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Kinetics of the Reaction of 2,4-Dinitrochlorobenzene with 4-Aminothianes and Measurements of the Base Strengths of the 4-Aminothianes

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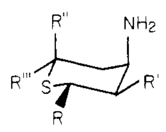
The kinetics of the reaction of 2,4-dinitrochlorobenzene with substituted 4-aminothianes have been investigated at 50 °C in 80% dioxane. Amines with an axial C(4)–NH_2 bond react at a slightly faster rate than the corresponding epimers. The kinetic data are interpreted in terms of solvation of the lone pair of electrons on the nitrogen atom and steric hindrance to solvation of the ammonium ion. The *N*-2,4-dinitrophenyl derivatives of the amines were also prepared. The pK_a values of the substituted 4-aminothianes were determined at 27 °C in 80% methyl Cellosolve. Aryl-substituted aminothianes were less basic than the unsubstituted 4-aminothianes apparently due to the polar effect of the aryl group which could be transmitted along the σ bond.

The synthesis and conformational analysis of several substituted 4-aminothianes have been communicated by us.[2] In continuation of our interest in 4-aminothianes we now report the kinetics of the reaction of 2,4-dinitrochlorobenzene with these amines and also the pK_a values of the aminothianes.

Kinetics of the Reaction of 2,4-Dinitrochlorobenzene with 4-Aminothianes

The kinetics of the reaction of a primary amine with 2,4-dinitrochlorobenzene has been studied by Bunnett and Randall.[3] The reaction follows a nucleophilic bimolecular substitution process. Eliel and co-workers[4] have reported the reaction rates for the reaction of a few substituted cyclohexylamines with 2,4-dinitrochlorobenzene. The already established conformations[2] for the 4-aminothianes **1a–f**, **2a–f**, **3a**, and **3b** are corroborated in the present study by the kinetics of the reaction of 2,4-dinitrochlorobenzene with the aminothianes.



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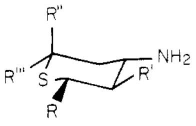
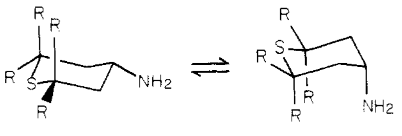


2

a, R = C_6H_5; R' = H; R'' = H; R''' = C_6H_5
b, R = *p*-ClC_6H_4; R' = H; R'' = H; R''' = *p*-ClC_6H_4
c, R = C_6H_5; R' = CH_3; R'' = H; R''' = C_6H_5
d, R = C_6H_5; R' = C_2H_5; R'' = H; R''' = C_6H_5
e, R = C_6H_5; R' = H; R'' = CH_3; R''' = CH_3
f, R = *p*-ClC_6H_4; R' = H; R'' = CH_3; R''' = CH_3



3a, R = H **3'**
b, R = CH_3

Table I. Second-Order Rate Constants for the Reaction of Substituted 4-Aminothianes with 2,4-Dinitrochlorobenzene in 80% Dioxane at 50 °C

compd	10^4k_2, L mol^{-1} s^{-1}	k_a/k_e
1a	5.31 ± 0.04	1.50
1b	3.46 ± 0.03	1.42
1c	1.33 ± 0.01	0.99
1d	0.97 ± 0.01	1.18
1e	9.06 ± 0.10	1.35
1f	6.58 ± 0.01	1.21
2a	3.54 ± 0.04	
2b	2.43 ± 0.02	
2c	1.35 ± 0.02	
2d	0.82 ± 0.02	
2e	6.72 ± 0.05	
2f	5.45 ± 0.05	
3a	8.51 ± 0.01	
3b	18.16 ± 0.02	

The reaction follows second-order kinetics and the rate constants at 50 °C for the aminomethianes **1a–f**, **2a–f**, **3a**, and **3b** are given in Table I. The results in Table I indicate that amines **1a**, **1b**, **1d**, **1e**, and **1f**, with an axial C(4)–NH_2 bond, react at a slightly faster rate than their epimers [C(4)–NH_2 equatorial] **2a**, **2b**, **2d**, **2e**, and **2f**. Eliel and co-workers[4] reported a similar order of reactivity for the reaction of substituted cyclohexylamines with 2,4-dinitrochlorobenzene. In a mixture of dioxane and water, the amines would presumably be surrounded by a primary solvation cage of water molecules, and solvation will, of course, be centered on the lone pair of electrons on nitrogen.[5] The pK_a values of the pairs of epimeric amines listed in Table III suggest that equatorial amines **2a–f** are more solvated than the axial amines **1a–f**. The electron pair on equatorial NH_2 is more tightly surrounded by a shell of solvent molecules which constitutes a barrier between it and the 2,4-dinitrochlorobenzene. Thus, equatorial amines react at a slower rate. In the axial epimers **1a–b**, the nitrogen lone pair is less accessible for solvation and is relatively free for nucleophilic attack. However, solvation can not be the entire answer since the specific rate constant ($k_2 = 1.33 \times 10^{-4}$ L mol^{-1} s^{-1}) of **1c** was almost identical with the specific rate constant ($k_2 = 1.35 \times 10^{-4}$ L mol^{-1} s^{-1}) of **2c**. This suggests that steric effects may be more important than solvation in the case of **1c** and **2c**. On the basis of the conformation assigned for the aminothiane **1c** by NMR studies,[2] the steric hindrance for the

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(1) Forms part of the Ph.D. Dissertation of P. K. Subramanian to be submitted to the University of Madras, India.

(2) Subramanian, P. K.; Ramalingan, K.; Satyamurthy, N.; Berlin, K. D. *J. Org. Chem.*, preceding paper in this issue.

(3) Bunnett, J. F.; Randall, J. J. *J. Am. Chem. Soc.* **1958**, *80*, 6020.

(4) Eliel, E. L.; Della, E. W.; Williams, T. H. *Tetrahedron Lett.* **1963**, 831.

(5) For a review of ionic solvation in water, see Feats, F. S.; Ives, D. J. G. *J. Chem. Soc.* **1956**, 2798. See also Bockris, J. O. M. "Modern Aspects of Electrochemistry"; Butterworths: London, 1954; p 47.

Table II. Substituted *N*-(2,4-Dinitrophenyl)-4-aminothianes

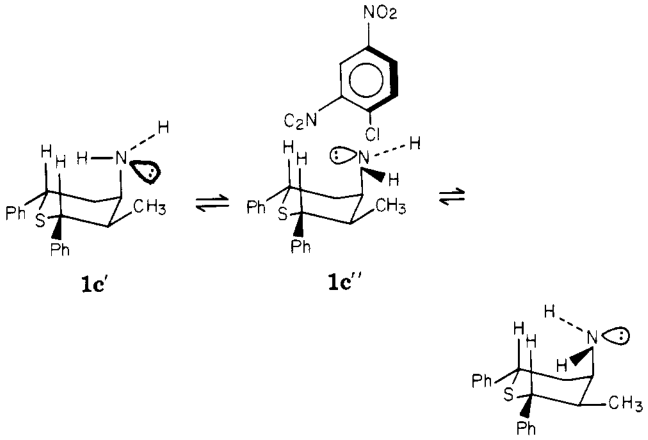
compd	% yield	mp,[a] °C	formula
4a	35	185-186	$C_{23}H_{21}N_3O_4S$
4b	32	186-187	$C_{23}H_{19}N_3O_4SCl_2$
4c	27	202-204	$C_{24}H_{23}N_3O_4S$
4d	44	216-218	$C_{25}H_{25}N_3O_4S$
4e	32	190-192	$C_{19}H_{21}N_3O_4S$
4f	34	157-159	$C_{19}H_{20}N_3O_4SCl$
5a	39	228-229	$C_{23}H_{21}N_3O_4S$
5b	36	232-233	$C_{23}H_{19}N_3O_4SCl_2$
5c	32	182-183	$C_{24}H_{23}N_3O_4S$
5d	32	179-180	$C_{25}H_{25}N_3O_4S$
5e	34	178-179	$C_{19}H_{21}N_3O_4S$
5f	32	142-144	$C_{19}H_{20}N_3O_4SCl$

[a] Recrystallized from absolute alcohol. C, H, and N analyses agreed to within 0.3% of theoretical values.

Table III. Dissociation Constants of Substituted 4-Aminothianes

compd	pK_a	compd	pK_a
1a	7.76 ± 0.03	**2b**	8.07 ± 0.02
1b	7.59 ± 0.03	**2c**	7.97 ± 0.01
1c	7.40 ± 0.01	**2d**	7.86 ± 0.01
1d	7.26 ± 0.01	**2e**	8.32 ± 0.02
1e	8.25 ± 0.00	**2f**	8.33 ± 0.03
1f	8.18 ± 0.03	**3a**	8.72 ± 0.02
2a	8.29 ± 0.01	**3b**	8.41 ± 0.03

solvation of the lone pair on the nitrogen could be probed by considering the preferred rotational conformations of the axial NH_2 group and an equilibrium of three conformers **1c′**, **1c″**, and **1c‴** related by rotation about the C–N bond.

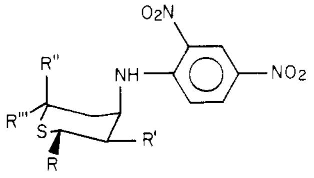


1c′ **1c″** **1c‴**

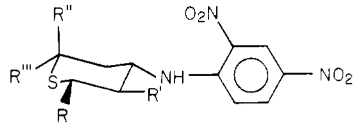
The reaction rate of **1c** indicates that the most preferred rotational conformation for the axial amino group is as in **1c″**. The lone pair pointing toward the center of the thiane ring is less readily available for nucleophilic attack and hence the lower reaction rate. This view is also supported in the case of the near constancy of the reaction rates for the 3-ethyl derivatives **1d** and **2d** (Table I).

The specific rate constant (k_2 = 9.06 × 10^{-4} L mol^{-1} s^{-1}) for the reaction of 2,4-dinitrochlorobenzene with **1e** was considerably higher than that of **1a** (k_2 = 5.31 × 10^{-4} L mol^{-1} s^{-1}). This same trend was observed with **1f** reacting faster than **1a**. The axial amine **1f** (k_2 = 6.58 × 10^{-4} L mol^{-1} s^{-1}) gave a much higher rate constant than that of **1b** (k_2 = 3.46 × 10^{-4} L mol^{-1} s^{-1}). It is probable that the axial methyl group hinders the formation of the solvation shell to a greater extent in these cases, making the lone pair in **1e** and **1f** free for nucleophilic attack.

The *N*-2,4-dinitrophenyl derivatives **4** and **5** were prepared for the amines **1a–f** and **2a–f**. Relevant details are furnished in Table II.



4

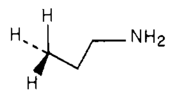


5

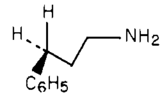
a, R = C_6H_5; R′ = H; R″ = H; R‴ = C_6H_5
b, *p*-ClC_6H_4; R′ = H; R″ = H; R‴ = *p*-ClC_6H_4
c, R = C_6H_5; R′ = CH_3; R″ = H; R‴ = C_6H_5
d, R = C_6H_5; R′ = C_2H_5; R″ = H; R‴ = C_6H_5
e, R = C_6H_5; R′ = H; R″ = CH_3; R‴ = CH_3
f, R = *p*-ClC_6H_4; R′ = H; R″ = CH_3; R‴ = CH_3

pK_a Values of 4-Aminothianes

Prelog and Hafliger[6] have shown that configuration can be assigned to epimeric pairs of 2-aminocyclohexanols from a knowledge of their pK_a values. Bird and Cookson[7] determined pK_a values of the epimeric pairs of aminocholestanes in order to clarify the influence of hindrance of solvation. To evaluate the effect of substituents on the basicity of 4-aminothianes, we have measured the dissociation constants of variously substituted epimeric amines in 80% methyl Cellosolve at 27 °C. The pK_a values for six pairs of epimeric amines **1a–f** and **2a–f** and related compounds **3a** and **3b** are listed in Table III. An inspection of the Table III shows that 2,6-diaryl-substituted 4-aminothianes **1a–d** and **2a–d** are much less basic than the unsubstituted (parent) amine **3a**. This lowering in basic strength may be attributed to the polar effect of the aryl groups which could be transmitted along the σ bonds.



6
p$K_a{}^8$ = 10.59



7
p$K_a{}^8$ = 10.39

3a
pK_a = 8.72

2a
pK_a = 8.29

Quite similar observations have been reported in the literature:[8] for example γ-phenylpropylamine (**7**) (pK_a = 10.39) is less basic than *n*-propylamine (**6**) (pK_a = 10.59) and this is possibly due to a polar effect of the phenyl group at a γ position. Amines **1e**, **1f**, **2e**, and **2f** with a single equatorial aryl group are stronger bases compared to **1a**, **1b**, **2a**, and **2b** with two equatorial aryl groups at 2- and 6-positions. The basicity of the tetramethyl derivative **3b** (pK_a = 8.41) is less than that of **3a** (pK_a = 8.72). In **3b**, the axial methyl groups hinders the solvation of

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(6) Prelog, V.; Hafliger, O. *Helv. Chim. Acta* **1950**, 33, 2021.
(7) Bird, C. W.; Cookson, R. C. *J. Chem. Soc.* **1960**, 2343.
(8) Lange, N. A. "Handbook of Chemistry"; McGraw-Hill: New York, 1967; p 1215.

$^{+}NH_3$ cation and hence reduces the basicity of the amine group.

Experimental Section

The preparation of the 4-aminothianes **1a–f**, **2a–f**, and **3a,b** have been communicated.[2]

Kinetic Procedure. The pure aminothianes were dried in vacuo before use. The 2,4-dinitrochlorobenzene was also dried before use. Dioxane was purified as described in the literature[9] and 80% dioxane was used as the solvent.

The rate was followed conductometrically.[10] The concentration of the amine was maintained at twice the concentration of 2,4-dinitrochlorobenzene in order to trap the HCl formed during the reaction. The amine (0.4 mol) and the 2,4-dinitrochlorobenzene (0.2 mol) solutions were prepared and thermostated at 50 ± 0.01 °C. Equal volumes (2 mL) of the solutions were mixed in the conductance cell. Immediately after mixing, the conductance was measured. At appropriate time intervals, the conductance values of the reaction mixture were then recorded. The infinity readings were determined after keeping the reaction mixture in the conductance cell at 75 °C for 72 h. The rate constant k_2 is given by

$$k_2 = (1/2tb)[(C_t - C_0)/(C_\infty - C_t)]$$

where b = concentration of 2,4-dinitrochlorobenzene in moles/liter, C_0 = initial conductance, C_t = conductance at time t, and C_∞ = conductance at infinite time

Measurement of Dissociation Constants.[7] The pure amines were dried in vacuo before use. Methyl Cellosolve was purified by fractional distillation. Distilled water free from carbon dioxide was prepared and 80% methyl Cellosolve was used as the solvent.

The amine (about 15 mg) was dissolved in 80% methyl Cellosolve (25 ml). While the solution was stirred under nitrogen, 0.05 N hydrochloric acid was added dropwise from a burette that could be read to 0.005 mL. The pH values were measured in a pH meter, precalibrated with buffers at pH 4.0 and 9.2 with a glass electrode. All measurements were made at 27 ± 0.01 °C. The equivalence point was determined from a plot of pH against volume of HCl added. An average value (pK_a) of one-fourth, one-half, and three-fourth neutralizations was taken, and at least two independent titrations were carried out on each compound.

Preparation of Substituted *N*-(2,4-Dinitrophenyl)-4-aminothianes. A solution of the aminothiane (0.0019 mol) and 2,4-dinitrochlorobenzene (0.41 g, 0.002 mol) in 90% ethanol (25 mL) was boiled on a water bath for 6 h. When the solution cooled, the derivative crystallized out. It was filtered, washed with cold ethanol (10 mL), and recrystallized (ethanol). Other relevant data were given in Table II.

Registry No. **1a**, 69832-20-8; **1b**, 70095-68-0; **1c**, 78837-43-1; **1d**, 78837-44-2; **1e**, 78837-45-3; **1f**, 78837-46-4; **2a**, 69832-19-5; **2b**, 70071-36-2; **2c**, 78918-40-8; **2d**, 78918-41-9; **2e**, 78837-47-5; **2f**, 78837-48-6; **3a**, 21926-00-1; **3b**, 78837-49-7; **4a**, 78837-50-0; **4b**, 78837-51-1; **4c**, 78837-52-2; **4d**, 78837-53-3; **4e**, 78837-54-4; **4f**, 78837-55-5; **5a**, 78918-42-0; **5b**, 78918-43-1; **5c**, 78918-44-2; **5d**, 78918-45-3; **5e**, 78837-56-6; **5f**, 78837-57-7; 2,4-dinitrochlorobenzene, 97-00-7.

Supplementary Material Available: An expanded Table II showing combustion analytical data (1 page). Ordering information is given on any current masthead page.

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[9] Weissburger, A.; Pros Kauer, E. S., Eds. "Organic Solvents"; Interscience: New York, 1955; p 371.

[10] Guggenheim, E. A.; Prue, J. F. "Physiocochemical Calculations"; North-Holland Publishing Co.: Amsterdam, 1959; p 445.

New Method for Building Carbon–Phosphorus Heterocycles

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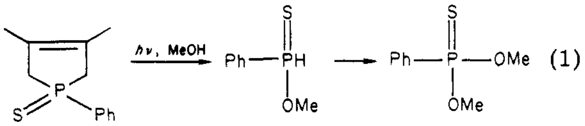
Received May 12, 1981

The photolysis of 1-substituted 3,4-dimethylphosphole sulfides–*N*-phenylmaleimide cycloadducts in alcohols (R′OH) has been found to proceed with high yields whatever the nature of the R substituent. It provides a ready access to the almost unknown phosphinothioates RP(S)(H)OR′. When R = $(CH_2)_nBr$ the phosphinothioates thus obtained are readily cyclized by NaH in THF. Five-, six-, and seven-membered rings have been obtained in this way.

Recently some efforts have been devoted to the devising of new general methods for building carbon–phosphorus heterocycles. Indeed, older classical methods were often plagued by low yields and/or limited practical applicability.[1] As far as monocyclic compounds are concerned, two new methods have appeared very recently in the literature. The first one was devised by Quin[2] and relied upon an ozone cleavage of the double bond at the junction of a bicyclic phospholene. Its main purpose was the synthesis of large-membered functional rings. On our side we described a method relying upon two successive Arbuzov rearrangements so as to convert two P–O–C bonds into two P–C bonds.[3] This method was satisfactory but was relatively complex. Thus we decided to carry on new research in order to devise a simpler method. The results of our work are described hereafter.

Results and Discussion

Our starting point was an observation of Tomioka[4] describing the cleavage of phospholene sulfide **1** under UV irradiation in alcohol (eq 1). The primary product **2** was



1

2 (max yield 6%)

3 (max yield 27%)

obtained in very poor yield, and additional work[5a] on the

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[1] For a very recent account, see: Quin, L. D. "The Heterocyclic Chemistry of Phosphorus"; Wiley-Interscience: New York, 1981.

[2] Quin, L. D.; Middlemas, E. D. *J. Am. Chem. Soc.* **1977**, *99*, 8370.

[3] Mathey, F.; Mercier, F. *J. Chem. Soc., Chem. Commun.* **1980**, 191.

[4] Tomioka, H.; Takata, S.; Kato, Y.; Izawa, Y. *J. Chem. Soc. Perkin Trans. 2* **1980**, 1017.

[5] (a) Tomioka, H.; Nakamura, S.; Ohi, T.; Izawa, Y. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 3707. (b) The photolysis of the dimer of 1-phenylphosphole oxide (which contains a 7-phosphanorbornene skeleton) shows an enhancement of the rate of the photocleavage when compared to the photolysis of 1-phenyl-3-phospholene oxide; see: Tomioka, H.; Hirano, Y.; Izawa, Y. *Tetrahedron Lett.* **1974**, 1865, 4477.

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