-58° (4) and 58-60° (5). The ir and nmr spectra of the literature compound and **4d** were identical (see reference 9). (e) Calcd. for $C_{13}H_{13}ClN_2O_5$: Cl, 11.33. Found: Cl, 11.23. (f) A 12% yield of **4a** was also obtained. (g) Literature (5) m.p. 232-235°. The ir and nmr spectra of **7e** and the literature compound were identical (see reference 9). (h) Calcd. for $C_{12}H_9ClN_2O_4$: Cl, 12.63. Found: C, 12.74. (i) Literature (2) m.p. 154°.

Table II

Spectral Properties of Amidoxime-Dimethyl Acetylene Dicarboxylate Adducts and Derived 1,2,4-Oxadiazinones

Compound No.	Uv λ Max (log ε) (a)	Ir (cm^{-1}) (b)	Nmr (δ ppm) (c)
4a	224 (4.07), 273 (3.19)	3530, 3425, 3270, 1740, 1722, 1650, 1588	3.67 (s, 3H), 3.85 (s, 3H), 5.47 (m, 2H) (d), 5.85 (s, 1H), 7.24-7.70 (m, 5H)
4b	229 (4.37), 269 (4.21)	3445, 3330, 1730, 1718, 1628, 1586	2.32 (s, 3H), 3.63 (s, 3H), 3.80 (s, 3H), 5.37 (m, 2H) (d), 5.78 (s, 1H), 7.08 (d, 2H, J = 8.0), 7.42 (d, 2H, J = 8.0)
4c	228.5 (4.23), 275 (3.97)	3535, 3425, 3365, 1723, 1640, 1603, 1583	3.69 (s, 3H), 3.83 (s, 3H), 5.47 (m, 2H) (d), 5.86 (s, 1H), 7.58 (q, 4H, J = 8.5)
4d	213 (4.08), 246.5 (4.15), 278 sh (4.03)	3530, 3430, 3365, 1720, 1635, 1615, 1588	3.69 (s, 3H), 3.79 (s, 3H), 3.83 (s, 3H), 5.40 (m, 2H) (d), 5.78 (s, 1H), 6.82 (d, 2H, J = 8.8), 7.48 (d, 2H, J = 8.8)
4e	215 (4.09), 257 (4.10), 300 (3.86)	3534, 3430, 1724, 1644, 1606, 1522	3.70 (s, 3H), 3.83 (s, 3H), 5.48 (m, 2H) (d), 5.88 (s, 1H), 7.72 (d, 2H, J = 8.6), 8.16 (d, 2H, J = 8.6)
5	222 (4.07), 275.5 (4.16)	3545, 3440, 1760, 1718, 1620, 1589, 1571	3.70 (s, 3H), 3.92 (s, 3H), 5.21 (m, 2H) (d), 6.14 (s, 1H), 7.25-7.72 (m, 5H)
7a	240 (4.15), 262 (4.13), 310 (3.94)	3420, 3240, 1700, 1630, 1614 (e)	3.73 (s, 3H), 6.04 (s, 1H), 7.25-7.43 (m, 3H), 7.60-7.67 (m, 2H) (f)
7b	237 (4.14), 263.5 (4.15), 305 sh (3.87)	3450, 3245, 3220, 1715, 1691, 1647, 1617 (e)	5.83 (s, 1H), 7.28-7.55 (m, 3H), 7.60-7.84 (m, 2H) (f)
7c	235 (4.16), 260 (4.12), 305 (3.89)	3420, 3230, 1697, 1645, 1617 (e)	1.31 (t, 3H, J = 7), 4.25 (q, 2H, J = 7), 6.15 (s, 1H), 7.40-7.91 (m, 5H)
7d	258 (4.20), 305 (3.92)	3445, 3220, 3150, 1698, 1648, 1611 (e)	2.40 (s, 3H), 3.70 (s, 3H), 5.97 (s, 1H), 7.23 (d, 2H, J = 8.2), 7.66 (d, 2H, J = 8.2)
7e	245.5 (4.22), 270 (4.19) 310 sh (3.95)	3245, 1735, 1730, 1698, 1661, 1647, 1620, 1597 (e)	3.73 (s, 3H), 6.03 (s, 1H), 7.35 (d, 2H, J = 8.8) 7.57 (d, 2H, J = 8.8) (f)
7f	271 (4.35), 320 sh (3.87)	3240, 3150, 1735, 1697, 1647, 1603 (e)	3.73 (s, 3H), 4.00 (s, 3H), 6.04 (s, 1H), 6.82 (d, 2H, J = 8.7), 7.72 (d, 2H, J = 8.7) (f)
7g	215 (4.05), 255 (4.06) 303 (4.09)	3220br, 1719, 1625, 1600, 1527 (e)	3.67 (s, 3H), 5.90 (s, 1H), 8.09 (q, 4H, J = 8.7) (f)
8a	241 (4.08), 270 (4.05) 310 (3.80)	3430, 3240, 1703, 1655 w, 1626 w, 1618, 1577 (e)	3.70 (s, 3H), 6.00 (s, 1H), 7.38-7.54 (m, 3H), 7.72-7.88 (m, 2H)
8b	237 (4.11), 263 (4.11) 310 (3.81)	3450, 3245, 3210, 2720, 2615, 2515, 1715, 1692, 1648, 1618, 1573 (e)	6.00 (s, 1H), 7.42-7.48 (m, 5H) (f)
8c	230 (4.10), 260 (4.08), 305 (3.83)	3500, 3410, 3245, 3215, 1727, 1707, 1647, 1619	1.32 (t, 3H, J = 7), 4.24 (q, 2H, J = 7), 6.12 (s, 1H), 7.40-7.84 (m, 5H), 9.95 (m, 1H) (d)

(a) Measured in methanol solution. (b) Measured in chloroform solution unless specified otherwise. (c) Measured in deuteriochloroform unless specified otherwise. (d) Exchanges with deuterium oxide. (e) Measured in potassium bromide. (f) Measured in deuteriochloroform-deuteriodimethylsulfoxide solution.

nant *trans*-oid addition occurred in solvents of low dielectric constant (benzene) while mainly *cis* addition took place in methanol or acetonitrile. This trend is also different from the reported (10) stereochemistry of addition of primary and secondary amines to dimethyl acetylenedicarboxylate, which is mainly *cis*-oid in all solvents except methanol. Culbertson (6) has reported that a 1:3 mixture of *cis-trans* adducts (*i.e.*, **4a** and **5**) was obtained from benzamidoxime and dimethyl acetylene dicarboxylate, in methanol solution, but no evidence to support this assignment was presented. Inasmuch as the nmr spectral data, given by this author, for the major and the minor components correspond to that measured by us (Table II) for the *cis*-**4a** and the *trans*-**5** adducts, respectively, it is probable that his assignment should be reversed.

EXPERIMENTAL

The melting points were determined in a Mel-Temp apparatus and are corrected. The infrared spectra were measured with a Perkin-Elmer model 237 grating infrared spectrophotometer. The ultraviolet spectra were recorded with a Perkin-Elmer model 402 ultraviolet visible spectrophotometer. The nmr spectra were obtained with a Varian T-60 spectrometer. The chemical shifts are expressed as ppm(δ) from internal tetramethylsilane. The mass spectra were measured with an Atlas CH-4 spectrometer.

The amidoximes which were utilized are known and were prepared by the addition of hydroxylamine to the appropriate benzonitrile (see Table 2 in reference 3).

Reaction of the Amidoximes with Dimethyl Acetylenedicarboxylate

(A) Preparation of the (*E*)-Adducts (**4a-4c**).

A solution of the amidoxime (1 equivalent) in methanol (20 ml./g. of amidoxime taken) containing dimethyl acetylenedicarboxylate (1.3

equivalent) was either heated at reflux temperature for 0.5 hours (**4a**) or left at room temperature for 2 hours (**4b-4c**). The solvent was removed *in vacuo* and the residue was subjected to column chromatography on florisil (40 g./g. of amidoxime taken). The product was eluted from the column with a suitable solvent system: **4a**, **4b** [hexane-ethyl acetate (9:1)], **4c**, **4d** [hexane-ethyl acetate (4:1)], and **4e** [hexane-ethyl acetate (7:3)]. The adducts were purified for analysis by crystallization or by tlc on silica gel (see Tables I and II for analytical and spectroscopic data).

(B) Synthesis of the (*Z*)-adduct (**5**).

A solution of benzamidoxime (1 equivalent) and dimethyl acetylenedicarboxylate (1.3 equivalent) in benzene (15 ml./g., of benzamidoxime) was heated at reflux temperature for 16 hours. After workup (see A) the crude product was subjected to column chromatography on florisil using hexane-ethyl acetate to elute the desired product. See Tables I and II.

Synthesis of Oxadiazinone (**6**).

A solution of the (*E*)-adduct (**4a**, 5.0 g., 18 mmoles) in methanol (15 ml.), containing an equimolar amount of sodium methoxide, was heated at reflux temperature for 2 hours. The solution was cooled, neutralized with acetic acid, and the resultant was evaporated *in vacuo*. Water was added to the residue and the solid thus obtained (3.2 g., 64%, m.p. 120-123°) was collected by filtration. Crystallization of this material from ethyl acetate-hexane gave a solid, m.p. 129-131°; ir (chloroform): 3405, 3220, 1747, 1631 (w) cm^{-1}; nmr (deuteriochloroform): 2.98 (d, 1H, J = 16 Hz), 3.33 (d, 1H, J = 16 Hz), 3.38 (s, 3H), 3.62 (s, 3H), 7.31-7.47 (m, 3H), 7.56-7.77 (m, 2H); ms: (relative intensity) 278 (4), 133 (32), 119 (35), 118 (100), 104 (27), 103 (59), 101 (32), 91 (13), 77 (23), 59 (34), 57 (15), 51 (10), 43 (11).

Anal. Calcd. for $C_{13}H_{14}N_2O_5$: C, 56.11; H, 5.07; N, 10.07. Found: C, 56.49; H, 4.87; N, 10.20.

Synthesis of the Carbomethoxymethylene Oxadiazines (**7a**, **7d-7g**, and **8a**).

The amidoxime dimethyl acetylenedicarboxylate adduct (1 equivalent) in acetonitrile (15-20 ml./g. of adduct), containing DBN (1.1-1.3 equivalent) was heated at reflux temperature; 3 hours in the case of **4b-4c** and 18 hours for **4a** and **5**. The solvent was removed *in vacuo* and the residue was subjected to column chromatography on florisil (30 g./g. of adduct taken). In all cases except **7f**, the product was removed from the column by initial elution with an ethyl acetate-hexane solution (4:1) which was gradually decreased in hexane contact until pure ethyl acetate was used. Compound (**7f**) was eluted from the column with ethyl acetate. The products thus obtained were crystallized from a suitable solvent system. See Tables I and II for analytical and spectroscopic data.

(*E*) or (*Z*)-3-Phenyl-6-carboxymethylene-4,5-dihydro-6*H*-1,2,4-oxaidazin-5-one (**7b** or **8b**).

A solution of the ester (2.0 g., 8.14 mmoles) in a mixture of 10% sulfuric acid (60 ml.) and glacial acetic acid (80 ml.) was heated at 40-50° for 64 hours. Water was added, the precipitated solid was collected by filtration and crystallized from a suitable solvent (see Tables I and II).

3-Phenyl-6*H*-furo[2,3-*c*]-1,2,4-oxadiazin-6-one (**9**).

A solution of the (*E*)-carboxylic acid (**7b**, 0.300 g., 1.29 mmoles) in acetic anhydride (2 ml.) was heated at 50° for 16 hours. The solvent was removed *in vacuo* and benzene was added to the residue. The resultant was evaporated *in vacuo* (repeated twice) and the residue was passed over a column of silica gel (10 g.) using anhydrous dichloromethane as the eluting solvent. The solid (0.115 g., 42%) thus obtained was crystallized from ethyl acetate-hexane and had m.p. 146.5-147.5°; ir (chloroform): 1827, 1720 (w), 1620 cm^{-1}; nmr (deuteriochloroform): 5.72 (s, 1H), 7.33-7.61 (m, 3H), 7.97-8.17 (m, 2H).

Anal. Calcd. for $C_{11}H_6N_2O_3$: C, 61.68; H, 2.82; N, 13.08. Found: C, 61.77; H, 3.11; N, 13.32.

Synthesis of the Symmetrical Anhydride (**10**).

A solution of the (*Z*)-acid (**8b**, 0.300 g.) in acetic anhydride (3 ml.) was heated at reflux temperature for 24 hours. The reaction was worked up exactly as described for **9** to give the anhydride (**10**) in quantitative yield. After crystallization from dichloromethane-hexane, it had m.p. 135.5-136.5°; ir (potassium bromide): 3450, 3116, 1808, 1670, 1620 cm^{-1}; nmr (deuteriochloroform): 5.62 (s, 2H), 7.36-7.60 (m, 6H), 7.82-8.13 (m, 4H), 8.56 (s, 2H, W_H = 12 Hz).

A satisfactory microanalysis could not be obtained for this substance. The ir spectrum and the fact that ethanolysis of this compound (see below) gave a mixture of the expected ethyl ester (**8c**) and the starting acid (**8b**) leave little doubt concerning the structure thereof.

(*E*)-3-Phenyl-6-carbomethoxymethylene-4,5-dihydro-6*H*-1,2,4-oxadiazin-6-one (**7a**).

(A) Esterification of (*E*)-Carboxylic Acid (**7b**).

A solution of the (*E*)-carboxylic acid (**7b**, 0.300 g.), in methanol (60 ml.), and benzene (60 ml.), containing concentrated sulfuric acid (2 drops), was heated with slow distillation to remove the water formed in the reaction. After 64 hours, the solvent was removed *in vacuo* and the residue was taken up in ethyl acetate. The solution was washed with saturated sodium chloride solution, it was dried over sodium sulfate, and evaporated *in vacuo*. The residue was subjected to tlc on silica gel using hexane-ethyl acetate (1:1) as the developing solvent. The product thus obtained (0.136 g., 43%) had m.p. 176-178°, after crystallization from ethyl acetate-hexane, and was identical in all respects to **7a** synthesized by cyclization of (*E*)-adduct (**4a**).

(B) Methanolysis of Compound **9**.

A mixture of compound **9** (0.214 g., 1.0 mmoles), methanol (0.05 ml.), and pyridine (2 drops) was left at room temperature for 16 hours. Water was added and the mixture was made acidic with 10% hydrochloric acid. The product was extracted into ethyl acetate, the extract was washed with saturated sodium chloride solution, dried over sodium sulfate and evaporated *in vacuo*. After purification by tlc and crystallization the ester (0.168 g., 68%) had m.p. 176-178° and was indistinguishable from an authentic specimen.

Synthesis of (*Z*)-3-Phenyl-6-carbomethoxymethylene-4,5-dihydro-6*H*-1,2,4-oxadiazin-5-one (**8a**) by esterification of **8b**.

The esterification of **8b** with methanol was carried out exactly as desired above for the esterification of (**7b**). The reaction product was subjected to tlc on silica gel [hexane-ethyl acetate (7:3)]. The material thus obtained (54%) had m.p. 175-179°, and was indistinguishable from **8a** prepared by the cyclization of the (*Z*)-adduct (**5**).

Synthesis of (*E*)-3-Phenyl-6-carobethoxymethylene-4,5-dihydro-6*H*-1,2,4-oxadiazin-5-one (**7c**) by esterification of **7b**.

The sulfuric acid catalysed esterification of **7b** with ethanol was carried out as described for the synthesis of **7a**, except that the ternary benzene-ethanol-water mixture was distilled during 48 hours. The crude ester was purified by column chromatography on florisil (50 g./mmole of acid taken) using hexane-ethyl acetate (9:1) to elute the product (39%). After crystallization from dichloromethane-hexane it had m.p. 138° (see Table I and II).

(*Z*)-3-Phenyl-6-carboethoxymethylene-4,5-dihydro-6*H*-1,2,4-oxadiazin-5-one (**8c**).

(A) From the Sodium Salt of Benzamidoxime and Ethyl Chlorofumarate.

An equimolar mixture of the sodium salt of benzamidoxime and ethyl chlorofumarate was heated at reflux temperature, in ethanol solution, for 3 hours. The product was worked up as reported by Wolf (2) and after purification by tlc on silica gel [benzene-dioxan-acetic acid (95:5:0.2)] the ester (35%) was crystallized from ethanol to give a solid m.p. 154-156° (lit. (2) m.p. 154°) (see Tables I and II).

(B) Esterification of (*Z*)-Acid (**8b**) with Ethanol.

The esterification was effected exactly as described for the synthesis of **7c**. The product was purified by tlc (see (A) above) and after crystallization from ethanol, it had m.p. 153-155° (53%) and was identical to the compound prepared by the method of Wolf.

(C) Ethanolysis of the Symmetrical Anhydride (**10**).

The symmetrical anhydride (0.150 g., 0.33 mmoles), absolute ethanol (0.02 ml.) and pyridine (2 drops) were left at room temperature for 16 hours. The reaction was worked up as described for the synthesis of **7a** from **9**. The crude product was subjected to tlc on silica gel [same solvent system as in (A)] to give the ethyl ester (**8c**, 0.052 g., 60% and the (*Z*)-acid (**8b**, 0.032 g., 41%). The ester had m.p. 153-155° after crystallization from methanol.

REFERENCES AND NOTES

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(8) In most cases, the nmr spectra of the crude products showed the presence of a small amount of another, presumably isomeric, substance.

(9) We thank Professor Heindel for providing us with the spectral data for compounds **4a** and **4b** and Dr. Santilli for the nmr and ir spectra of **4c** and **7c**.

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