Reactions of Mercury(II) Acetate with Nitrogen Compounds. Part 3.† Contrasting Reactions of Mercury(II) and Lead(IV) Acetates with Some Semicarbazones: Bis(5,6-diphenyl-1,2,4-triazin-3-onato)mercury

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Treatment of benzil monosemicarbazone with lead tetra-acetate in acetic acid gave O-acetylbenzoin in a fragmentation involving phenylbenzoyldiazomethane as an intermediate. Treatment of benzil monosemicarbazone with mercury(II) acetate gave bis(5,6-diphenyl-1,2,4-triazin-3-onato)mercury. Benzil bis-semicarbazone and some benzaldehyde semicarbazones gave stable aminomercury compounds when treated with mercury(II) acetate and, in contrast with lead tetra-acetate, dehydrogenations or fragmentations did not occur. Lead tetra-acetate fragmentation of the hydrazone system ArC(ArC=Y)=NNHX (Y = O or NR) to a diazo species, which may cyclise or react further, appears to be a useful general reaction when X is a good leaving group, e.g. CONH₂ or SO₂Ar.

LEAD TETRA-ACETATE (LTA) oxidations of semicarbazone systems gave rise to a range of interesting cyclisations.[1] For example, ketone semicarbazones were cyclised to 1,3,4-oxadiazolines,[2] benzil bis-semicarbazones gave 1-(N-ureido)-1,2,3-triazoles,[3] and benzaldehyde semicarbazones gave 2-amino-1,3,4-oxadiazoles.[4] Reactions of such systems with the comparable [5] mercury reagent, mercury(II) acetate (Hg2A) have not been reported. We have now [6] examined the behaviour of Hg2A with some of these substrates. While mercury(II) acetate can be useful in dehydrogenation reactions,[7] it is a weaker oxidising agent than LTA, and with these hydrazone systems it failed to give the dehydrogenative cyclisations which are readily available with the lead(IV) reagent.

RESULTS AND DISCUSSION

(i) *Benzil Semicarbazones.*—Cyclisation of substituted benzil bis-semicarbazones (1) to 1-(N-ureido)-1,2,3-triazoles (6) with LTA, in a new route to 1-amino-1,2,3-triazoles, was recently reported by Alexandrou and

strate (1) was recovered. When the reaction was carried out in cold acetic acid, the mercury complex (2; M = Hg, n = 1, Y = NNHCONH₂) was formed. Further heating of this complex in acetic acid did not give a fragmentative cyclisation but regenerated the parent semicarbazone, reflecting the weaker oxidising power of Hg^II relative to Pb^IV.

Treatment of the monosemicarbazone (4) with 1 mol equiv. of LTA in acetic acid gave O-acetylbenzoin (7) (85%), via the diazo intermediate (3; Y = O). The presence of the diazo intermediate in this LTA fragmentation was proved by carrying out the reaction in dichloromethane containing triethylamine (to remove acetic acid expected to be formed). Evaporation of the solvent gave a residue showing intense i.r. bands at 2 080 and 1 750 cm⁻¹ assigned to compound (3; Y = O) and also a band at 2 170 cm⁻¹ which we assign to –N=C=O present in the lead salts (from the fragmented CONH₂ moiety). The main component of the residue in dichloromethane, however, was compound (8) (65%) from a dehydrative cyclisation which was not encountered with acetic acid
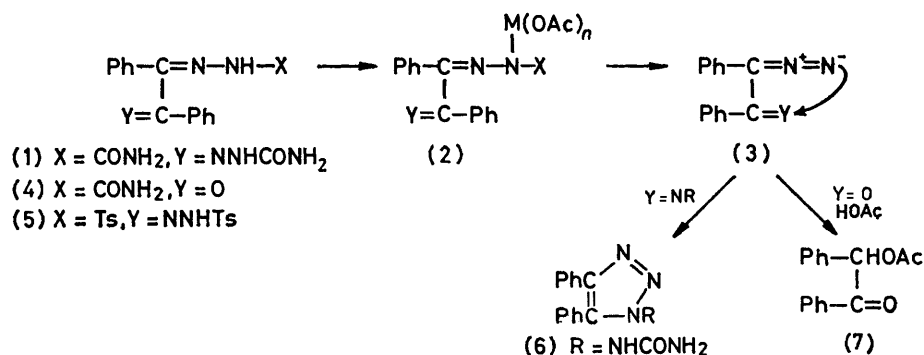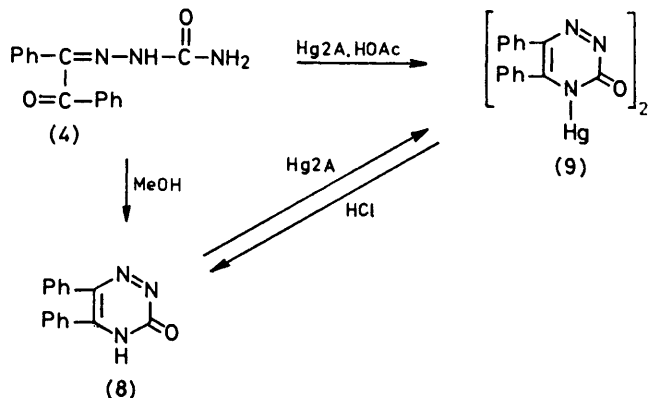

SCHEME 1

Adamopoulos [3] and it is confirmed herein. This reaction parallels the cyclisation of benzil bis(p-tolylsulphonyl)-hydrazone (5) which occurred on treatment with either LTA or Hg2A and where evidence for metallo and diazo intermediates has been presented.[8] Attempts to obtain a similar cyclisation of compound (1) by heating with Hg2A in acetic acid proved unsuccessful and the sub-

† Part 2, ref. 8.

as solvent. When the residue was treated with acetic acid, the i.r. bands at 2 080 and 2 170 cm⁻¹ disappeared and t.l.c. showed the presence of O-acetylbenzoin in the mixture. The diazo species (3; Y = O) was also obtained by LTA oxidation of benzil mono(p-tolylsulphonyl)hydrazone,[8] where it was readily converted to O-acetylbenzoin by acetic acid. The observation of these fragmentation reactions with the semicarbazones

(1) and (4), as well as with the corresponding *p*-tolyl-sulphonylhydrazone derivatives,[8] suggests that the reaction sequence of Scheme 1 may be general for LTA oxidations when X is a good leaving group.

Treatment of the semicarbazone (4) with Hg2A for 20 h in acetic acid interestingly gave the product (9) (Scheme 2) and, in agreement with the bis-semicarbazone
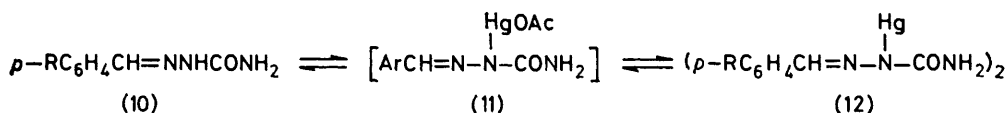
SCHEME 2

(1), oxidative fragmentation was not observed. In this reaction product (9) arose from an initial dehydrative cyclisation to the triazinone (8) which subsequently reacted with the remaining Hg2A. The triazinone (8) (70%) was obtained independently by heating the semi-carbazone (4) under reflux in methanol for 5 h. Separate brief treatment of compound (8) with Hg2A readily gave high yields of the bistriazinonatomercury derivative (9) which could revert to the triazinone upon treatment with dilute hydrochloric acid. The influence of reactant ratios on the reactions of the semicarbazone (4) with Hg2A is in the Table. When less than a molar pro-portion of Hg2A was used, mixtures of compounds (4) and (8) or (8) and (9) were formed. The results (Table) suggest that the Hg2A assisted in establishing an equilibrium concentration of the triazinone (8) which, in the presence of excess of reagent, was shifted strongly in favour of compound (8) by its removal in the form-ation of the mercury derivative (9). With a sufficient excess of Hg2A quantitative yields of compound (9) may be obtained. The dehydration of compound (4) observed with LTA and Hg2A probably arose because a ready cyclisation of this system provides an alternative and more favoured mode of reaction than electrophilic complex formation. LTA is hygroscopic [1] and a useful solvent drying agent,[9-11] with a strong affinity for water and this probably influenced its behaviour in the non-hydroxylic medium dichloromethane–Et$_3$N. With the bis-semicarbazone (1) such a dehydration is not possible and complex formation may occur without competition.

In the reaction of compound (4) with LTA competition between dehydration and complex formation was indeed clearly indicated by the product mixture.

Recently, uracil mercury derivatives have been studied [12] as models for the binding of mercury(II) or alkylmercury(II) with the bases of DNA molecules, where mercury bonding to the amido moiety may occur at nitrogen or oxygen.[12] In compound (9), which is a dehydroxyazauracil derivative, bonding at nitrogen was confirmed by the absence of the amido N–H absorptions in both i.r. and ^{1}H n.m.r. spectra and by the broad amido $>$C=O band at 1 630 cm^{-1} which was shifted by 50 cm^{-1} to lower frequencies relative to the parent compound (8) ($>$C=O, 1 680 cm^{-1}). This shift was similar to the carbonyl band of uracil mercury com-pounds containing a mercury–nitrogen bond and is ascribed to a higher electron density on the amido moiety when bonded to Hg^{II}.[12] The ^{1}H and ^{13}C n.m.r. spectra of the compounds further confirmed the struc-tures (see Experimental section).

(ii) *Substituted Benzaldehyde Semicarbazones.*—When a series of substituted benzaldehyde semicarbazones (10) was treated with Hg2A in acetic acid, oxidative cyclis-ations did not occur. With compounds (10; R = MeO or Me) mixtures of the bis-semicarbazonatomercury derivatives (12) and the parent semicarbazones (10), in the ratio *ca.* 1 : 1, were obtained on treatment of the acetic acid solutions with water. With the parent semi-carbazone (10; R = H) the ratio of compounds (12) : (10) in the mixture was 4 : 11 and for electron-with-drawing substituents in the methine phenyl ring (10; R = NO$_2$ or Cl) no reaction was observed, either on prolonged stirring at ambient temperature or on heating at 50—60° for 2 h. It appears that an equilibrium of exchange reactions, as in Scheme 3, was set up but that Hg^{II} was again too weak an oxidising agent for further reactions to occur. The bonding site of Hg in com-pounds (12) was established from ^{1}H n.m.r. and i.r. spectra. The semicarbazones (10) showed δ([^{2}H$_6$]-DMSO) 7.76—7.90 (CH=N), 10.1—10.52 (NH), and 6.40—6.75 (NH$_2$), while for compounds (12) the CH=N signal was characteristically [13] deshielded by the nearby mercury to δ 8.16—8.36 and the NH signal was absent. The relative intensities of both CH=N signals in the mixtures were consistent with the reduction in intensity of the secondary NH signal and gave the proportion of both components in the mixtures. I.r. spectra of com-pounds (12) showed the amido carbonyl band and the NH$_2$ stretching vibrations (see Experimental section) confirming the secondary N–H bonding site. In general, bonding of Hg2A to amido moieties occurs at the nitrogen atom [14] but with cyclic amides bonding at oxygen has also been observed.[12] With benzaldehyde

SCHEME 3

thiosemicarbazones complexation with mercury(II) chloride occurred at both the sulphur atom and the imino nitrogen.[15] The components of these mixtures were held tenaciously and it did not prove possible to effect satisfactory separations. However, for compounds (10; R = H and Me) careful leaching of the mixtures with hot alcohol removed most of the semicarbazone and allowed the isolation of compounds (12; R = H and Me) in crude form. When these compounds (12; R = H and Me) were redissolved in [^{2}H$_4$]acetic acid, ^{1}H n.m.r. signals due to the parent semicarbazones only were observed. This suggests that the equilibrium (Scheme 3) lies strongly on the semicarbazone side in acetic acid solution and the observation of compounds (12) at all may be due to a more rapid precipitation of these highly insoluble mercury derivatives, and accompanying equilibrium shift, on treatment with water. In agreement with this, attempts to directly observe the development of the equilibrium by adding Hg2A to acetic acid solutions of the semicarbazones in the n.m.r. tube were unable to detect a build-up of compounds (12) (suggesting low concentrations), while treatment of the same solutions with water caused compounds (12) to separate in the high proportion mixtures described.

EXPERIMENTAL

M.p.s were measured with an Electrothermal apparatus. I.r. spectra were measured for KBr discs or mulls with Perkin-Elmer 377 and 457 spectrophotometers. N.m.r. spectra were measured with JEOL JNM-MH-100 and FX-60 spectrometers. Benzil monosemicarbazone (4) [m.p. 176—178° (from ethanol) (Found: C, 67.65; H, 4.8; N, 16.0. Calc. for C$_{15}$H$_{13}$N$_3$O$_2$: C, 67.4; H, 4.8; N, 15.7%), δ([^{2}H$_6$]-DMSO) 10.2 (NH) and 6.6 (NH$_2$) confirming configuration (4) (cf. ref. 8)] was prepared by stirring equimolar quantities of benzil and semicarbazide hydrochloride in methanol–water (5 : 1 v/v) for 20 min. Benzil bis-semicarbazone (1), m.p. 250—252° (Found: C, 59.2; H, 4.9; N, 25.8. Calc. for C$_{16}$H$_{16}$N$_6$O$_2$: C, 59.2; H, 4.9; N, 25.5%), was prepared by heating a mixture of benzil, semicarbazide hydrochloride (2 mol. equiv.), sodium acetate (2 mol. equiv.), and methanol–water (9 : 1 v/v), under reflux for 5 h. The benzaldehyde semicarbazones were prepared as previously described.[16]

(1) Reactions of Benzil Monosemicarbazone.—(a) With LTA. A mixture of the semicarbazone (4) (534 mg), LTA (1.088 g), and acetic acid (20 ml) containing acetic anhydride (0.5 ml) was stirred for 16 h at ambient temperature. The initially yellow solution, which turned colourless, was brought to 200 ml, with water and extracted with ether (4 × 50 ml). The combined ethereal extract was washed with water and dilute sodium carbonate solution, dried, and evaporated to yield O-acetylbenzoin (150 mg, 82%), m.p. 83° [from chloroform–pentane (b.p. 40—60°)] (lit.,[17] 83°), identified by mixed m.p. and comparison of i.r. and ^{1}H n.m.r. spectra with those of an authentic sample.

A mixture of the semicarbazone (4) (1.068 g) and dichloromethane (30 ml) containing triethylamine (6.7 ml) was treated with LTA (2 g), stirred at ambient temperature for 1 h, and heated under reflux for a further 1 h. The deep red solution was then divided into two fractions (A) and (B). Fraction (A) was evaporated and the residue dissolved in

acetic acid (20 ml), heated under reflux for ca. 2 h, cooled, brought to 200 ml with water, and extracted with ether (4 × 50 ml). The combined ethereal extract was washed with water and dilute sodium carbonate solution, dried, and evaporated. The yellow residue (530 mg) contained the triazinone (8) (210 mg) (removed by swirling in ether). The remaining ether-soluble component contained mainly O-acetylbenzoin identified by t.l.c. and i.r. spectrum. Fraction (B) was brought to 40 ml with dichloromethane and washed with water. Evaporation of the solvent gave a residue containing compound (8), compound (3; Y = O), and some remaining lead salts and showing $v_{max.}$ 2 170 (Pb–N=C=O), 2 080 ($>$C=N$^+$=N$^-$), and 1 750 cm^{-1} ($>$C=O). The i.r. band at 2 170 cm^{-1} disappeared when the residue was treated with either water or alcohol.

(b) With mercury(II) acetate. A mixture of the semi-carbazone (4) (534 mg), Hg2A (636 mg), and acetic acid (20 ml) was stirred for 16 h at ambient temperature giving a clear lemon solution which on treatment with water gave a yellow precipitate of bis(5,6-diphenyl-1,2,4-triazin-3-onato-N^4)mercury (9) (680 mg, 98%), m.p. 210—212° (from ethanol) (Found: C, 51.95; H, 2.9; N, 12.1. C$_{30}$H$_{20}$-HgN$_6$O$_2$ requires C, 51.65; H, 2.9; N, 12.05%), δ$_C$ ([^{2}H$_6$]-DMSO) 164.6 (C-3), 157.9 (C-5), and 144.5 p.p.m. (C-6), δ$_H$ 7.28—7.40 (Ph), $v_{max.}$ 1 630 br. cm^{-1} (amide $>$C=O) and no N–H absorption. Bonding to Hg at N-4 is suggested by the ^{13}C shifts of C-3 and -5 [both deshielded by 15 p.p.m. relative to those of compound (8)] and by the different phenyl ^{1}H n.m.r. pattern for (9) relative to (8) suggesting proximity of the bonding site to the phenyl substituents. The semicarbazone (4) was treated with different molar ratios of mercury(II) acetate (Table). Treatment of com-

Influence of reactant ratios [a]

Molar ratio Hg(OAc)$_2$: (4)	Product yield (%)		
	(4) [b]	(8) [c]	(9) [b]
2 : 1	<1	<1	95
1 : 1	<1	<1	97
0.75 : 1	<1	74	24
0.5 : 1	53	46	<1
0.25 : 1	61	30	<1
0.1 : 1	71	19	<1

[a] Reactions were carried out in acetic acid for 16 h at 20 °C. [b] Separated on treatment with water. [c] Extracted into ether after treatment with water.

pound (9) with dilute hydrochloric acid (20 ml) at ambient temperature for 1 h gave compound (8) (80%). When the semicarbazone (4) was stirred for 16 h at 20° in acetic acid in the absence of Hg2A, it was recovered and no cyclisation was observed.

(ii) Synthesis of 5,6-Diphenyl-1,2,4-triazin-3-one (8).—A mixture of benzil monosemicarbazone (4) (1 g) and methanol (50 ml) was heated under reflux for 5 h. The cooled solution on evaporation gave the triazinone (8) (650 mg, 70%), m.p. 228—230° (from ethanol) (Found: C, 72.6; H, 4.4; N, 16.8. C$_{15}$H$_{11}$N$_3$O requires C, 72.3; H, 4.4; N, 16.85%), δ$_H$([^{2}H$_6$]DMSO) 10.8 (NH) and 7.12—7.52 (Ph, m), δ$_C$([^{2}H$_6$]-DMSO) 149.05 (C-3), 142.4 (C-5), and 140.0 p.p.m. (C-6) $v_{max.}$ 1 680br (amide C=O) and 3 050br, cm^{-1} (NH) [$v_{max.}$ 1 710 cm^{-1} (PhC=O) and δ 6.6 (NH$_2$) as in compound (4) were absent].

(iii) Reaction of Benzil Bis-semicarbazone with Mercury(II) Acetate.—A mixture of benzil bis-semicarbazone (1) (648 mg) and Hg2A (636 mg) suspended in acetic acid (20 ml) was stirred at ambient temperature for 16 h. Acetoxy-

(*benzil semicarbazonato*-N^2)*mercury* (2; X = CONH$_2$, Y = NNHCONH$_2$) (1.02 g, 88%), m.p. 253—254°, separated (Found: C, 37.5; H, 3.20; H, 14.4. C$_{18}$H$_{18}$H$_8$N$_6$O$_4$ requires C, 37.0; H, 3.1; N, 14.4%), $\nu_{max.}$ 1 650 (HgOAc), 3 450 (NH), 1 700 (CONH$_2$), and 1 600 ($>$C=N); δ 1.9 (HgOAc) and 7.52, 7.38, and 7.12 (Ar, NH).

Treatment of this compound (440 mg) with dilute hydrochloric acid (20 ml) gave the bis-semicarbazone (1) (230 mg, 83%). Further heating or stirring of the mercury complex in acetic acid gave the parent bis-semicarbazone (1) (>90%). When treated with LTA, compound (1) gave reactions similar to those described.[3]

(iv) *Reactions of Substituted Benzaldehyde Semicarbazones with Mercury*(II) *Acetate.*—The following is a typical example. A mixture of benzaldehyde semicarbazone (10; R = H) (500 mg), Hg2A (1 or 2 mol equiv.), and acetic acid was stirred at ambient temperatures for periods of 30 min to 16 h or heated at 50—55° for a few hours and then added to ice-cold water when a mixture of compounds (12) and (10), m.p. 212—219°, separated, δ ([^{2}H$_6$]DMSO) 8.20s, CH=N of compound (12; R = H)], 7.84 [s, CH=N of compound (10)] (intensity ratio 8 : 11 corresponding to a molar ratio of 4 : 11 in the mixture), 10.24br [NH of (10)], 6.48—6.60 [NH$_2$ of (10) and (12)], and 7.32—7.76 (m, Ar). On careful leaching of this mixture with warm ethanol semi-carbazone (10) was removed leaving the crude insoluble mercury complex *bis*(1-*benzylidenesemicarbazidato*-N^2)*mercury*, m.p. 216—218° (Found: C, 35.6; H, 2.65; N, 15.3. C$_{16}$H$_{16}$HgN$_6$O$_2$ requires C, 36.6; H, 3.0; N, 16.0%), $\nu_{max.}$ 3 480 (NH$_2$ stretch), 1 650 (amido NH$_2$ bend), and 1 600 ($>$C=N stretch), δ([^{2}H$_6$]DMSO) 8.24 (1 H, s, CH=N), 7.36—7.76 (5 H, m, Ph), and 6.50br (2 H, CONH$_2$). When the reaction between the semicarbazone and Hg2A was carried out under reflux in acetic acid, the semicarbazone was recovered along with mercury globules and some mercury(I) acetate.

Similar reactions of the compounds (10; R = Me and MeO) gave comparable mixtures containing one part of compounds (12) to one of compounds (10). The insoluble compound *bis*(1-p-*tolylidenesemicarbazidato*-N^2)*mercury* (12;

R = Me), m.p. 219—221° (Found: C, 38.1; H, 3.3; N, 15.15. C$_{18}$H$_{20}$HgN$_6$O$_3$ requires C, 39.0; H, 3.6; N, 15.2%), δ([^{2}H$_6$]DMSO) 8.16 (CH=N), 6.50br (NH$_2$), 7.14 and 7.56 (Ar, A$_2$B$_2$), and 2.30 (*p*-Me), was obtained by careful leaching of the mixture with warm ethanol. For compounds (10; R = Cl and NO$_2$) no reactions or complex formation was observed and the semicarbazones proved inert under the conditions.

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