Evidence for the Existence of a New 8 π-Electron System, 1,3,5-Thiadiazinide Anion

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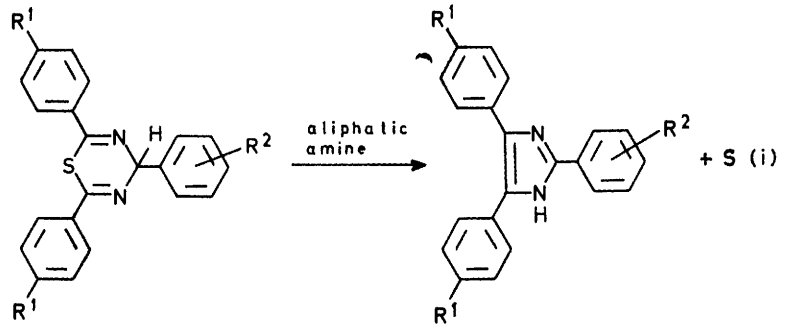
2,4,6-Triaryl-4*H*-1,3,5-thiadiazines react with catalytic amounts of aliphatic amines to afford 2,4,5-triarylimidazoles and sulphur in nearly quantitative yield. The proposed intermediate of this reaction is the very reactive, planar, conjugated 8 π-electron system, 2,4,6-triaryl-1,3,5-thiadiazinide anion. Kinetic evidence for formation of this anion is reported. Moreover a hydrogen isotope effect for ring contraction of 2,4,6-triphenyl-[4-^{2}H]4*H*-1,3,5-thiadiazine is reported. The reaction has been extended to 2,6-diaryl- and 4-alkyl-2,6-diaryl-4*H*-1,3,5-thiadiazines.

BRESLOW [1] and DEWAR [2] have pointed out that cyclic, conjugated $4n$ π-electron systems are destabilized by resonance. They named this phenomenon 'anti-aromaticity'. Schmidt [3] has shown that six-membered, conjugated, planar heterocyclic anions (1,3-oxazinide, 1,3-thiazinide, *etc.*), with bond angles of *ca.* 120° are suitable models for studying this destabilizing effect. He prepared such systems by treating the appropriate heterocyclic compounds with strong base.

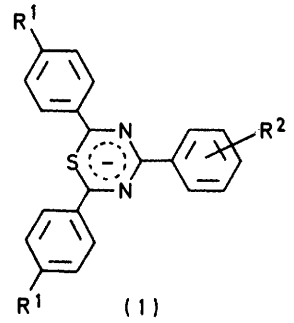
Recently we have reported the formation of 2,4,5-triarylimidazoles[4] by base catalysed ring contraction of 2,4,6-triaryl-4*H*-1,3,5-thiadiazines [5] (Scheme 1). For this reaction we proposed a mechanism involving the formation of a new reactive planar 8 π-electron system,

[1] R. Breslow, *Angew. Chem.*, 1968, **80**, 573; *Angew. Chem. Internat. Edn.*, 1968, **7**, 565.
[2] M. J. S. Dewar, *Angew. Chem.*, 1971, **83**, 859; *Angew. Chem. Internat. Edn.*, 1971, **10**, 761.
[3] R. R. Schmidt, *Angew. Chem.*, 1975, **87**, 603; *Angew. Chem. Internat. Edn.*, 1975, **14**, 581.
[4] C. Giordano and A. Belli, *Synthesis*, 1975, 167.
[5] C. Giordano, A. Belli, and V. Bellotti, *Synthesis*, 1975, 266.

2,4,6-triaryl-1,3,5-thiadiazinide anion (1). We now report a kinetic study of the reaction which provides evidence for the formation of anion (1). In addition we report the extension of the reaction to another set of 4*H*-1,3,5-thiadiazines using potassium t-butoxide as base (Scheme 2).



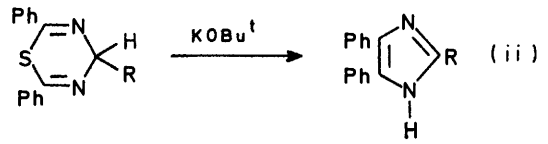
SCHEME 1



(1)

EXPERIMENTAL

Amines were commercially available. They were purified by distillation or crystallization. 4*H*-1,3,5-Thiadiazines were prepared by a previously described procedure.[5] α-Deuteriobenzaldehyde (isotopic purity >98%) was obtained from Merck, Sharp, and Dohme (Canada). M.p.s were determined by the Kofler method. U.v. spectra were recorded with a Unicam SP 1800 spectrophotometer.



R = H or CH_3

SCHEME 2

General Procedure.—Kinetic data were determined by monitoring the increase in absorbance of imidazoles at 320 nm for at least two half-lives. A thermostatted 10 mm cell was used as reaction chamber.

2,4,6-*Triphenyl*-[4-^{2}H]4H-1,3,5-*thiadiazine.*—Boron trifluoride–ether (0.75 ml, 6 × 10^{-3} mol; *d* 1.13) was added, at 0—5 °C, to a stirred mixture of thiobenzamide (0.41 g, 3 × 10^{-3} mol), α-deuteriobenzaldehyde (0.32 g, 3 × 10^{-3} mol), and benzonitrile (0.31 g, 3 × 10^{-3} mol) in chloroform (3 ml). The mixture was stirred for 18 h at room temperature. It was poured into ice, made alkaline with saturated sodium carbonate solution, and extracted with diethyl ether. The solvent was distilled off *in vacuo*. Chromatography of the residue on SiO_2 (50 g; 70—230 mesh) using light petroleum (b.p. 40—60°)–diethyl ether (90 : 10) as eluant gave the product, which was crystallized from n-heptane; yield 0.64 g (65%), isotopic purity 98 ± 1% (n.m.r.), m.p. 146—147°.

Hydrogen–Deuterium Exchange.—Path A. Anhydrous piperidine (0.85 ml, 8.5 × 10^{-3} mol; *d* 0.861) was added, under nitrogen, at room temperature, to a stirred solution of 2,4,6-triphenyl-[4-^{2}H]4*H*-1,3,5-thiadiazine (360 mg, 1.1 × 10^{-3} mol) in benzene (110 ml). The solution was kept at room temperature for 50 min and then washed with D_2SO_4 (2 ml) in D_2O (30 ml) to remove the resultant imidazole (180 mg). The aqueous layer was extracted with benzene and the combined benzene extracts were evaporated *in vacuo*. The residue (160 mg) was crystallized from n-heptane to give 2,4,6-triphenyl-[4-^{2}H]4*H*-1,3,5-thiadiazine (70 mg), isotopic purity 93 ± 1% (mass spectroscopy), 95 ± 1% (n.m.r.).

Path B. Anhydrous piperidine (1.7 ml, 1.7 × 10^{-2} mol; *d* 0.861) was added under nitrogen at room temperature to a stirred solution of [4-^{2}H]2,4,6-triphenyl-4*H*-1,3,5-thiadiazine (720 mg, 2.2 × 10^{-3} mol) in benzene (220 ml). The solution was kept at room temperature for 50 min, then washed with 2N-H_2SO_4 (2 × 50 ml) and the aqueous layer was extracted with benzene. The combined benzene extracts were evaporated *in vacuo*, and the residue was crystallized from n-heptane to give 2,4,6-triphenyl-[4-^{2}H]4*H*-1,3,5-thiadiazine (200 mg), isotopic purity 93 ± 1% (mass spectroscopy).

2-*Methyl*-4,5-*diphenylimidazole.*—Potassium t-butoxide (3.4 g, 3 × 10^{-2} mol) was added in small portions at room temperature to a stirred solution of 4-methyl-2,6-diphenyl-4*H*-1,3,5-thiadiazine (5.3 g, 2 × 10^{-2} mol) in dry tetrahydrofuran (200 ml). The resulting suspension was stirred at room temperature for 45 min. The mixture was poured onto ice and extracted with chloroform (3 × 150 ml), the solvent was distilled off *in vacuo*, and chromatography of the residue on SiO_2 gave the imidazole (4.5 g, 96%), m.p. 246—248° (lit.,[6] 241°) (Found: C, 82.0; H, 6.1; N, 11.7. Calc. for $C_{16}H_{14}N_2$: C, 82.0; H, 6.0; N, 12.0%).

4,5-*Diphenylimidazole.*—Potassium t-butoxide (3.4 g, 3 × 10^{-2} mol) was added in small portions at room temperature to a stirred solution of 2,6-diphenyl-4*H*-1,3,5-thiadiazine (5 g, 2 × 10^{-2} mol) in dry tetrahydrofuran (200 ml). The resulting suspension was stirred at room temperature

[6] G. Theilig, *Chem. Ber.*, 1953, **86**, 96.

for 30 min. The mixture was poured onto ice and extracted with chloroform (3 × 150 ml), the solvent was distilled off *in vacuo*, and chromatography of the residue on SiO_2 followed by treatment with active charcoal in ethanol gave the product (3.9 g, 80%), m.p. 235—236° (from CH_3CN) (lit.,[7] 231°) (Found: C, 81.7; H, 5.5; N, 12.7. Calc. for $C_{15}H_{12}N_2$: C, 81.8; H, 5.5; N, 12.7%).

Isolation of Sulphur in the Preparation of 2,4,5-Triphenylimidazole.—Triethylamine (0.8 ml, 5.75 × 10^{-3} mol; *d*, 0.728) was added at room temperature to a stirred solution of 2,4,6-triphenyl-4*H*-1,3,5-thiadiazine (6 g, 1.8 × 10^{-2} mol) in benzene (100 ml). The reaction mixture was stirred for 72 h at room temperature and chromatographed on SiO_2. The first fraction, eluted with benzene, gave sulphur (550 mg, 95%). The second, eluted with methanol, gave 2,4,5-triphenylimidazole (5.3 g, 98%).

RESULTS

Formation of 2,4,5-triarylimidazoles and sulphur from 2,4,6-triaryl-4*H*-1,3,5-thiadiazines occurs in the presence of catalytic amounts of aliphatic amines. An isosbestic point (271 nm; CH_2Cl_2; 27°) was observed in the reaction between 2,4,6-triphenyl-4*H*-1,3,5-thiadiazine and piperidine. Rate constants determined under pseudo-first-order conditions (excess of triethylamine) for 2,6-diaryl-4-phenyl- and 4-aryl-2,6-diphenyl-4*H*-1,3,5-thiadiazines are reported in Table 1. The rate has a linear dependence on the concentrations of amine and 2,4,6-triaryl-4*H*-1,3,5-thiadiazine. A linear dependence on the concentration of 2,4,6-triphenyl-4*H*-1,3,5-thiadiazine was also observed for high amine: 2,4,6-triphenyl-4*H*-1,3,5-thiadiazine ratios (Table 2).

TABLE 1

Rate constants for reaction (i) with Et_3N as base [a]

R^1	R^2	$[Et_3N]$/ M	10^3k_{obs}/ s^{-1}	$10^3k_{obs}[Et_3N]^{-1}$/ l mol^{-1} s^{-1}
H	*p*-OCH_3	0.23	1.6	7.0
H	*p*-OCH_3	0.11	0.75	6.8
H	*p*-CH_3	0.23	2.4	10.4
H	*p*-CH_3	0.11	1.2	10.9
H	*p*-CH_3	0.06	0.65	10.8
H	H	0.23	3.8	16.5
H	H	0.11	1.9	17.3
H	H	0.06	0.97	16.2
H	*p*-Cl	0.11	3.3	30
H	*m*-Br	0.11	6.9	63
H	*m*-Br	0.06	3.8	64
CH_3	H	0.23	0.87	3.8
Cl	H	0.06	7.9	131
OCH_3	H	0.68	0.55	0.81
OCH_3	H	0.45	0.40	0.88

[a] 65 °C; solvent, benzene; [4*H*-1,3,5-thiadiazine] *ca.* 10^{-5}M.

TABLE 2

Rate constants for reaction (i; $R^1 = R^2 = H$) with Et_3N as base [a]

10^5[Thiadiazine]/ M	10^{-4}[Et_3N] : [Thiadiazine]	$10^3k_{obs}[Et_3N]^{-1}$/ l mol^{-1} s^{-1}
3.3	3.03	3.0
6.6	1.51	3.0
9.9	1.01	3.1
13.2	0.16	3.0

[a] 27 °C; solvent, benzene; [Et_3N] 1M.

A good correlation between relative rate constants (Table 1) and Hammett σ values [8] for 2,6-diaryl-4-phenyl- and 4-aryl-2,6-diphenyl-4*H*-1,3,5-thiadiazines was found. The calculated ρ values are 2.1 * (*r* 0.990) and 1.4 (*r* 0.994) respectively. 2,4,6-Triphenyl-[4-^{2}H]4*H*-1,3,5-thiadiazine reacted in various solvents and with different bases 2—3.5 times slower than 2,4,6-triphenyl-4*H*-1,3,5-thiadiazine (Table 3). By stopping the reaction between [4-^{2}H]2,4,6-triphenyl-4*H*-1,3,5-thiadiazine (isotopic purity 98 ± 1%) and piperidine at 45% conversion, the recovered starting material showed an isotopic purity of 95 ± 1% (see Experimental section). This indicates a small hydrogen–deuterium exchange between piperidine and the substrate.

TABLE 3

Rate constants for reaction 2,4,6-triphenyl-[4-^{2}H]4*H*-1,3,5-thiadiazine [a]

Amine	Solvent	10^3k_{obsH}[amine]$^{-1}$/ l mol^{-1} s^{-1}	10^3k_{obsD}[amine]$^{-1}$/ l mol^{-1} s^{-1}	k_H/k_D
Triethylamine	Benzene	16.7	7.83	2.1
Piperidine	Benzene	73	30	2.4
Triethylamine	Methyl ethyl ketone	300	85	3.5
Triethylamine	Ethanol	62	21	3

[a] 65 °C; [amine] 4.5 × 10^{-2}M; [1,3,5-thiadiazine] *ca.*10^{-5}N.

In Table 4, the rate constants for the reaction between 2,4,6-triphenyl-4*H*-1,3,5-thiadiazine and triethylamine in several solvents are reported. The rate is enhanced by increasing polarity for aprotic solvents. The reaction does not occur in heptane while in dimethyl sulphoxide it is 120 times faster than in benzene. Rate constants for the reactions between 2,4,6-triphenyl-4*H*-1,3,5-thiadiazine and several bases are reported in Table 5. The temperature effect on reaction rate is shown in Table 6. Over the range investigated, the rate is only slightly affected.

TABLE 4

Rate constants, measured in different solvents, for reaction (i; $R^1 = R^2 = H$) with Et_3N as base [a]

Solvent	*T*/°C	10^3[Et_3N]/ M	10^3k_{obs}/s^{-1}	$10^3k_{obs}[Et_3N]^{-1}$/ l mol^{-1} s^{-1}
Dimethyl sulphoxide	45	6	5.2	867
Methyl ethyl ketone	65	11	3.3	300
Diglyme	65	23	2.5	109
Ethanol	65	45	2.8	62
Benzene	65	113	1.9	17
Benzene	45	113	0.83	7
Heptane	65	113	*b*	

[a] [1,3,5-thiadiazine] 3 × 10^{-5}M. [b] Too slow to be measured.

The availability [5] of 2,6-diphenyl- and 4-methyl-2,6-diphenyl-4*H*-1,3,5-thiadiazines (Scheme 2) gave us the opportunity to extend the scope of the reaction. Bases stronger than aliphatic amines such as potassium t-butoxide in tetrahydrofuran are required to catalyse the ring contraction of this set of thiadiazines (see Experimental section).

DISCUSSION

Our results are in good agreement with the general reaction mechanism exemplified in Scheme 3 for the reaction between 2,4,6-triphenyl-4*H*-1,3,5-thiadiazine

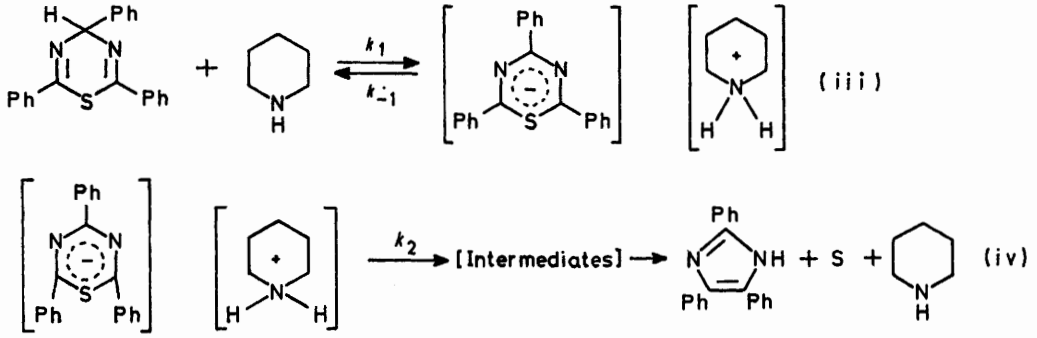
* The correlation was made by adding the σ values of the two substituents R^1.

[7] H. Bredereck and G. Theilig, *Chem. Ber.*, 1953, **86**, 88.

[8] D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, 1958, **23**, 420.

and piperidine. The occurrence of equilibrium (iii) is confirmed by the hydrogen–deuterium exchange in the reaction between 2,4,6-triphenyl-[4-^{2}H]4*H*-1,3,5-thiadiazine and piperidine.

Formation of an anion is supported by the following observations: the reaction rate is enhanced by



SCHEME 3

electron-withdrawing substituents (positive ρ values), increasing amine basicity, and increasing solvent polarity. The primary kinetic deuterium isotope effect and the small degree of hydrogen–deuterium exchange indicate that hydrogen abstraction is the rate-determining step of the reaction. The reaction rate can be

TABLE 5

Rate constants for reaction (i; $R^1 = R^2 = H$)[a]

Amine	[amine]/ N [d]	$10^3 k_{obs}$/s^{-1}	$10^3 k_{obs}$[amine]$^{-1}$/ N^{-1} s^{-1}
1,1,3,3-Tetramethyl-guanidine	0.01	4.8	480
DABCO [b]	0.03	3.0	100
Piperidine	0.03	2.2	73
Triethylamine [c]	0.11	1.8	16.4
Morpholine	0.18	1.5	8.3
n-Hexylamine	0.11	0.50	4.6
N-Methylmorpholine	0.57	0.50	0.88
Di-s-butylamine	0.28	0.17	0.61
NN-Dimethyl-*m*-toluidine	0.57	*e*	
Pyridine	0.57	*e*	

[a] [1,3,5-thiadiazine] 3×10^{-5} M; 65 °C; solvent, benzene. [b] For the same reaction in dimethyl sulphoxide at 45 °C k_{obs}[Et$_3$N]$^{-1} = 3.2$ l mol^{-1} s^{-1}. DABCO = 1,4-diazabicyclo-[2.2.2]octane. [c] 2,4,6-Triphenyl-4*H*-1,3,5-thiadiazine reacts, at room temperature, much faster with triethylamine than with di-isopropylethylamine. [d] 1N = 1 equiv. amine per dm^3. [e] Too slow to be measured.

properly expressed by an equilibrium steady-state treatment, which leads to equation (v). From the data on hydrogen–deuterium exchange we assume that k_2 is

$$-\mathrm{d}[4H\text{-}1,3,5\text{-thiadiazine}]/\mathrm{d}t = \mathrm{d}[\text{imidazole}]/\mathrm{d}t = \frac{k_1 k_2 [4H\text{-}1,3,5\text{-thiadiazine}]\,[\text{amine}]}{k_{-1} + k_2} \quad (v)$$

4-aryl-2,6-diphenyl-4*H*-1,3,5-thiadiazines suggest that substituents on the aryl groups have roughly the same influence on the reaction rate. From Table 5 it appears that the reaction rate is enhanced by increasing amine basicity. Amines are listed in Table 5 from greater to lesser effectiveness in catalysing the reaction and the relative position depends on both basicity and steric hindrance.

We conclude that the formation of 1,3,5-thiadiazinide

TABLE 6

Rate constants at different temperatures for the reaction (i; $R^1 = H$) with Et_3N as base [a]

R^2	T/°C	[Et$_3$N]/ M	$10^3 k_{obs}$/s^{-1}	$10^3 k_{obs}$[Et$_3$N]$^{-1}$/ l mol^{-1} s^{-1}
H	44.7	0.11	0.85	7.6
H	56.3	0.11	1.4	12.7
H	65.4	0.11	1.9	17.2
H	74.0	0.11	2.6	23.7
Cl	42.7	0.06	0.43	15.5
Cl	52.8	0.06	1.2	20
Cl	65.0	0.11	3.3	30
Cl	73.6	0.06	2.5	42

[a] [1,3,5-thiadiazine] 10 mg l^{-1}; solvent, benzene.

anion, a six-membered, planar, conjugated 8 π-electron system, is responsible for the ring contraction of 4*H*-1,3,5-thiadiazines.

[6/1088 *Received*, 7th *June*, 1976]

[9] F. G. Bordwell, *Accounts Chem. Res.*, 1972, 374.