Kinetics and Mechanism of the Reaction of Substituted Phenylhydrazones with Thallium(III) Acetate. Reactions of Mercury(II) Acetate with Nitrogen Compounds. Part 8 †

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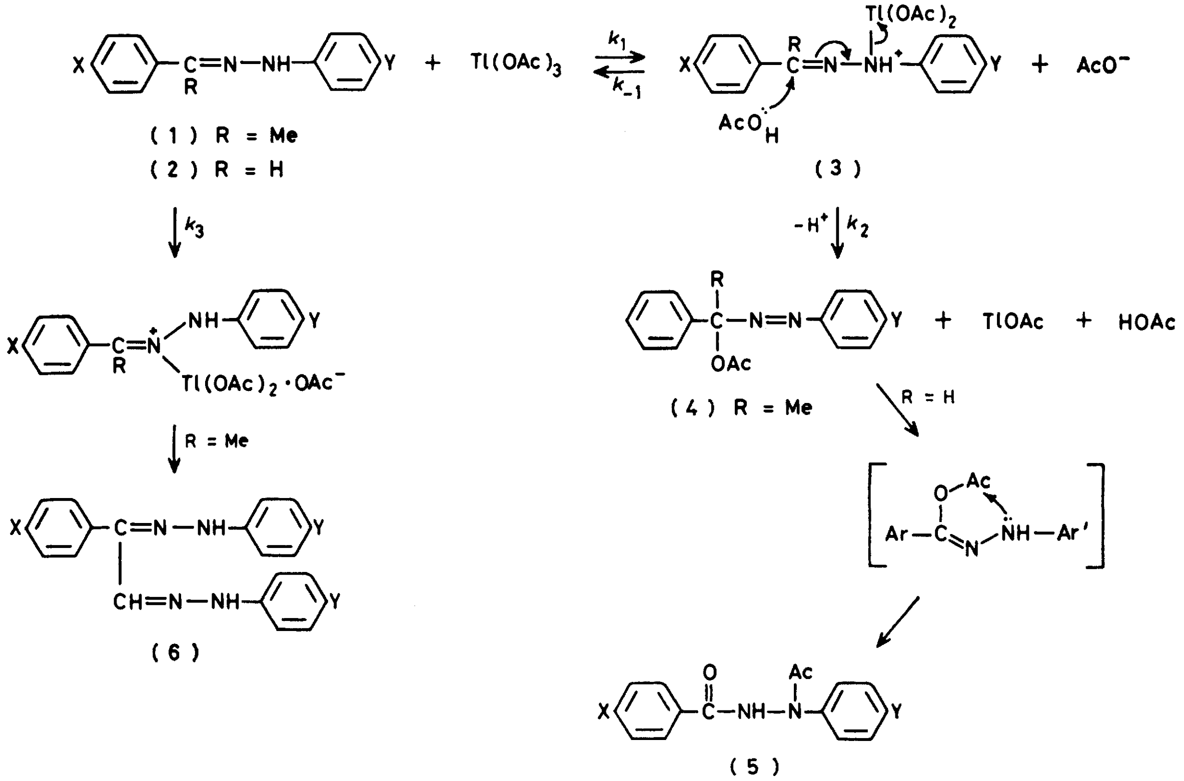
The reaction of substituted phenylhydrazones with thallium(III) acetate in acetic acid involved an electrophilic attack at the hydrazone amino-NH moiety giving an intermediate which is attacked by solvent at the methine carbon. The Hammett ρ values for substituents in the methine and the *N*-phenyl rings were −1.05 and −3.6, respectively. Activation thermodynamic parameters ΔE_a 17.9, ΔH_a 17.2 kcal mol^{-1}, and ΔS_a −14.65 cal K^{-1} mol^{-1} were measured for *p*-chlorobenzaldehyde *p*-nitrophenylhydrazone. The main products from aromatic aldehyde arylhydrazones were *N*'-acetyl-*N*-aroyl-*N*'-arylhydrazines (5). The main products from ketone arylhydrazones were α-acetoxy-α-phenylazo-derivatives of the ketone (4). The unexpected divergence of reactivity of phenylhydrazones with the acetates of Hg^{II}, Tl^{III}, and Pb^{IV} is discussed.

THERE is but one report[1] of the reaction of a phenylhydrazone system with a thallium(III) salt. In a study of the reactions of oximes with thallium(III) nitrate, the phenylhydrazones of two ketones, acetophenone and benzophenone, were treated with thallium(III) nitrate in moist methanol and the ketones were regenerated.[1] With dried methanol as solvent the product from benzophenone phenylhydrazone was methyl phenylazo-(diphenyl) methyl ether.[1] Studies of the reactions of phenylhydrazones with lead(IV) acetate [2,3] and mercury(II) acetate [4,5] have shown remarkably different behaviour of these reagents towards phenylhydrazone substrates. For example, treatment of acetophenone 4-nitrophenylhydrazone (1a) (Scheme) with lead(IV) acetate (LTA) in acetic acid gave the azoacetate (4a) in high yield [6] while a similar reaction with mercury(II) acetate (Hg2A) gave the substituted osazone (6a) in high yield.[5] In order to explain this unexpected divergence of reactivity, it was necessary to examine the reactions of phenylhydrazones with thallium(III) acetate (TTA) under identical conditions because of the special relationship of these isoelectronic reagents where Tl^{III} is the intermediate member of the series. This work with TTA is described herein.[7]



SCHEME Y = NO$_2$, X = (a) H; (b) Cl; (c) NO$_2$; (d) Me; (e) MeO

RESULTS AND DISCUSSION

(a) *Products and Solvent Effects*.—When a series of substituted phenylhydrazones of aldehydes and ketones was treated with thallium(III) acetate in acetic acid,

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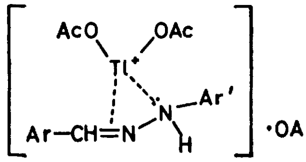
the carbonyl compounds were not regenerated. The aldehyde hydrazones (2) gave the *NN'*-diacylhydrazines (5) in yields of 85—90%. The ketone hydrazone (1a) gave the azoacetate (4a) as the main product (65%) along with the substituted osazone (6a) as a minor product (5%) and some decomposition resins. In giving these products the behaviour of TTA was lying towards that of LTA but with a significant difference insofar as the acetate moiety of the products (4) and (5) arose from solvent involvement and not from an intramolecular acetoxy-migration in the redox step as was the case [2] with LTA. Thus when acetophenone 4-nitrophenylhydrazone (1a) was treated with TTA in dichloromethane containing triethylamine (to remove acetic acid expected to be liberated), no azoacetate was formed and the hydrazone was recovered. A comparable LTA oxidation of compound (1a) in dichloromethane–triethylamine readily gave the product (4a) confirming the intramolecular nature of the redox step with the Pb^{IV} oxidant. Products such as (5) arose from an addition of acetic acid to a nitrilimine intermediate in the LTA oxidation.[2,3] There was no dehydrogenation to a nitrilimine in the thallium(III) acetate reaction but the formation of the products (5) involved the acetic acid solvent. Thus when the substrate (2a) was treated with thallium(III) acetate at 25° for periods of 1—7 days, in the following solvents, the product (5a) only was obtained along with hydrazone recovered: solvent, yield of (5a): acrylonitrile, 2—4% (from HOAc generated); acrylonitrile–Et_3N (to trap HOAc generated), 0 [compound (5a) was not detected]; acrylonitrile–HOAc (90 : 10 v/v), 25—28%; HOAc, 90%. No trace of cyanopyrazoles or cyanopyrazolines, the expected acrylonitrile trapping products of nitrilimines, was encountered and the products (5) did not arise from addition of acetic acid to a nitrilimine intermediate.

(b) *Kinetics.*—Reaction rates for a series of hydrazones (2) (Table) were measured by monitoring the concentration of thallium(III) acetate [8] under second-order conditions with equimolar ratios of reactants. Linear second-order plots were obtained over the early stage (<50%) of the reaction and gave a Hammett ρ value of -1.05 (r 0.988) for the methine phenyl ring using σ^+ values [9] for the substituents (Nos. 1—6, Table). Removal of the p-NO_2 group from the *N*-phenyl ring caused a large increase in rate such that accurate rates could not be obtained using the iodine titration method of Ouellette,[8] which we found to be the most satisfactory and reproducible method for dealing with the kinetics of this phenylhydrazone–thallium(III) acetate system. However, by using a p-NO_2 group in the methine phenyl ring it was possible to slow the reactions sufficiently for a measurement of some substituent variation in the *N*-phenyl ring, and the three points (Nos. 4, 7, and 8, Table) correspond to a Hammett ρ value of -3.6 (± 0.2) for the *N*-phenyl ring. An Arrhenius plot (Table, No. 2 and footnote *a* gave thermodynamic data for the reaction with compound (2b): ΔE_a 17.9 kcal mol^{-1}, ΔH_a 17.2 kcal mol^{-1}, and ΔS_a -14.65 cal K^{-1} mol^{-1}. These data indicate an electrophilic attack and the σ^+ correlation suggests a transition state with an incipient positive charge capable of resonance with the methine aromatic ring, *e.g.* (A), arising from attack at the planar conjugated π–n electron cloud. The ratio of the ρ values suggests ultimate bonding at the hydrazone amino-NH moiety giving a species (3) with a positive charge adjacent to the *N*-phenyl ring. This intermediate, when attacked by solvent at the methine carbon, would give rise to the products (4) in an intermolecular redox step. With aldehyde hydrazones the products (4) would be readily converted to the compounds (5) *via* a tautomerism and a 1,4 O→N acetyl migration under the prolonged stirring which was necessary for the reaction.

No.	Compound (2) X	Y	$10^2 k$ (298 K)/ l mol^{-1} s^{-1}	(σ^+) [c]	Intercept $x/(a-x)$
1	H	NO_2	1.57 ± 0.04	(0.0)	0.26
2 [a]	Cl	NO_2	0.85 ± 0.08	(+0.114)	0.195
3 [b]	Br	NO_2	0.91 ± 0.04	(+0.150)	0.22
4	NO_2	NO_2	0.29 ± 0.03	(+0.79)	0.21
5	Me	NO_2	3.75 ± 0.35	(−0.311)	0.30
6	MeO	NO_2	9.95 ± 0.45	(−0.778)	0.26
7	NO_2	Br	138.2 ± 6.7		0.33
8	NO_2	H	284.4 ± 11		0.98

[a] Other Arrhenius data: $\times 10^2 k$, temperature: 3.33, 310; 9.43, 322; 22.95 l mol^{-1} s^{-1}, 333 K. [b] For a series of initial concentrations (a) the half-life for this substrate was, $\times 10^3 a$ M, $\times 10^{-3} t_{\frac{1}{2}}$ s: 8.31, 10.38; 6.23, 13.98; 5.17, 23.16; 4.15, 30.24. [c] σ^+ Values from ref. 9.



(A)

While linear second-order plots were obtained, these did not pass through the origin as expected for a pure second-order reaction but instead gave intercepts which were close to the origin on the $x/(a-x)$ axis (Table). For a second-order system involving an equilibrium these intercepts should represent k_{-1} (Scheme) which would be a pseudo-first-order reversal of the first step.[10] However, because of the added complexity [10] of the competing side-reaction, k_3, (Scheme), these intercepts are not measurements of k_{-1} but probably encompass that value. When the overall order of the reaction was carefully determined by the half-life method by plotting log a (initial concentration) against log $t_{\frac{1}{2}}$ (Table, footnote *b*), a linear plot was obtained giving an order slightly below second order for the reaction, *i.e.* 1.8 ± 0.1. If k_3 (Scheme) is small relative to k_1, then the rate is governed by equation (i) where HyH represents hydrazone and F is the fraction [11] of the species (3) which proceeds to pro-

$$\text{Rate} = k_1[\text{HyH}][\text{TTA}]F \qquad \text{(i)}$$

$$F = \frac{k_2[(3)]}{k_{-1}[(3)] + k_2[(3)]} \qquad \text{(ii)}$$

$$\text{Rate} = \frac{k_1[\text{HyH}][\text{TTA}]}{k_{-1}/k_2 + 1} \qquad \text{(iii)}$$

ducts [*i.e.* equation (ii)]. Hence the overall rate expression is (iii) which reduces to the simple second order expression (i) ($F = 1$) if $k_{-1} \ll k_2$. However, if k_{-1} were to become significant and k_3 was not much less than k_1 then equation (iii) would need further modifications giving rise to a complicated kinetic expression.[12] The reactions which gave products of type (6) with mercury(II) acetate arose from an attack by the electrophile at the imino moiety [5] with rate constants over an order of magnitude smaller than the present values for TTA and about three orders of magnitude smaller than k_1 values [2] for LTA. Assuming that k_3 for TTA would be not less than that for Hg2A, then this relative closeness of the k_3 and k_1 values coupled with the relative stability of the intermediates (3) (which survive long enough for a solvent attack) and the observed small deviation from pure second-order kinetics suggest that k_{-1} and k_3 (Scheme) are indeed beginning to exert some influence on the measured rate but the second-order linear equations are still applicable. This also points to the origin of the spectrum of reactivity exhibited by the series of acetates of Pb^{IV}, Tl^{III}, and Hg^{II} with phenylhydrazones. For the Pb^{IV} reagent $k_2 \gg k_{-1}$ and $k_1 \gg k_3$ and the rate expression reduces to the second-order equation (i) ($F = 1$). For the Tl^{III} reagent the intermediate (3) is longer lived and, while k_1 and k_2 are still greater than k_3 and k_{-1}, respectively, the ratios are smaller and the competition of k_3 gives small amounts of side products. With the Hg^{II} reagent $k_{-1} \gg k_2$ and the dominant reaction then becomes that of k_3 (Scheme). In agreement with this, when an unprotonated form of the mercury analogue of the species (3) was prepared under different conditions,[4] it reverted to the parent hydrazone, when stirred in acetic acid, confirming that k_{-1} was large relative to k_2.

EXPERIMENTAL

M.p.s were measured with an Electrothermal apparatus. N.m.r. spectra were measured with a JEOL JNM-MH-100 spectrometer. The hydrazone substrates were prepared by standard procedures.[13]

(i) *Kinetics*.—Rate constants (Table) were measured under conditions similar to the synthetic reactions. Typically a solution of hydrazone (500 mg) in acetic acid was treated with an equimolar quantity of TTA in acetic acid such that the concentration of each substrate was 0.01M. Portions (1 ml) were withdrawn at appropriate time intervals (t) and added to a 5% KI solution (50 ml) and the liberated iodine [8] was titrated with standard sodium thiosulphate solution using a starch indicator. Plots of $x/(a - x)$ against t were linear with slope ka. The data used were for the early stages, <50%, since after *ca.* 60% reaction the rates began to gradually slope downwards probably due to complexation of Tl^{III} by the thallium(I) salts generated. Such a difficulty has been observed with other systems [8] also. Data quoted (Table) and experimental errors are the mean values for three measurements.

(ii) *Reactions of the Phenylhydrazones with Thallium*(III) *Acetate*.—The following are typical examples. (*a*) A solution of acetophenone 4-nitrophenylhydrazone (1a) (500 mg) in acetic acid (35 ml) was treated with TTA (747 mg), stirred at 55° for 2 h followed by 17 h at 25° and poured into water (120 ml). The cloudy mixture was extracted with ether (5 × 75 ml) and the combined ethereal extract was washed with water, dilute sodium carbonate solution, dried, and evaporated. The sticky orange-red residue (610 mg) was swirled in small quantities of cold chloroform and phenylglyoxal bis-(4-nitrophenylhydrazone) (6a) separated (15 mg), m.p. 308° (lit.,[5] 306—308°). The chloroform solution on evaporation yielded starting hydrazone (30%) and a yellow oil which was removed in ether and proved to be 1-(4-*nitrophenylazo*)-1-*phenylethyl acetate* (4a) (65%) (Found: C, 61.7; H, 4.6; N, 12.9. $C_{16}H_{16}N_3O_4$ requires C, 61.4; H, 4.8; N, 13.4%); $\nu_{max.}$ 1 745 (ester C=O) and 1 100 cm^{-1} (ester C–O–C); δ_H($CDCl_3$) 8.26 and 7.78 (4 H, A_2B_2, J_{AB} 8 Hz, *p*-$NO_2C_6H_4$), 7.64 (m, 2 H), 7.2—7.4 (m, 3 H, Ph), 2.2 (s, 3 H, Me-C), and 2.08 (s, 3 H, Ac); $\lambda_{max.}$ (EtOH) 278 nm (log ε 3.89). A similar reaction carried out in dichloromethane containing triethylamine gave a 90% recovery of starting hydrazone with small quantities of gums and the azoacetate (4a) was not encountered. Treatment of acetophenone 4-nitrophenylhydrazone with lead tetra-acetate (1 mol) in acetic acid for 2 h at ambient temperatures gave compound (4a) in 96% yield. A similar reaction in dichloromethane containing triethylamine gave the azoacetate (4a) in 40% yield and starting hydrazone (52%).

(b) A solution of benzaldehyde 4-nitrophenylhydrazone (2a) (500 mg) in acetic acid (50 ml) containing acetic anhydride (0.3 ml) was treated with TTA (1 mol) heated at 50° for 20 min, stirred at ambient temperature for 6 h, and carefully added to water. Starting hydrazone (32%), which separated, was removed and on standing *N*-benzoyl-*N'*-acetyl-*N'*-4-nitrophenylhydrazine (5a) separated, m.p. 186° (from ethanol) (lit.,[14] 186—187°). Ethereal extraction of the filtrate gave further quantities of this compound (overall yield 66%). Higher yields, with less recovery of starting material, were achieved with longer reaction times. Reactions carried out in acrylonitrile were worked-up by distribution between ether and water. The combined ethereal layers were evaporated and the residues separated by fractional crystallisation from absolute alcohol and column chromatography. The only compounds encountered were starting hydrazone and compounds (5). No cyano-absorptions were detected in the i.r. spectra of the mixture and no cyanopyrazolines were encountered.

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