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MECHANISM OF ORTHO-MERCURIATION OF SUBSTITUTED PHENYLHYDRAZONES - A NOVEL INTERNAL CYCLOMETALATION IN A HYDRAZONE ELECTROPHILIC ATTACK.

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The reactions of some aromatic aldehyde phenylhydrazones with mercury (II) oxide gave dimeric bishydrazone type products,[1, 2] but the reaction of p-nitrophenylhydrazones with mercury (II) acetate surprisingly[3] gave N-phenyl ortho-mercuriation, e.g. (1) ⟶ (3), apparently not involving the hydrazone chain. This reaction is herein established as an abnormal aromatic mercuriation which does indeed involve the hydrazone chain and an accompanying internal electrophile migration.

Selectivity: The reaction occurred with p-bromo phenylhydrazone systems as well as the p-nitro derivatives and the mercuriation was specific to the ortho position. (Table). Products from attack at the meta- site of the N- phenyl ring were not detected. When the nitro group was moved to the ortho- position, no reaction was observed and for both benzaldehyde- and p-methoxybenzaldehyde o-nitrophenylhydrazone the substrates were recovered.

Substituent Effects: Product studies (Table) indicated an unexpectedly strong influence by distant para-substituents of the methine phenyl ring. Kinetic studies[4] at 25° in acetic acid confirmed the substituent response (Table). The rates[4] were second order and gave a ρ value of -0.81 ($r = 0.999$) for the reaction (Figure 1). This is typical of electrophilic attack on a hydrazone system and is a higher negative ρ value than for electrophiles such as diazonium ion,[5] bromine[6] and lead tetraacetate,[7] all of which attack at the chain. Significantly, the σ^+ values[8] for the substituents were necessary (Figure 1) and normal σ values did not give a correlation. These data imply a strong interaction of the methine para-substituent with a cationic reaction centre.

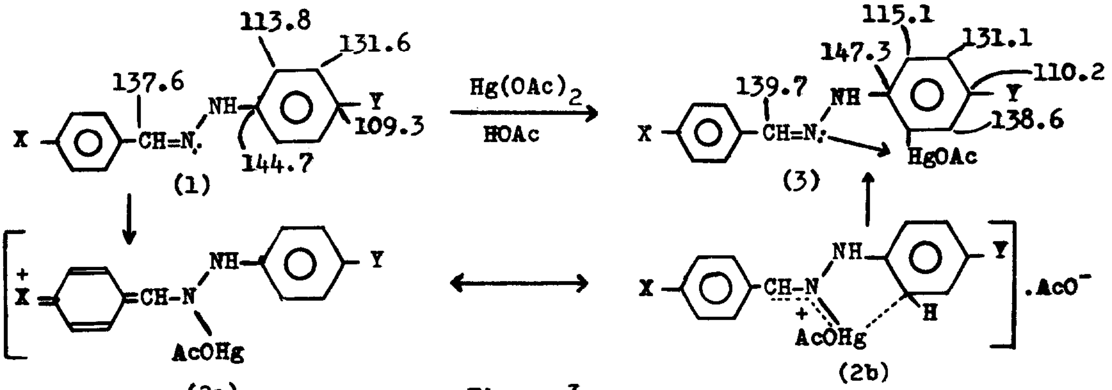
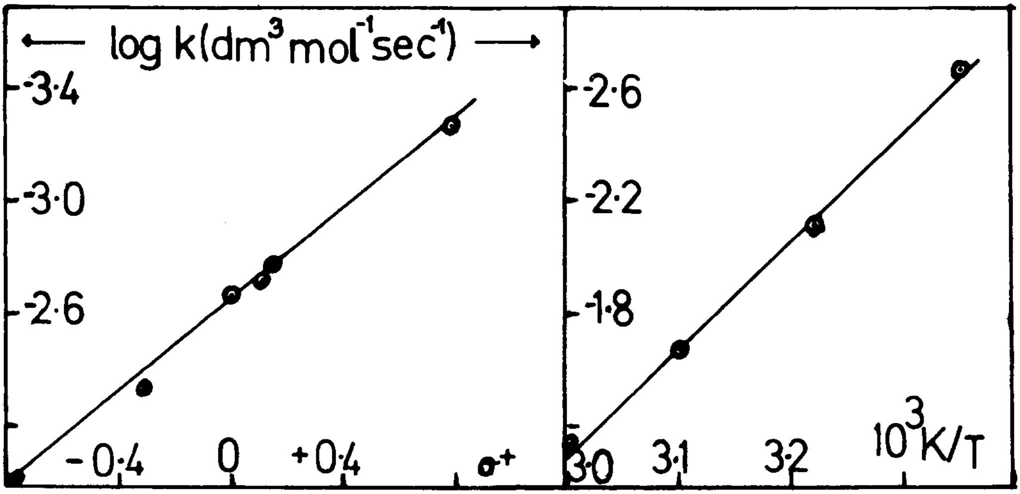


Figure 3.

The synthetic results also suggested a strong influence by para-substituents in the N-phenyl ring (Table). Kinetic measurements for Nos. 2, 7, 12 and also 1, 8 (Table) gave ρ, -2.8 ± 0.3 for this ring (using σ^+ values which correlated normal aromatic mercuriation[9]). This N-phenyl ρ value is intermediate between the value for normal aromatic mercuriation (ρ, - 4.0),[9] and the value for hydrazone electrophilic attack by bromine (ρ, - 2.2)[6] and lead tetraacetate (ρ, - 1.95).[10] It agrees with the methine substituent effects in suggesting an involvement of the hydrazone moiety. (It was not possible to use electron-donating para-substituents to measure ρ for the N-phenyl ring because removal of the para-electron withdrawing substituent surprisingly changed the nature of the reaction. With some aromatic aldehyde- phenylhydrazones (**1**, Y = H), p-methoxylphenylhydrazones (**1**, Y = MeO), and o-tolylhydrazones the products were mixtures of red resins and mercury (I) acetate. These reactions may be similar to those reported[12] for the reagents mercury (II) oxide and manganese dioxide. They are being examined further and will be reported elsewhere).

Thermodynamics: Kinetic measurements for the parent compound (1, X = H); Y = Br) gave thermodynamic data for the reaction (Figure 2.), ΔE_{act}, 17.5 k.cal mol.$^{-1}$, ΔH_{act} 16.9 k.cal mol.$^{-1}$ and ΔS_{act} - 14.1 e.u. The entropy is significantly lower than for mercuriation of other substituted benzenes (ca. - 20 to - 25 e.u.)[9] suggesting a transition state in which the activation energy is distributed among a greater number of bonds. It is comparable with the value, - 12.3 e.u.[11] for ortho-mercuriation of azobenzenes which is reported[11] to involve complexation at the β - azo-nitrogen. The activation energy is also lower than for normal aromatic mercuriations (ca. 21 - 25 k.cal mol.$^{-1}$)[9] and is consistent with a reaction-pathway stabilised by extra charge delocalization.

These data suggest that the mercuriation of the ortho-position is facilitated by the hydrazone imino moiety via attack at the n-electrons. A transition complex (Figure 3) which is stabilized by strong delocalization to the methine



Figures:1.Hammett plot for Nos. 1-6(Table); 2.Arrhenius plot for No. 3(Table)

TABLE

	Hydrazone		—— Conditions ——→	Product (3)		k.10^3 at 25°
No.	X	Y	Min., 25°	Yield (%)	M.p.	dm^{3}mol^{-1}sec^{-1}
1.	MeO	Br	20	72[a]	160-161°	9.58 (-0.778)[d]
2.	Me	Br	30	70[a]	172-174	4.56 (-0.311)
3.	H	Br	40	75[a]	163-165	2.13 (0)
4.	Cl	Br	45	85	165-166	1.91 (0.114)
5.	Br	Br	-	-	-	1.66 (0.150)
6.	NO_2	Br	80	90	181-183	0.53 (0.79)
7.	Me	NO_2	70	78[b]	-	0.06
8.	MeO	NO_2	70	88	-	0.28
9.	Cl	NO_2	70	35[b]	-	-
10.	NO_2	NO_2	70	0.5[c]	-	-
11.	Me	MeO	12	-	-	52.9 - 12.6[e]
12.	Me	H	45	-	-	27.6 - 22.4[e]

[a] Red oils were obtained due to decomposition of the product(confirmed by control reactions). [b]From ref. 3. [c]A reaction could not be achieved, ref. 3. [d] Parentheses contain σ^+ values used in Fig. 1, from ref. 8.

[e] These reactions gave red-brown resins and HgOAc as products. Attempted rapid kinetic measurements in the early stages were erratic. They are being examined further by comparing the reactions of other oxidising agents. However, despite this difficulty number 12 did correlate with numbers 7 and 2 in the ρ value for the N-phenyl ring.

phenyl ring, (2a), and in which HgOAc$^+$ ultimately migrates to the N-phenyl ring (2b) fits the data well. The reaction provides a new example of the recently[12] classified "cyclometalation" reactions in which an organic ligand of a transition metal complex undergoes intramolecular metalation with the formation of a metal-carbon σ bond. As far as we are aware, a quantitative estimation of electronic effects on such a reaction has not been reported previously but qualitative trends have been established for a number of other metals.[12] The mechanism suggests a preferred orientation for the compounds (3) in which the imino n-electrons are complexed with the Hg(II). Carbon-13 shifts (DMSO-d_6) are shown for compounds (1) and (3) (X = Me, Y = Br) and were assigned by observing the expected proton coupling and by using models. The difference in the methine carbon shifts, although small, lends some support for such a complexed structure. We have noted with other systems that when a Hg atom is bonded to a hydrazone amino NH, the methine carbon signal was generally shifted to a higher field by a small extent (Δ = - 0.5 to - 5 ppm). A reversed effect by a more remote ortho- Hg atom (Δ , 2 ppm.) is, therefore, unexpected unless there is some interaction with the imino moiety.

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REFERENCES

1. H. Minato, H. Tateno and H. Yokakawa, Bull.Chem.Soc.Japan, 1966, 39, 2724.
2. K. S. Balachandran, I. Bhatnagar and M. V. George, J.Org.Chem., 1968, 33, 3891.
3. R. N. Butler and W. B. King, J.C.S.Perkin I, 1976, 986.
4. Rate constants (± 5 %) were measured under conditions similar to the synthetic reactions. Typically, a solution of hydrazone (0.5 g.) in acetic acid (25.0 ml.) was equilibrated at 25° and treated with an equimolar proportion of mercuric acetate. At appropriate times aliquots (1.00 ml.) were withdrawn, treated with water (100 ml.), containing concentrated nitric acid (2.0 ml.) and extracted with chloroform. The unreacted mercuric acetate was determined by thiocyanate titrations and the rate constants were obtained from a plot of t vs. $x/(a-x)$ which was linear, through the origin, with slope ka.
5. A. F. Hegarty and F. L. Scott, J.Org.Chem., 1967, 32, 1957.
6. A. F. Hegarty and F. L. Scott, J.Chem.Soc.(B), 1966, 672.
7. T. A. F. O'Mahony, R. N. Butler and F. L. Scott, J.C.S.Perkin II, 1972, 1319.
8. L. P. Hammett, "Physical Organic Chemistry", McGraw-Hill, Toyko, 1970, p.356.
9. H. C. Brown, M. Dubcek and G. Goldman, J.Amer.Chem.Soc., 1962, 84, 1229, 1650.
10. M. J. Harrison, R. O. C. Norman and W. A. F. Gladstone, J.Chem.Soc.(C), 1967, 735.
11. P. V. Roling and R. A. Pickering, J.Organometal.Chem., 1976, 122, 289.
12. S. Trofimenko, Inorg.Chem., 1973, 12, 1215; M. I. Bruce, Angew.Chem.Int.Ed. Engl., 1977, 16, 73.