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The Reactions of Lead Tetra-acetate with Substituted Benzothiazolylhydrazones

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In the reaction of benzothiazolylhydrazones of some aromatic aldehydes with lead tetra-acetate the presence of a sulphur atom in the potential cyclisation site of the heteroaryl moiety inhibits the cyclisation reaction. Thus, the reaction of substituted benzothiazolylhydrazones involves an acetoxylation of the hydrazone and not a cyclisation reaction as had previously been reported. Cyclisation of the hydrazone to a triazolobenzothiazole moiety does, however, occur as a minor competitive process. A convenient route for converting the acetoxylated products to cyclised triazolobenzothiazoles has been developed thereby overcoming the most serious limitation in the use of the lead tetra-acetate-hydrazone reaction in the benzothiazole series.

IN recent years the reactions of lead tetra-acetate with substituted hydrazones have undergone a renewal of active interest.¹ In earlier studies the reagent was

¹ R. N. Butler, Chem. and Ind., 1968, 437; D. H. R. Barton, J. F. McGhie, and P. L. Batten, J. Chem. Soc. (C), 1970, 1033; cf. also ref. 7 and previous papers in the series; B. T. Gillis and M. P. La Montague, J. Org. Chem., 1968, **33**, 762; A. M. Cameron, P. R. West, and J. Warkentin, J. Org. Chem., 1969, **34**, 3230. looked upon solely as a means of cyclising hydrazones with an appropriately located heterocyclic ring and many of the complicated processes which are involved were missed. We have recently 2,3 pointed out the existence of a competitive acetoxylation process in the

F. L. Scott and R. N. Butler, J. Chem. Soc. (C), 1966, 1202.
R. N. Butler and F. L. Scott, J. Chem. Soc. (C), 1968, 1711.

cyclisation reactions and have indicated the predominance of one or other of these processes in certain instances. In connection with our studies of the principles which govern cyclisation or acetoxylation in these reactions we are presently investigating the effect of a second heteroatom X in the starting hydrazone on the overall course of the reaction. This present paper concerns the reaction when X is a sulphur atom.



RESULTS AND DISCUSSION

The system we chose to study was the benzothiazolylhydrazone system (I). The reactions of two of these materials with lead tetra-acetate were previously investigated by Bower and Doyle 4 as a means of obtaining triazolobenzothiazoles, and we have confirmed their results. These authors reported 4 that the products, which they considered to be triazolobenzothiazoles, contained a molecule of acetic acid of solvation. This



Scheme

was detected by elemental analysis. We have found that their structural assignments were, in fact, incorrect and that the main products arose from an acetoxylation reaction and are the N-aroyl-N'-acetylhydrazines (II) and not triazolobenzothiazoles. The structure (II) was indicated by the i.r. spectra of the materials which displayed the strong N-H (3320-3340 cm.-1) and the

* Preliminary results on the influence of an oxygen atom seem to parallel the present observations.

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carbonyl doublet (1670-1690 cm.⁻¹ conjugated; 1715-1730 cm.⁻¹ unconjugated) absorptions associated with the N-acetylhydrazide structure.^{2,3} This structure was confirmed by synthesising the materials from the corresponding hydrazides (IV) as outlined in the Scheme. However, by maintaining a careful product balance in the lead tetra-acetate reactions small quantities of a second product, the triazolobenzothiazoles (III), were isolated. These materials were different to those previously reported with this structure. The results of the reactions which are summarised in Table (I), indicate that the presence of the sulphur atom in a potential cyclisation site oriented the reaction strongly in favour of acetoxylation at the expense of cyclisation.*

However, the reaction, nevertheless, provided a good indirect route to the cyclised product (III) since it was found possible to obtain these materials in yields up to 60% by heating the diacylhydrazines (II) under reflux in phenol (Table 1). Compound (IIIa) has previously been reported by Reynolds and Van Allen,⁵ who prepared it by dehydrating the hydrazide (IVa) in refluxing phenol. We have confirmed the results of these workers. The compound which we obtained was identical with the sample obtained by treating the hydrazone (Ia) with lead tetra-acetate or by heating the hydrazide (IIa) under reflux in phenol. This latter reaction is an important innovation in heterocyclic synthesis since, as we have pointed out, the most serious limitation of this method has been the competitive acetoxylation process leading to materials such as (II).

TABLE 1

Reactions of hydrazones with lead tetra-acetate to give hydrazines and triazolobenzothiazoles

	H_{2}	ydrazine	es	Triazolobenzothiazoles			
Hydr-	<u> </u>	Yield		Yield			
azone	Compd.	(%)	M.p.	Compd.	(%)	M.p.	
(Ia)	(IIa)	69 a	$\begin{array}{c} 227\\ 229^{\circ} \end{array}$	(IIIa)	5 (58·5) b	156- 157° d	
(Ib)	(IIb)	67 ª	$\begin{array}{c} 224 \\ 226 \end{array}$	(IIIb)	3·5 (46) b	200- 202	
(Ic)	(IIc)	55 a	236 - 238	(IIIc)	10·5 (41) °	209— 211	
(Id)	(IId)	81	$\begin{array}{r} 204 \\ 206 \end{array}$	(IIId)	1·5 (50) b	164	
(Ie)	(IIe)	75	231-233	(IIIe)	3 (38) ⁵	151 - 153	

 Small quantities of gums from which no further crystalline products could be obtained were also isolated from these products observations and the second rest in the second rest in the second rest in the second 153°.

The formation of the products (III) involves ring closure by the nitrogen atom of the benzothiazole moiety. Ring closure by the sulphur atom is also conceivable though unlikely since the product of such a process would have a mesoionic structure. One further possibility is that the products could be substituted tetrazines

⁴ J. D. Bower and F. P. Doyle, *J. Chem. Soc.*, 1957, 727. ⁵ G. A. Reynolds and J. A. Van Allen, *J. Org. Chem.*, 1959, 24, 1478.

arising from dimerization of a nitrilimine intermediate. However, molecular-weight determinations showed the materials to be monomers and ruled out this possibility. The presence of nitrilimine intermediates in the reactions of lead tetra-acetate with hydrazones has been well established.⁶ However, such intermediates do not seem to be involved in the present reactions since attempts to trap them by using acrylonitrile as solvent, a process which was successful with other systems,⁶ gave no indication of their presence. When compounds (Ib) and (Id) were treated with lead tetra-acetate in acrylonitrile and the products were chromatographically separated, the corresponding compounds (III) and (II) were isolated in up to 20% yields along with a number of oils. We have so far been unable to identify the structures of the various oils but their i.r. spectra showed no nitrile absorptions and hence these materials are not the cyanosubstituted pyrazoles which would arise from a trapping of nitrilimine intermediates.

EXPERIMENTAL

M.p.s were measured on an Electrothermal apparatus. I.r. spectra were measured on a Perkin-Elmer Infracord (model 137E) spectrophotometer with sodium chloride optics. Solids were examined as discs with potassium bromide. U.v. spectra were measured on a Unicam model SP 800 spectrophotometer with methanol as solvent. Molecular weights were determined from mass spectra of the compounds measured on a AEI MF 902 double focusing mass spectrometer.

Preparation of Hydrazone Substrates.—The following is a typical example. A solution of 2-hydrazinobenzothiazole (8.25 g.) in warm glacial acetic acid (100 ml.) was slowly added to a solution of p-bromobenzaldehyde (9.25 g.) in the same solvent (100 ml.); the mixture was stirred at 100° for 10 min. The mixture was cooled and compound (Ic) (14.04 g.) separated, m.p. 280—281° (from glacial acetic acid) (lit.,⁴ 280°) (Found: C, 50.1; H, 3.4; Br, 24.4; N, 12.7. Calc. for $C_{14}H_{10}BrN_3S$: C, 50.6; H, 3.0; Br, 24.1; N, 12.6%. Addition of water to the acetic acid mother-liquor yielded a further 1.7 g. of the material (total yield, 15.75 g., 94%).

All the substituted benzaldehydes used were *para*substituted. The appropriate hydrazones were all prepared in a similar fashion to the above. Compound (Ia), m.p. 230—231° (lit.,⁷ 230—231° (Found: C, 66·0; H, 4·35. Calc. for $C_{14}H_{11}N_3S$: C, 66·4; H, 4·4%). Compound (Ib), m.p. 267—269° (Found: C, 58·75; H, 3·55; N, 14·65. $C_{14}H_{10}ClN_3S$ requires C, 58·4; H, 3·5; N, 14·65%). Compound (Id), m.p. 232—234° (Found: C, 67·9; H, 5·05; N, 16·05. $C_{15}H_{10}N_3S$ requires C, 67·4; H, 4·9; N, 15·75%). Compound (Ie), m.p. 209—210° (Found: C, 68·7; H, 5·85; N, 14·75. $C_{17}H_{17}N_3S$ requires C, 69·1; H, 5·75; N, 14·25%). In each case the yield was greater than 90%.

Lead Tetra-acetate Oxidations.—The following is a typical example. Lead tetra-acetate $(3\cdot3 \text{ g.})$ was added during a few minutes to a suspension of compound (Ib) (2.0 g.) in glacial acetic acid (30 ml.); the mixture was stirred at ambient temperatures for 1 hr. and then poured into water (600 ml.) cooled with crushed ice. A white solid (2.08 g.),

⁶ M. Callona and R. Andrisano, Publ. Ist. Chem. Univ. Bologna, 1943, 5, 3.

m.p. 170—185°), separated (Filtrate A). The solid was leached with ligroin (200 ml.) and the insoluble portion (1.60 g., 67%), m.p. 223—225° (raised to 224-225° by recrystallisation from absolute ethanol) was compound (IIb). The ligroin extract was set aside for 12 hr. in an ice-bath when it deposited 200 mg. of an impure solid which on recrystallisation from absolute ethanol yielded compound (IIIb) (70 mg., 3.5%), m.p. 199—200°.

The filtrate (A) was extracted with ether $(2 \times 200 \text{ ml.})$. The ethereal solution was washed with sodium carbonate solution, dried, and evaporated. The residue was a sticky gum from which no pure products could be obtained. However, for the reaction with compound (Id) a small quantity of the cyclised product (IIId) was isolated from this gum by careful crystallisation from absolute ethanol.

The results of a series of these reactions are summarised in Table 1. Analytical data for the products are provided in Table 2.

TABLE 2

Analytical data

Found (%)						Required (%)		
Compd.	c	Н	N	Formula	c	H	N	
(IIa)	62.0	$4 \cdot 2$	13.2	$C_{16}H_{13}N_{3}O_{2}S$	61.7	$4 \cdot 2$	13.5	
(IIb) •	56.15	$3 \cdot 5$	12.45	C ₁₆ H ₁₂ ClN ₃ O ₂ S	55.7	3.5	12.2	
(IIc)	49.5	$3 \cdot 3$	11.0	C ₁₆ H ₁₂ BrN ₃ O ₂ S	5 49.1	$3 \cdot 3$	10.75	
(IId)	$62 \cdot 1$	4.35	12.80	C ₁₇ H ₁₅ N ₃ O ₂ S	62.3	4 ·6	12.9	
(IIe)	64.9	5.35	11.7	$C_{19}H_{19}N_3O_2S$	64.8	$5 \cdot 1$	11.9	
(IIIa) ^b	67.3	3.55	16.65	C ₁₄ H ₉ N ₃ S	67.0	3.6	16.75	
(IIIb) •	58.6	$2 \cdot 8$	15.05	C14H8CIN8S	58.8	2.8	14.7	
(IIIc) ^d	51.2	2.45	12.35	C ₁₄ H ₈ BrN ₈ S	51.0	2.4	12.7	
(IIId) •	67.6	4.1	16.3	$C_{15}H_{11}N_{3}S$	68 .0	4.15	15.85	
(IIIe)	69.85	4 ·9	14.0	C ₁₇ H ₁₅ N ₃ S	69.7	$5 \cdot 1$	14.35	
∉ Fo	ound:	Cl,	10 ·2.	Required Cl,	10·3.	^b Four	nd and	
required M. 251. • Found and required M. 285.5). • Found								

required M, 251. • Found and required M, 285.5). • Found: Br, 23.9; M, 330. Required Br, 24.2; M, 330. • Found and required M, 265. • Found and required M, 293.

Synthesis and Acetylation of the Hydrazides (IV).—The following are typical examples. A suspension of p-bromobenzoyl chloride (1.04 g.) in pyridine (15 ml.) was added during 5 min. to a warmed solution of 2-hydrazinobenzothiazole (790 mg.) in the same solvent (15 ml.). The mixture was heated at 45° for 15 min., stirred at room temperature for 2 hr., and poured into water (300 ml.) cooled with crushed ice to give compound (IVc) (1.10 g., 75%), m.p. 237—239° (from absolute ethanol) (Found: C, 48.3; H, 2.7; Br, 22.0; N, 12.1. $C_{14}H_{10}BrN_3OS$ requires C, 48.3; H, 2.9; Br, 23.0; N, 12.05%).

The following compounds were prepared in similar fashion. Compound (IVa) (64%), m.p. 191—193° (from benzene) (Found: C, 62·4; H, 4·15; N, 15·4. $C_{14}H_{11}N_3OS$ requires C, 62·5; H, 4·2; N, 15·6%). Compound (IVb) (38%), m.p. 236—237° (from chloroform) (Found: C, 55·3; H, 3·3; N, 14·1. $C_{14}H_{10}CIN_3OS$ requires C, 55·6; H, 3·55; N, 13·9%). Compound (IVd) (49%), m.p. 189—190° (Found: C, 63·65; H, 4·6; N, 14·5. $C_{15}H_{13}N_3OS$ requires C, 63·6; H, 4·6; N, 14·85%).

Acetylation of the materials (IV) yielded products which were identical (mixture m.p. and i.r. spectra) with the *N*-aroyl-*N'*-acetylhydrazines obtained from the lead tetraacetate reactions above. The following is a typical example. A solution of compound (IVc) (500 mg.) in 50%

⁷ W. A. F. Gladstone, R. O. C. Norman, and J. B. Aylward, J. Chem. Soc. (C), 1969, 2587; W. A. F. Gladstone, Chem. Comm., 1969, 179.

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(v/v) acetic acid-acetyl chloride solution (20 ml.) was heated under reflux for 30 min. The mixture was cooled to give compound (IIc) (0.40 g.), m.p. 236-238° (from absolute ethanol). Addition of water to the filtrate yielded a further 50 mg. of the compound (total yield, 0.45 g., 80%). The yield for each of these reactions was 80-90%.

Substituted s-Triazolo[4,3-b]benzothiazoles (III).—The following is a typical example. A solution of compound (IId) (1 g.) in phenol (10 ml.) was heated under reflux for 24 hr.; the solvent was then removed by steam distillation. Recrystallisation of the residue from absolute ethanol yielded compound (IIId) (410 mg., 50%), m.p. 164—166°. The results of a series of these reactions are included in Table 1. The materials (III) obtained in this manner were identical (mixture m.p. and i.r. spectra) with those obtained from the lead tetra-acetate reactions above.

The materials (IIIa) and (IIIc) were also prepared from the corresponding compounds (IV) in the manner described by Reynolds and Van Allen.⁵

Reactions in Acrylonitrile. The following is a typical

example of a number of experiments which were carried out on compounds (Ib) and (Id) in attempts to detect nitrilimine intermediates.

A suspension of compound (Id) (2 g.) in acrylonitrile (100 ml.) was treated with lead tetra-acetate (3.25 g.) and the mixture was stirred for 2 hr. at ambient temperatures. Insoluble inorganic material was removed and the solution was evaporated. A suspension of the residue in ethanol was carefully added to water and the insoluble material (1.9 g.), m.p. 180-200° was removed. Recrystallisation of this material from carbon tetrachloride-light petroleum (b.p. 100-120°) yielded compound (IId) (0.5 g., 21%). The carbon tetrachloride-light petroleum solution which remained was evaporated and the residue was dispersed on a column of neutral alumina. This was eluted in turn with light petroleum, light petroleum-benzene, benzene, ether, and ethyl acetate. Various oils (discussed above) were encountered and the ethyl acetate fraction deposited compound (IIId) (0.20 g., 10%).

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