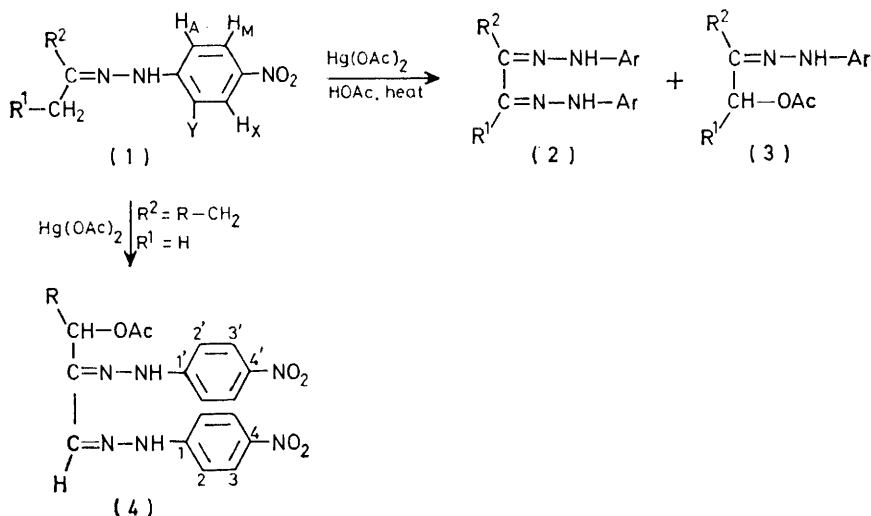# A Novel Hydrazino-transfer Reaction to a Saturated Carbon: Direct Conversion of Substituted Acetophenone and Aliphatic Ketone 4-Nitrophenylhydrazones into 1,2-Bis-hydrazones. Reactions of Mercury(II) Acetate with Nitrogen Compounds. Part 6 †

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Treatment of a series of substituted acetophenone 4-nitrophenylhydrazones with mercury(II) acetate in acetic acid gave the corresponding substituted phenylglyoxal bis-(4-nitrophenylhydrazones) in varying yields. Similar reactions involving hydrazino-transfers to methyl groups were observed with the 4-nitrophenylhydrazones of acetone, propiophenone, methyl ethyl ketone, methyl benzyl ketone, and also with the 2,4-dinitrophenylhydrazones of acetone and acetophenone. Substituent influences on product distribution and a possible mechanism are discussed.

THE reaction of phenylhydrazones with mercuric oxide gives mixtures of dimeric products.[1,2] With mercuric acetate (Hg2A) as reagent aldehyde phenylhydrazones gave an unexpected mercuriation at the *ortho*-position of

osazones (2) were accompanied by the α-acetoxy-products (3) and the trend for the series of acetophenone hydrazone derivatives (1a)—(1d) (Table) suggested a competitive process where electron-donating groups in the

the *N*-phenyl ring *via* an initial complexation at the imino-function.[3] Herein, we report[4] an equally unexpected hydrazino-transfer to a saturated carbon atom which has now been observed in the reaction of mercuric acetate (Hg2A) with substituted ketone phenylhydrazones containing a *C*-alkyl group at the methine carbon. Overall, this provides a 'one-flask' conversion of simple monophenylhydrazone derivatives into substituted osazones. Although the reaction is limited as to scope and yields, it can provide a useful route to substituted osazones in some cases where the yields are reasonable.

RESULTS AND DISCUSSION

Treatment of a range of *p*-nitrophenylhydrazones of acetophenones and aliphatic ketones (1a—j) (Table) with 1 mol equiv. of Hg2A in hot acetic acid resulted in a novel hydrazino-transfer to a methyl group giving as main products the 1,2-bis-hydrazones (2) of the corresponding 1,2-dicarbonyl compounds (Table). In some cases the

† Part 5, R. N. Butler and M. G. Cunningham, *J.C.S. Perkin I*, 1980, 744.

methine phenyl ring favoured the hydrazine-transfer, and electron-withdrawing groups favoured the α-

$$\text{Compound (1)} \xrightarrow[\text{HOAc}]{\text{Hg2A}} \text{Compound (2)} + \text{Compound (3)}$$

	Y	R¹	R²	M.p. (°C)	Yield (%)[a]	M.p. (°C)	Yield (%)
a	H	H	Ph	306—308 [b]	60		
b	H	H	C₆H₄Me-p	303—305	57		
c	H	H	C₆H₄Cl-p	308—309	45	129—131	9
d	H	H	C₆H₄NO₂-p	300—303	11 [g]	174—176	50
e	H	H	Me	296 [c]	70		
f	NO₂	H	Me	299—300 [d]	60		
g	NO₂	H	Ph	297—299 [e]	32 [h]		
h	H	Me	Ph	258—259 [f]	10 [i]		

				Compound (4) (R)			
i	H	H	MeCH₂	246—249 (Me)	35		
j	H	H	PhCH₂	243—245 (Ph)	40		

[a] Yields are calculated for a disproportionation, *i.e.* when 2 mol of compound (1) gives 1 mol of compound (2), the yield was 100%. [b] Lit.,[13a] m.p. 310 °C. [c] Lit.,[13c] m.p. 302 °C. [d] Lit.,[14] m.p. 299—300 °C. [e] Lit.,[13a] m.p. 295—297 °C. [f] Lit.,[13a] m.p. 256—257 °C. [g] Conditions: heated under reflux for 5 h; substrate recovered, 8%. [h] Conditions: heated at 70—80 °C for 11 h; substrate recovered, 65%. [i] Compound (3) (C=O for CHOAc) was obtained in 16% yield along with extensive gums.

acetoxylation reaction. In all cases varying quantities of intractable deep red-coloured resins were encountered, testifying to the complexity of the reaction which probably involved a number of steps. When the substituents on the hydrazone methine carbon were a methylene group and a methyl group [substrates (i and j) (Table)], the hydrazino-transfer occurred to the methyl group accompanied by an acetoxylation of the methylene group and a methyl groups [substrates (i and j) (Table)].

The structures of the products were proved from their i.r. and n.m.r. spectra which showed all of the expected signals. For compounds (1a, e, f, g, and h) (Table) the structures of the products (2) were further confirmed by direct synthesis by treatment of the corresponding 1,2-dicarbonyl compounds with 2 mol equiv. of 4-nitrophenylhydrazine and comparison of the products with authentic samples.

coming from the decomposition of the *ortho*-acetoxymercurio-compound; (iv) when a half molar proportion of Hg2A was used per mol of hydrazone substrate, a similar reaction with somewhat lower yields of bis-hydrazones was observed, *e.g.* with compound (1a) (Table), the yield of the corresponding bis-hydrazone (2a) was 54% for a reaction with 0.5 mol equiv. of mercuric acetate.

The competitive acetoxylation of the saturated carbon α-to the imino-group, giving products (3), compares with the allylic acetoxylation (involving prior mercuriation) observed [5-10] on heating alkenes with mercuric acetate in

$$-CH_2-CH=CH- \longrightarrow -CH(HgOAc)-CH=CH- \longrightarrow$$
$$-CH(OAc)-CH=CH- \quad (1)$$
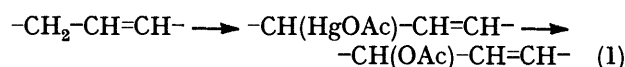
acetic acid [equation (1)]. This is considered to involve an allylic carbocation.[8-10] We tentatively suggest that
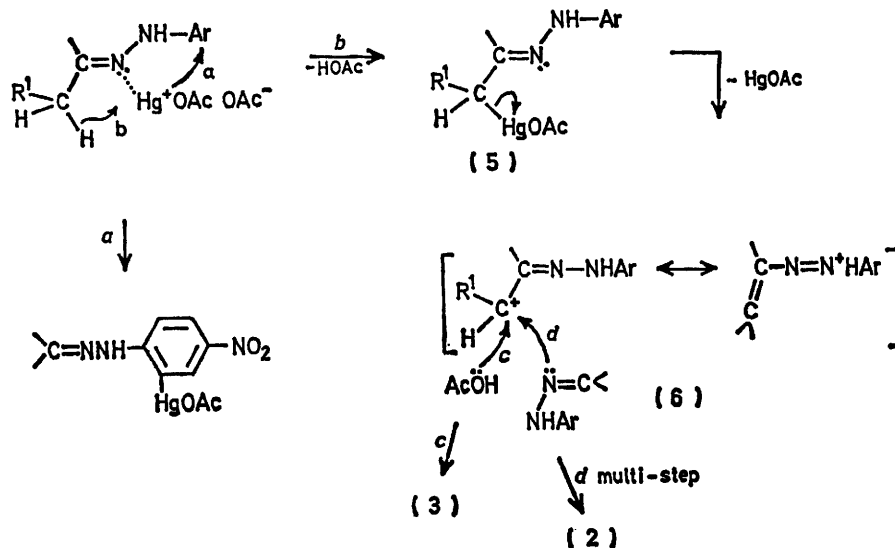
SCHEME

This interesting reaction was a surprising deviation from the N-phenyl *ortho*-mercuriation, which occurred under similar conditions with the corresponding aromatic aldehyde phenylhydrazones *via* complexation at the imino-function.[3] A number of features of the reaction give some mechanistic insight: (i) the reaction occurred in the presence of a radical inhibitor (*p*-benzoquinone) suggesting that radicals are not involved; (ii) careful analysis of the decomposition gums suggested that *ca.* 10—15% of the reaction had indeed involved an *ortho*-mercuriation of the N-phenyl ring with the *ortho*-mercurio-product undergoing decomposition in the hot acetic acid; when the substrate (1a) (Table) was treated with Hg2A in methanol, the *ortho*-acetoxymercurio-product (1; R¹ = H, R² = Ph, Y = HgOAc) was isolated in 20% yield [along with starting material (60%)] and, when this acetoxymercurio-compound was heated separately in acetic acid, it gave decomposition resins identical to some of those which were separated from the hydrazino-transfer reaction mixture; (iii) the products also contained mixtures of HgOAc and Hg⁰, the latter

the present reaction is a nitrogen analogue of this but open to a number of more complicated competitive steps (Scheme). We have previously shown[3] that mercuriation of the N-phenyl *ortho*-position involves complexation at the imino-function (Scheme, step *a*). A competitive electrophilic migration to the α-carbon would give the species (5) (Scheme, step *b*), which, in hot acetic acid, may lose HgOAc generating a relatively stable[11] aza-allylic cation (6). Competitive attack on this cation by solvent (step *c*) would give the products (3) and a nucleophilic attack by unchanged hydrazone (step *d*) would give a potential precursor to the 1,2-bis-hydrazones (2). Such a mechanism accommodates the observed data, including the substituent effects where electron-withdrawing groups at the methine carbon reduce the basicity of the imino-function and inhibit step *d*. It also accommodates the requirement of only 0.5 mol equiv. of Hg2A to give the products (2) and the somewhat lower yields of compounds (2) when a 0.5 molar proportion of Hg2A was in fact used, due to the consumption of some of the reagent in the competitive

ortho-mercuriation of the *N*-phenyl ring. The proposed mechanism also satisfactorily relates this observed complicated reaction of the ketone hydrazones to the more easily probed *ortho*-mercuriation of the corresponding aldehyde derivatives.

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. ¹H and ¹³C N.m.r. spectra were measured with JEOL JNM-MH-100 and FX-60 spectrometers. Some of the 1,2-bis-hydrazones (2) proved quite insoluble causing difficulty with n.m.r. spectral measurements and inability to detect some NH signals. The *p*-nitrophenylhydrazone substrates were prepared by standard procedures.[12]

Mercuric Acetate Oxidations.—General procedure. A mixture of hydrazone (500 mg) in acetic acid (15 ml) was treated with mercuric acetate (1 mol equiv.) dissolved in acetic acid (20 ml) and stirred at ambient temperatures for 2.5 h followed by 3.5 h at 64—68 °C. Metallic mercury and salts were removed and the red products (2) separated slowly. In cases where mixtures of mercury and the products were obtained, the organic compounds were separated by leaching into dimethyl sulphoxide–acetone (1 : 1 v/v) or nitrobenzene. Thus, typically, a mixture of *p*-chloroacetophenone 4-nitrophenylhydrazone (1c) (500 mg) in acetic acid (15 ml) was treated with a solution of mercuric acetate (550 mg) in acetic acid (20 ml) and the mixture was stirred at ambient temperature for 2.5 h, followed by heating at 64—68 °C for 3.5 h. Metallic mercury and mercury salts were removed and the red solution, when treated with water (20 ml), gave a mixture (filtrate A) of red p-*chlorophenylglyoxal bis-*(p-*nitrophenylhydrazone*) (2c) and yellow 2-(p-*chlorophenyl*)-2-(p-*nitrophenylhydrazono*)*ethyl acetate* (3c), the latter of which was separated by dissolving in ether. The filtrate A, on standing, yielded a second crop (filtrate B) of compound (2c) (overall yield, 170 mg, 45%). Further work-up of filtrate B by fractional evaporation yielded intractable red-brown resins. Compound (2c) had m.p. 308—309 °C (from dimethyl sulphoxide–water) (Found: C, 55.05; H, 3.6; N, 19.15. $C_{20}H_{15}ClN_6O_4$ requires C, 54.75; H, 3.4; N, 19.15%); $\nu_{max.}$ 3 260 (NH) and 1 600—1 610 cm⁻¹ (C=N); δ_H (HMPA) 8.0—8.4 (m, 4 H, overlapping A_2B_2, H_M), 7.4—7.6 (m, 5 H, overlapping −CH= and *p*-ClC₆H₄), 6.88—7.0 (m, 4 H, overlapping A_2B_2, H_A) (NH signals not observed in HMPA solvent; compound was insoluble in DMSO or other solvents). Compound (3c) (Found: C, 55.3; H, 3.95; N, 11.9. $C_{16}H_1$ ClN_3O requires C, 55.15; H, 4.0; N, 12.1%); $\nu_{max.}$ 3 295 (NH), 1 712 (ester C=O), and 1 600 cm⁻¹ (C=N); δ_H (CDCl₃), 9.92 (s, br, 1 H, NH), 8.17 (d) and 7.20 (d) (A_2B_2, 4 H, J_{AB} 10 Hz, *p*-NO₂C₆H), 7.80 (d) and 7.36 (d) (A_2B_2, 4 H, J_{AB} 9 Hz, *p*-ClC₆H₄), 5.14 (s, 2 H, CH₂O), and 2.16 (s, 3 H, Ac).

Compounds (2a), (2e), (2f), (2g) and (2h) are known (Table).[13,14] The following new compounds were obtained in reactions similar to those described: p-*tolylglyoxal bis-*(p-*nitrophenylhydrazone*) (2b), m.p. 303—305 °C (from DMSO–acetone, 1 : 1 v/v, by addition of water) (Found: C, 60.0; H, 4.1; N, 19.8. $C_{21}H_{18}N_6O_4$ requires C, 60.3; H, 4.3; N, 20.1%); $\nu_{max.}$ 3 260 (NH) and 1 604 cm⁻¹ (C=N); δ_H ([²H₆]-DMSO, hot) 7.52—7.80 (m, 6 H, overlapping A_2B_2; 4 H, H_A and 2H *ortho* to *p*-Me), 8.02—8.11 (d, A_2B_2, 2 H, *ortho* to C=N, J_{AB} 9 Hz), 8.4—8.76 (m, 5 H, H_M of A_2B_2 and CH=N) and 2.44 (s, 3 H, *p*-Me); p-*nitrophenylglyoxal bis-*(p-*nitro-*

phenylhydrazone) (2d), m.p. 300—303 °C (Found: C, 53.8; H, 3.1; N, 22.0. $C_{20}H_{15}N_7O_6$ requires C, 53.5; H, 3.3; N, 21.8%); $\nu_{max.}$ 3 250 (NH) and 1 600 cm⁻¹ (C=N); (n.m.r. spectra could not be obtained due to insolubility even in HMPA and DMSO); 2-(p-*nitrophenyl*)-2-(p-*nitrophenyl-hydrazono*)*ethyl acetate* (3d), m.p. 174—176 °C (from EtOH) (Found: C, 54.1; H, 3.95; N, 15.5. $C_{16}H_{14}N_4O_6$ requires C, 53.65; H, 3.9; N, 15.6%); $\nu_{max.}$ 3 300 (NH), 1 730 (ester C=O), 1 600 (C=N), and 1 105 cm⁻¹ (ester C–O–C); δ_H ([²H₆]DMSO) 10.96 (br, NH), 7.96—8.28 (m, 6 H, 4 H *ortho* to NO₂ and 2 H *ortho* to C=N), 7.40—7.48 (d, A_2B_2, J_{AB}, 8 Hz, 2 H, H_A), 5.28 (s, 2 H, CH₂O), and 2.08 (s, 3 H, Ac); 1-*ethyl*-2,3-*bis-*(p-*nitrophenylhydrazono*)*propyl acetate* (4i), m.p. 246—249 °C (from EtOH) (Found: C, 52.5; H, 4.2; N, 20.6. $C_{18}H_{18}N_6O_6$ requires C, 52.2; H, 4.35; N, 20.3%); $\nu_{max.}$ 3 260 and 3 210 (N–H), 1 740 (ester C=O), 1 600 (C=N), and 1 108 cm⁻¹ (ester C–O–C); δ_H ([²H₆]-DMSO) 11.8br and 11.58br (NH), 8.04—8.24 (m, 4 H, overlapping A_2B_2, H_M), 7.86 (s, 1 H, CH=N), 7.08—7.34 (m, 4 H, overlapping A_2B_2, H_A), 5.80 (q, 1 H, MeC*H*–O), 2.04 (s, 3 H, OAc) and 1.50 (d, 3 H, *Me*CH); δ_C [(²H₆]DMSO) 10.5 (Me-C), 20.92 and 171.8 (OAc), 112.08 and 111.29 (C-2 and C-2′), 125.7, (C-3 and C-3′), 139.6 (C-4 and C-4′), 142.3, (C=N), 149.0 and 149.9 (C-1 and C-1′), and 153.1 (CH=N) (assignments were confirmed by off-resonance proton decoupling); 2,3-*bis-*(p-*nitrophenylhydrazono*)-1-*phenylpropyl acetate* (4j), m.p. 243—245 °C (from EtOH) (Found: C, 58.1; H, 4.15; N, 17.7. $C_{23}H_{20}N_6O_6$ requires C, 58.0; H, 4.2; N, 17.65%); $\nu_{max.}$ 3 250 and 3 200 (NH), 1 745 (ester C=O), 1 600 (C=N) and, 1 105 cm⁻¹ (ester C–O–C); δ_H ([²H₆]DMSO) 11.84 and 11.62br (NH), 8.12—8.28 (m, 4 H, H_M), 7.88 (s, 1 H, CH=N), 7.04—7.52 (m, 9 H, overlapping A_2B_2 and Ph), 6.70 (s, 1 H, Ph–C*H*–OAc), and 2.20 (s, 3 H, Ac); 1-*phenyl*-1-(p-*nitrophenylhydrazono*)*propan*-2-*one* (3h; C=O for CHOAc), m.p. 209—212 °C (from EtOH) (Found: C, 63.5; H, 4.3; N, 15.2. $C_{15}H_{13}N_3O_3$ requires C, 63.6; H, 4.55; N, 14.8%); $\nu_{max.}$ 3 280 cm (NH) 1 630 (C=O), and 1 600 cm⁻¹ (C=N); δ_H 10.64br (NH), 8.12 and 7.24 (2 × d, 4 H, A_2B_2, J_{AB} 10 Hz, *p*-NO₂C₆H₄), 7.76—7.92 (m, 2 H, *o*-Ph), and 7.40—7.64 (m, 3 H, *m*- and *p*-Ph), and 2.20 (s, 3 H, Ac) [this compound was converted into the bis-hydrazone (2h) by treatment with 1 mol of *p*-nitrophenyl-hydrazine, further confirming its structure].

Acetophenone o-*Acetoxymercurio-p-nitrophenylhydrazone* (1; R² = Ph, R¹ = H, Y = HgOAc).—The compound was obtained (20% yield) by treating acetophenone *p*-nitrophenylhydrazone with mercuric acetate (1 mol) in methanol for 2.5 h at 25 °C followed by 3.5 h at 64 °C. Mercury(I) acetate was removed and fractional evaporation gave the *acetoxymercurio-derivative*, m.p. 182—183 °C (decomp.) (from EtOH) (Found: C, 37.3; H, 2.9; N, 8.5. $C_{16}H_{15}Hg$-N_3O requires C, 37.4; H, 2.9; N, 8.2%); $\nu_{max.}$ 3 280 (NH), 1 640 (C=O of HgOAc), and 1 610 cm⁻¹ (C=N); δ_H ([²H₆]-DMSO) 10.0br (NH), 8.32 (d, H_X, J_{AB} 2 Hz), 8.1 and 8.0 (1 H, H_M, J_{AM} 10 Hz), 7.32—7.46 (m, 4 H, overlapping, H_A of AMX and *m*- and *p*-Ph), 7.8 (m, 2 H, *o*-Ph), 2.4 (s, 3 H, Me-C), and 1.84 (s, 3 H, HgOAc).

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