

2,5-Diarylimidazo[4,5-*d*]imidazoles

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and

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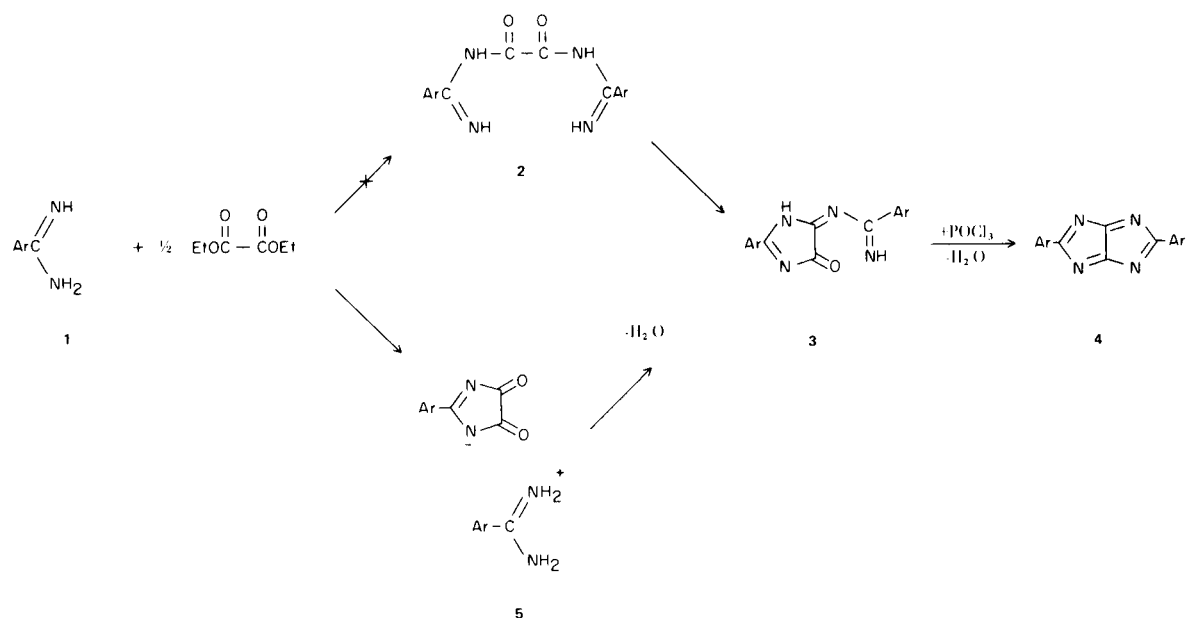
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In the course of screening a wide variety of heterocyclic compounds as insect sterilants (2), we became interested in preparing a few derivatives of the previously unreported imidazo[4,5-*d*]imidazole system 4 (3). We felt that if diethyl oxalate could be condensed with two equivalents of an amidine, it might be possible to cyclodehydrate the adduct 2 in one or two stages to the desired product 4. Examination of the literature revealed that a 2:1 adduct of benzamidine and diethyl oxalate had been reported, but that the product was evidently the benzamidinium salt of 2-phenylimidazole-4,5-dione (5a) (4).

It appeared to us that 5a might also serve as a pre-

cursor to 3a or 4a, and we therefore prepared a sample of 5a and heated it in the absence of solvent at 200° for ca. 20 minutes. The reported (4) decomposition and color loss was observed; a white solid was obtained whose empirical formula, C<sub>14</sub>H<sub>12</sub>N<sub>4</sub>O, corresponded to the loss of one molecule of water from 5a. Structure 3a was tentatively assigned to this product (5), although we have been unable to choose unambiguously between various tautomeric possibilities. Final dehydration of 3a to the desired 2,5-diphenylimidazo[4,5-*d*]imidazole (4a) was effected by heating 3a with phosphorus oxychloride in pyridine. The analogous derivatives 4b-d were prepared



- a: Ar = C<sub>6</sub>H<sub>5</sub>  
 b: Ar = *p*-CH<sub>3</sub>-C<sub>6</sub>H<sub>4</sub>  
 c: Ar = *p*-CH<sub>3</sub>OC<sub>6</sub>H<sub>4</sub>  
 d: Ar = 3,4,5-(CH<sub>3</sub>O)<sub>3</sub>C<sub>6</sub>H<sub>2</sub>

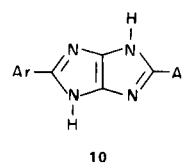
similarly from the appropriately substituted benzamidines.

The nmr spectrum (deuteriochloroform) of **4a** consists of two multiplets centered at 7.55 (6H) and 8.62 (4H) ppm, indicating substantial deshielding of the *ortho* hydrogens. In addition, the nmr spectra of the substituted derivatives **4b-d** clearly showed that the two phenyl rings were in identical environments and that cyclization onto one of the phenyl rings, *i.e.*, to give some other ring system, had not occurred.

Elemental analyses of the products were correct for the structures shown, and a molecular ion peak at *m/e* 258 (rel. intensity 56%) in the mass spectrum of **4a** confirmed the molecular weight. Fragments at *m/e* 155 (3.4%, M - PhCN), 129 (2.4%, M - PhC<sub>2</sub>N<sub>2</sub>), 103 (100%, PhCN), 76 (18%, C<sub>6</sub>H<sub>4</sub>), and 52 (4.3%, N≡C-C≡N), support the proposed structure. The phenyl derivative **4a** had  $\lambda_{\max}$  278 nm ( $\epsilon$  5 x 10<sup>2</sup>), and the infrared spectra of **4a-d** contained characteristic bands at 1590 (m), 1530 (s), 1505 (s), 1370 (s), and 1170 (s) cm<sup>-1</sup>.

1,1-Dimethylguanidine reacted with diethyl oxalate in absolute ethanol to give a water-soluble, *white* product that analyzed correctly for the expected 2:1 adduct. Attempted thermal dehydration did not provide an analog of **3**, but rather gave a low yield of a material that appeared to analyze for C<sub>5</sub>H<sub>13</sub>N<sub>3</sub>O<sub>2</sub> and that has not been further characterized. Attempted dehydration with phosphorus oxychloride was also unsuccessful.

As yet we have not investigated the chemistry of the imidazo[4,5-*d*]imidazole compounds except for several attempts (lithium/ammonia, lithium/THF, sodium borohydride/DMF) to reduce **4a** and **4b** to the 10 $\pi$ -electron system **10** (6). The reductions proceeded very slowly and complex mixtures resulted from which no fully characterized products have been obtained.



#### EXPERIMENTAL (6)

Melting points are uncorrected. Nuclear magnetic resonance spectra were recorded on a Varian Model T-60 spectrometer, infrared spectra on a Perkin Elmer Model 137 Infracord, ultraviolet spectra on a Cary Model 14 spectrophotometer, and mass spectra on a Finnigan Model 1015 Quadrupole mass spectrometer. Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tennessee. Benzamidine hydrochloride was purchased; other amidines were synthesized by the Pinner method (7).

Benzamidinium Salts of 2-Phenylimidazole-4,5-diones (**5a-d**).

The general procedure of Goerdeler and Sappelt (4) was followed. Melting points and recrystallization solvents are included in Table I.

TABLE I

No.	M.p., °C	Yield, %	Recryst. Solvent	Formula	C	Elemental Analyses				
						Calcd. H	N	C	Found H	N
<b>5a</b>	192 dec.			C <sub>16</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub>		ref. 4				
<b>5b</b>	195 dec.	86	(a)	C <sub>18</sub> H <sub>18</sub> N <sub>4</sub> O <sub>2</sub>	67.07	5.63	17.38		(a)	
<b>5c</b>	235-247 dec.	24	(b)	C <sub>18</sub> H <sub>18</sub> N <sub>4</sub> O <sub>4</sub>	61.01	5.12	15.81	60.94	5.25	15.60
<b>5d</b>	222.5-223.5 dec.	100	<i>i</i> -PrOH	C <sub>22</sub> H <sub>26</sub> N <sub>4</sub> O <sub>8</sub>	55.69	5.52	11.81	55.83	5.62	11.77
<b>3a</b>	240-242	74	Me <sub>2</sub> CO	C <sub>16</sub> H <sub>12</sub> N <sub>4</sub> O	69.55	4.38	20.28	69.66	4.26	20.09
<b>3b</b>	245-246.5	78	MePh-Py	C <sub>18</sub> H <sub>16</sub> N <sub>4</sub> O	71.03	5.30	18.41	70.91	5.29	18.54
<b>3c</b>	240-241 dec.	46	MeCN	C <sub>18</sub> H <sub>16</sub> N <sub>4</sub> O <sub>3</sub>	64.28	4.79	16.66	64.49	4.80	16.81
<b>3d</b>	217-219	25	DMF	C <sub>22</sub> H <sub>24</sub> N <sub>4</sub> O <sub>7</sub>	57.89	5.30	12.27	58.01	5.59	12.40
<b>4a</b>	181.5-183	50	EtOAc	C <sub>16</sub> H <sub>10</sub> N <sub>4</sub>	74.40	3.90	21.69	74.41	3.95	21.90
<b>4b</b>	236.5-239	47	DMF	C <sub>18</sub> H <sub>14</sub> N <sub>4</sub>	75.50	4.93	19.59	75.53	4.94	19.50
<b>4c</b>	175	41	MeCN-CHCl <sub>3</sub>	C <sub>18</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub>	67.92	4.43	17.60	68.04	4.27	17.80
<b>4d</b>	236-238	22	CHCl <sub>3</sub>	C <sub>22</sub> H <sub>22</sub> N <sub>4</sub> O <sub>6</sub>	60.27	5.06	12.78	60.07	4.97	12.73

- (a) We were unable to find a satisfactory recrystallization solvent for this compound, and a correct elemental analysis was not obtained.  
 (b) This salt was washed well with THF but was not recrystallized.

*N*-(5-Oxo-2-phenyl-2-imidazolin-4-ylidene)benzamides (**3a-d**).

A sample of a benzamidine salt **5** was placed in a pyrex tube or flask, and the vessel was heated in an oil bath at 200° for ca. 1 hour. The sample was cooled, triturated with benzene and collected, or recrystallized directly from an appropriate solvent (see Table I).

Imidazo[4,5-*d*]imidazoles (**4a-d**).

A typical example is the preparation of the *p*-methoxy derivative **4c** from **3c**. A solution of phosphorus oxychloride (4 ml.) in pyridine (20 ml.) was added to a solution of **3c** (7 g.) in pyridine (60 ml.), then the solution was heated in an oil bath at 90° for 3 hours. The solvent was stripped *in vacuo* and the residue was neutralized with aqueous sodium bicarbonate. The crude product was collected by filtration, dried, and chromatographed on Florisil. Elution with dichloromethane gave 4.2 g. of **4c** that was recrystallized from acetonitrile-chloroform to give 2.7 g. of **4c**, m.p. 175°.

## Reaction of 1,1-Dimethylguanidine with Diethyl Oxalate.

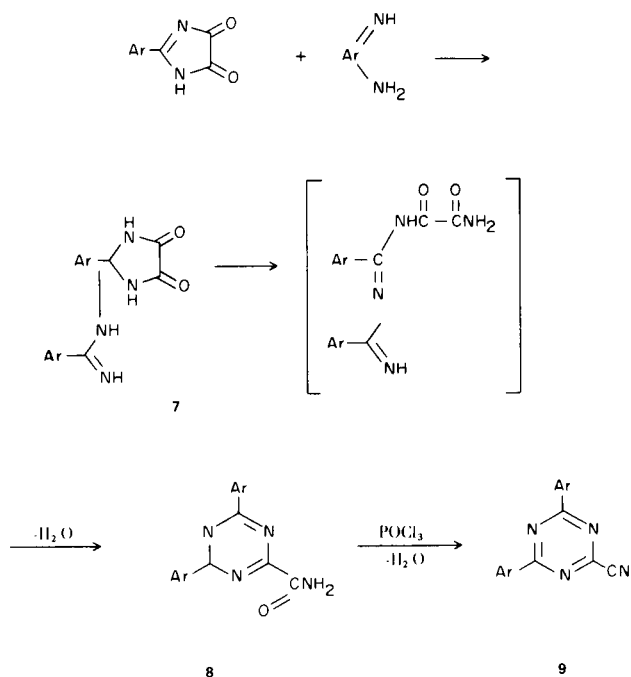
A solution of 25.1 g. of 1,1-dimethylguanidine dihydrochloride in absolute ethanol (80 ml.) was treated with a solution of sodium ethoxide (from 4.7 g. of sodium) in ethanol (150 ml.). The resulting mixture was stored in a refrigerator overnight, then centrifuged to remove sodium chloride. The clear solution thus obtained was treated with diethyl oxalate (14.8 g.) at room temperature. A solid separated and was collected; a second crop was obtained by concentrating the filtrate to give a total of 18.7 g. (81%), m.p. 243-244° dec. An analytical sample was recrystallized from ethyl acetate-ethanol, m.p. 232° dec.

*Anal.* Calcd. for C<sub>8</sub>H<sub>16</sub>N<sub>6</sub>O<sub>2</sub>: C, 42.10; H, 7.07; N, 36.82. Found: C, 42.17; H, 6.93; N, 36.97.

## REFERENCES

- (1) Author to whom correspondence should be addressed.
- (2a) J. E. Oliver, S. C. Chang, R. T. Brown, J. B. Stokes, and A. B. Borkovec, *J. Med. Chem.*, **15**, 315 (1972); (b) J. E. Oliver and M. M. Crystal, *J. Econ. Entomol.*, **65**, 303 (1972); (c) J. E. Oliver and A. B. DeMilo, *J. Heterocyclic Chem.*, **8**, 1087 (1971).
- (3) The ring system has been prepared in reduced forms, e.g., by condensing glyoxal with ureas (J. Nematollahi and R. Ketcham, *J. Org. Chem.*, **28**, 2378 (1963)), and benzil with guanidine (M. Lempert-Sreter, V. Solt, and K. Kempert, *Magy. Kem. Folyoirat*, **69**, 237 (1963)); cf. *Chem. Abstr.*, **59**, 10022b (1963)).
- (4) J. Goerdeler and R. Sappelt, *Chem. Ber.*, **100**, 2064 (1967).
- (5) An alternative condensation in which benzamidine adds across a C=N double bond of the 2-arylimidazole-4,5-dione was

considered (see reference 4); ring-opening and loss of water from the initial adduct **7** might be expected to result in the *s*-triazine-carboxamide **8** which could be further dehydrated with phosphorus oxychloride to the nitrile **9**. The absence of characteristic *s*-



triazine bending absorption at 800-820 cm<sup>-1</sup> (M. St. C. Fleet, "Characteristic Frequencies of Chemical Groups in the Infra-red", Elsevier Publishing Co., Amsterdam, 1963, p. 83) in the infrared spectra of **3** and **4**, and of C≡N absorptions in the spectra of **4** eliminate this possibility.

(6) The parent compound of this system has recently been reported. J. P. Ferris and F. R. Antonucci, *Chem. Commun.*, 126 (1972).

(7) Mention of a commercial or proprietary product in this paper does not constitute an endorsement of this product by the U. S. Department of Agriculture.

(8) A. Pinner and F. Klein, *Ber.*, 1889 (1877).