

Reactions of indoles with mercury (II) salts

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Abstract. A number of mercurated indoles were prepared. Their spectroscopic data (UV, IR, $^1\text{H-NMR}$ and $^{13}\text{C-NMR}$) are reported. Our results contradict certain data appearing in previous reports on similar compounds. When heated in acetic acid mercurated compounds decomposed, although the products formed were not identical with those obtained earlier from the same substrates by the action of thallium(III) acetate in acetic acid. Reaction of 1-methylindole-3-mercuriacetate with styrene in the presence of lithium tetrachloropalladate furnished a product which was tentatively assigned the structure 9-methyl-1,3-diphenyl-1, 2, 3, 4-tetrahydrocarbazole.

Keywords. Indoles; mercuration; organomercurials.

1. Introduction

In the course of our work on the reactions of heterocycles with metal salts; we investigated the reactions of indole and substituted indoles with thallium(III) acetate (Banerji and Ray 1978). A variety of oxidation products were obtained whose structures depended on the substituents at the 2- and 3-positions of indole. The results could be explained by assuming initial thallation of the indole to a 3-thallated indolenine, which reacted *in situ* to yield the products. In no case were we able to isolate the organo-thallium derivatives.

In contrast it was reported earlier (Mingoia 1930; Ramachandran and Witkop 1964; Yudin *et al* 1971) that mercury(II) salts react with indoles to give fairly stable isolable organo-mercuri derivatives. The complete characterisation of only a few of these has been described. Also, in the above-mentioned reports, there exists a great deal of confusion regarding the structures of these compounds as well as their spectroscopic data. Hence, we decided to re-investigate various aspects of the indole- HgX_2 ($\text{X} = -\text{OAc}$, $-\text{Cl}$) reaction with special reference to the spectroscopic properties of the products. The results of this investigation are reported in the present paper.

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2. Results and discussion

Indole was reacted with different proportions of mercuric acetate in ethanolic media at room temperature (Ramachandran and Witkop 1964). The physical properties of the products obtained by using (i) one molar, (ii) two molar and (iii) excess of mercuric acetate, were very similar to those reported by Ramachandran and Witkop who characterised these as the "mono", "di-" and "tri-acetoxymercuri" derivatives respectively. The elemental analyses, however, showed that none of these products was pure. Products from (i) and (ii) contained less nitrogen than the formulation suggested by Ramachandran and Witkop. Hence it appears that mercuration occurred to a greater extent than the "mono" and "di-acetoxymercuri" stage. It was not possible to accurately check mercuration at these stages. As all the products were extremely insoluble in nature they could not be purified by crystallisation.

1-Methylindole-3-mercuriacetate (I), 1-methylindole-3-mercurichloride (II) and 1,3-dimethylindole-3-mercuriacetate (III) were obtained following the method of Yudin *et al* (1971) while 3-methylindole-2-mercuriacetate (IV) was also prepared by the method of Ramachandran and Witkop. These compounds could be obtained in pure state and gave the expected elemental (C, H, N) analyses.

The UV spectra of all the compounds were measured in ethanol and the data are given in table 1. Our results indicate that for compounds (I-IV) the absorption maxima suffered only a small but significant hypsochromic shift whereas the extinction coefficients were virtually unchanged. The mercury substituent has two vacant *p*-orbitals and exerts a -*R* conjugative effect on the aromatic nucleus which causes the observed hypsochromic shift in the UV spectra. Similar observations for phenyl- thienyl- and furyl-mercury derivatives were noted earlier (Leandri and Tundo 1954). Ramachandran and Witkop (1964) had reported the UV spectral data of what they formulated as "mono-", "di," and "tri-acetoxymercuri" indoles in about 2.5% acetic acid. These workers reported marked changes in the position of absorption maxima as well as very large enhancements in extinction coefficients when compared with the starting materials. Our results contradict these reports. The absorption maxima of the "mono-" ($\lambda_{\text{max}}^{\text{EtOH}}$ 218, 272, 277.5, 288 nm), and "di-acetoxymercuri" ($\lambda_{\text{max}}^{\text{EtOH}}$ 218, 272, 277.5, 288 nm) compounds showed the same small hypsochromic shift compared to indole ($\lambda_{\text{max}}^{\text{EtOH}}$ 216, 266, 276, 287 nm) as observed for the other compounds. Moreover, no perceptible shifts of the absorption maxima of these two compounds, or in fact of any of the other mercurated products, were observed when the medium was changed from ethanol to 2.5% acetic acid. The extinction coefficients for the two products obtained from indole calculated on the basis of mono- and di-acetoxymercuration are considerably less than those expected. This is in conformity with the elemental analyses which showed the occurrence of mercuration beyond the desired stage.

We report here the IR spectra of the mercurated indoles for the first time. The important bands and their assignments are listed in table 2. The spectra were recorded in Nujol mull using polyethylene discs. The C-Hg stretching bands appeared at 400-415 cm^{-1} for all the compounds. When the IR spectra were recorded in KBr pellets, additional bands appeared at 335-340 and 505-550 cm^{-1}

indicating the formation of other compounds by metathetical reactions. The IR spectrum of 1,3-dimethyl-2-acetoxymethylmercuri-indole is given in figure 1, with the more important assignments. The different impure mercurated products ("mono-", "di-" and "tri-acetoxymethylmercuri") from indole also showed C-Hg stretching at 400–415 cm^{-1} .

NMR investigation of mercuri-indole was also carried out (table 3). Some ^1H -NMR data had been earlier reported by Ramachandran and Witkop (1964) using trifluoroacetic acid (TFA) as the solvent. They made certain structural assignments on the basis of these observations; in particular the "di-acetoxymethylmercuri" derivative was assigned the structure 2,3-diacetoxymethylmercuri-indole. It seems that no reliance can be placed on these data for the following reasons: Firstly in TFA medium the indoles will certainly exist as 3-protonated indolenine species rather than free species; Secondly in the strong acid medium used demercuration would easily occur so that the reported values may not refer to the mercurated compounds at all.

We found that for the 1-methyl-3-acetoxymethylmercuri-indole, the C-2 proton and N-methyl group were slightly de-shielded with respect to 1-methyl indole. There were also changes in the signals for the benzenoid protons. In the parent heterocycle all these protons appeared as a complex multiplet centred around $\delta 7.2$, whereas in the mercuri-derivative one of these moved downfield to appear as a double doublet at $\delta 7.50$ ($J_0 = 6.1$ Hz, $J_m = 1.5$ Hz). This signal was presumably due to the C-4 proton, which is shielded by the 3-acetoxymethylmercuri grouping.

The 20 MHz ^{13}C -NMR of 1-methyl-3-acetoxymethylmercuri-indole was recorded in $\text{DMSO}-d_6$. Tentative assignments based on single-frequency off-resonance decoupling (SFORD) multiplicities and chemical-shift theory are given in figure 2. ^{13}C -NMR spectra of the other compounds could not be recorded on account of their poor solubility in the more common deuterated solvents.

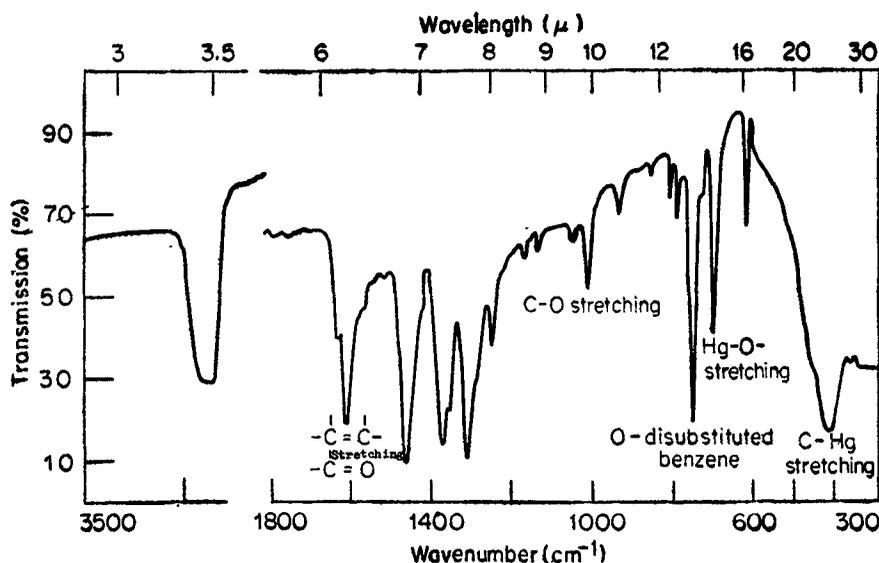


Figure 1. IR spectrum of 1,3-dimethyl-2-acetoxymethylmercuri-indole recorded in Nujol mull with polythene disc. Region below 600 cm^{-1} was recorded at higher concentration.

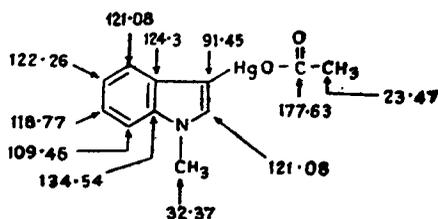


Figure 2. 20 MHz ^{13}C NMR Spectral data (CDCl_3) (in ppm) of 1-methyl-3-acetoxy mercuri-indole.

Table 1. uv absorption maxima of mercurated indoles (in 95% ethanol),

| Compound (in EtOH) | λ_{max} (log ϵ) in nm |
|---------------------------------------|---|
| 2-Acetoxymercuri-skatole | 226 (4.32), 290 (3.90), 296 (3.90) |
| Skatole* | 222 (4.50), 275 (3.73), 282 (3.78), 2.90 (3.69) |
| 1-Methyl-3-acetoxymercuri-indole | 222 (4.58), 272.5 (3.90), 284 (3.89), 295 (3.80) |
| 1-Methylindole-3-mercuri-chloride | 222 (4.58), 270 (sh) (3.76), 283 (3.77), 295 (3.67) |
| 1-Methylindole* | 219 (4.54), 275 (3.77), 282 (3.78), 293 (3.66) |
| 1,3-Dimethyl-2-acetoxy-mercuri-indole | 228 (4.43), 292.5 (3.99) |
| 1,3-Dimethyl-indole* | 225 (4.50), 248 (3.72), 278 (3.68) |
| Indole* | 216 (4.54), 266 (3.76), 276 (3.76), 287 (3.68) |

* Houlihan (1972).

Table 2. IR absorption bands of mercurated indoles (in nujol mull recorded in polythene discs).

| Compound | ν (in cm^{-1}) | | | | |
|---------------------------------------|------------------------------|------------------|---------------------------------|------|------|
| | Acetate* | | <i>o</i> -Disubstituted benzene | Hg-O | Hg-C |
| | >C=O | -O-C- stretching | | | |
| 2-Acetoxymercuri-skatole | 1580 | 1010 | 725 | 680 | 405 |
| 1-Methyl-3-acetoxymercuri-indole | 1600 | 1005 | 730 | 690 | 400 |
| 1,3-Dimethyl-2-acetoxy-mercuri-indole | 1600 | 1010 | 750 | 700 | 415 |
| 1-Methylindole-3-mercuri-chloride | ... | ... | 750 | ... | 410 |

* Strong bands were observed for the three acetoxymercuri compounds at 1580–1600 cm^{-1} which masked the >C=C< stretching band. For the mercuri-chloride derivative a very weak absorption (>C=C<) was observed at 1590 cm^{-1} .

Table 3. 80 MHz ¹H-NMR spectral data of mercurated indoles.

| Compound | Signal at δ (ppm) | | | |
|--------------------------------------|--------------------------|---------------------|---|---|
| | Solvent | -OCOCH ₃ | Aromatic protons | Other protons |
| Mono-acetoxy-mercuri-skatole | DMSO-d ₆ | 1.87 | 6.70-7.80 | -CH ₃ merged with DMSO peak |
| 1-Methylindole-3-mercuri-acetate | CDCl ₃ | 2.05 (3H, s) | 6.95 (1H, br, s) 7.08-7.30 (3H, m) 7.50 (1H, dd, $J_o = 6.1$ Hz, $J_m = 1.5$ Hz) | -N-CH ₃ 3.76 (3H, s) |
| 1,3-Dimethylindole-2-mercuri-acetate | CDCl ₃ | 2.01 (3H, s) | 6.94-7.37 (4H, m) | -N-CH ₃ 3.37 (3H, s) C-CH ₃ 2.21 (3H, s) |
| 1-Methylindole-3-mercuri-chloride | DMSO-d ₆ | | 6.94-7.30 (3H, m); 7.38 (1H, dd, $J_o = 8.8$ Hz, $J_m = 1.8$ Hz; 7.65 (1H, dd, $J_o = 7.7$ Hz, $J_m = 2.6$ Hz) | -N-CH ₃ 3.74 (3H, s) |

As mentioned earlier, the reaction of indoles with TTA in acetic acid gave oxidation products. It was of interest to find out whether the mercuri-indoles would also be converted to similar products under similar or more vigorous reaction conditions. It was found that the mercurated compounds remained largely unaffected when subjected to reaction conditions similar to those used for the TTA reaction. When more vigorous conditions were used, none of the products previously obtained with TTA was formed though some, demercuration to the original compounds occurred. Most of the material underwent decomposition to intractable products. In the case of mono-acetoxymmercuri-indole, oxindole was formed in low yield on heating with glacial acetic acid for 4 hours.

2.1. Reaction of 1-methylindole-3-mercuri-acetate with styrene

The palladium salt-catalysed olefin arylation reaction provides a very convenient route to a wide variety of olefinic compounds (Heck 1968). We attempted the use of 3-mercurated N-methylindole for arylating styrene in methanolic medium in the presence of lithium tetrachloropalladate at room temperature. A number

of unstable products were formed, of which only one of the major compounds could be isolated in a reasonably pure state by preparative TLC. None of the others could be isolated by TLC as they underwent decomposition. The isolated product, which exhibited a typical indolic UV spectrum ($\lambda_{\text{max}}^{\text{EtOH}}$ 225, 277–278 (sh) nm), was tentatively assigned the structure 9-methyl-1,3-diphenyl-1,2,3,4-tetrahydrocarbazole (3) primarily on the basis of its $^1\text{H-NMR}$ spectrum. A variety of possibilities exist for alternative combinations with styrene, of which only that shown was compatible with the $^1\text{H-NMR}$ (see experimental for chemical shifts) (figure 3).

The formation of the product (3) can be mechanistically rationalised as shown in scheme 1.

3. Experimental

All melting points are uncorrected and were determined on an electrically heated Kofler Block melting point apparatus. The UV spectra were measured on a Varian 634S spectrophotometer in 95% aldehyde free ethanol. The IR spectra were

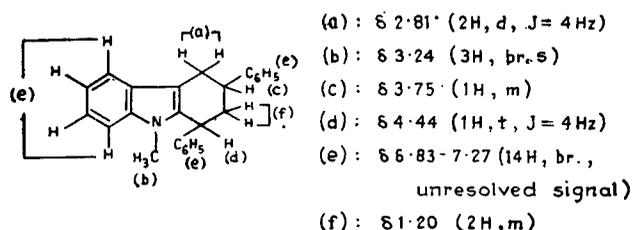
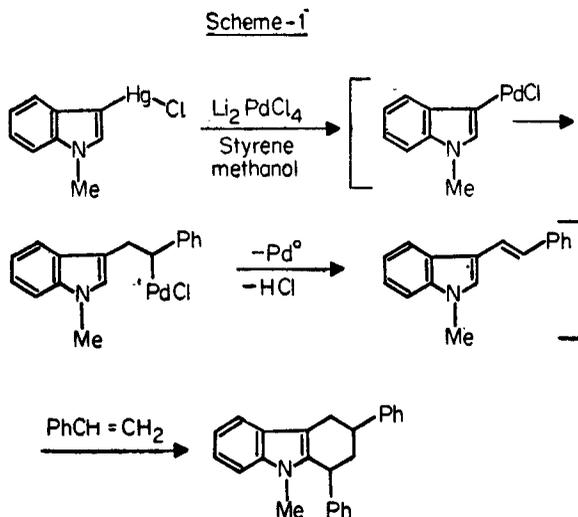


Figure 3. 80MHz $^1\text{H-NMR}$ spectral data of 9-methyl-1,3-diphenyl-1,2,3,4-tetrahydrocarbazole.



recorded in polythene disc on a Beckman IR-20 spectrophotometer. The ^1H - and ^{13}C -NMR spectra were recorded on Varian Associates CFT-20 NMR spectrometer.

3.1. 2-Acetoxymercuri-skatole

Mercuric acetate (1.59 g, 5 mmol) in absolute ethanol (15 ml) was added in portions to a magnetically stirred solution of skatole (0.66 g, 5 mmol) in absolute ethanol (10 ml) whereby a pale yellow dispersion was formed. The mixture was stirred for 2 hr and left overnight. The pale yellow precipitate was filtered and washed thoroughly with absolute ethanol (yield 1.1 g, 57.9%); m.p. 180° (d). Found C 35.5%, H 3.1%, N 3.6%; $\text{C}_{11}\text{H}_{11}\text{O}_2\text{NHg}$ requires C 35.7%, H 3.2%, N 3.6%.

3.2. 1-Methyl-3-acetoxymercuri-indole and 1,3-dimethyl-3-acetoxymercuri-indole

1-Methylindole and 1,3-dimethylindole were prepared according to Heaney and Steven (1973).

To a stirred solution of the methylated indole (5 mmol) in absolute ethanol (10 ml), mercuric acetate (1.59 g, 5 mmol) in absolute ethanol (15 ml) was added and left overnight. The white precipitate was filtered off, washed and dried.

3.2a. 1-Methyl-3-acetoxymercuri-indole. Yield 1.7 g, 89.4%; m.p. 187° (d). Found C 34.2%, H 2.2%, N 3.5%; $\text{C}_{11}\text{H}_{11}\text{O}_2\text{NHg}$ requires C 33.9%, H 2.3%, N 3.6%.

3.2b. 1,3-Dimethyl-3-acetoxymercuri-indole. Yield 1.1 g, 55.0%; m.p. 144-6°. Found C 35.6%, H 3.2%, N 3.7%; $\text{C}_{12}\text{H}_{13}\text{O}_2\text{NHg}$ requires C 35.7%, H 3.2%, N 3.4%.

3.3. 1-Methylindole-3-mercurichloride

1-Methylindole (0.66 g, 5 mmol) and sodium acetate (1.6 g, 20 mmol) were dissolved in anhydrous methanol (10 ml), and mercuric chloride (1.36 g, 5 mmol) in methanol (15 ml) was added. A white precipitate appeared instantaneously, which was filtered, washed and dried (yield 1.5 g, 83.3%), m.p. 170° (d) (Yudin *et al* 1971, 170-3°). Found C 35.6%, H 1.9%, N 3.7%; $\text{C}_9\text{H}_8\text{ClNHg}$ requires C 35.6%; H, 1.9%; N 3.8%.

3.4. Reaction of 1-methylindole-3-mercuriacetate and styrene in presence of Li_2PdCl_4

To a mixture of 1-methylindole-3-mercuriacetate (0.97 g, 2.5 mmol) and styrene (0.6 ml, > 5 mmol); 0.1 (M) Li_2PdCl_4 (50 ml, 5 mmol) in methanol was added dropwise over a period of 1 hr and then stirred for 48 hr in an atmosphere of nitrogen. The mixture was filtered, the solvent removed and the residue was extracted with methylene chloride. The residue from the methylene chloride extract was purified by column chromatography and PLCC. 9-methyl-1,3-diphenyl-1,2,3,4-tetrahydrocarbazole (*R*, 0.40, alumina; developing solvent: petrol-benzene 1:2) was isolated as an amorphous solid.

80 MHz NMR spectral data of (3) (in $CDCl_3$): (a) δ 2.81 (2H, *d*, $J = 4$ Hz); (b) δ 3.24 (3H, broad *s*); (c) δ 3.75 (1H, *m*); (d) δ 4.44 (1H, *t*, $J = 4$ Hz); (e) δ 6.83–7.27 (4H, broad unresolved signal), (f) δ 1.20 (2H, *m*).

3.5. Mono-acetoxymercuri-indole

To a stirred solution of indole (0.59 g, 5 mmol) in absolute ethanol (10 ml); mercuric acetate (1.59 g, 5 mmol) in absolute ethanol (15 ml) was added portionwise. The reaction mixture was allowed to stand overnight, filtered, the residue washed with ethanol and dried (yield 1.2 g, 66.6% on basis of mono-mercuration); m.p. 266° (d) [Ramachandran and Witkop 1964, 270° (d)]. Found N 2.2%, $C_{10}H_9O_2NHg$ requires N 3.7%.

3.6. Di-acetoxymercuri-indole

Di-acetoxymercuri indole was prepared similarly using two moles of mercuric acetate (3.17 g, 10 mmol). The product was isolated in a similar manner (yield 2.7 g, 98.1% on basis of di-mercuration); m.p. 205° (d) [Ramachandran and Witkop 1964, 205° (d)]. Found N 1.9%; $C_{12}H_{11}O_4NHg_2$ requires N 2.2%.

3.7. Tri-acetoxyme-mercuri-indole

Indole was mercurated with excess of mercuric acetate (6.36 g, 20 mmol) following the same procedure. A precipitate rapidly formed and then redissolved. The alcohol was removed under reduced pressure. The residue was triturated with water, filtered and then washed successively with water, ethanol and ether (yield 0.5 g, 10.7% on basis of tri-mercuration); m.p. 268–9° (d) [Ramachandran and Witkop 1964, 270° (d)]. Found N 1.8%, $C_{14}H_{13}O_6NHg_3$ requires N 1.6%.

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References

- Banerji A and Ray R 1978 *Indian J. Chem.* B16 422
Heck R F 1968 *J. Am. Chem. Soc.* 90 5518
Heanly H and Steven V L 1973 *J. Chem. Soc. Perkin Trans. I* 499
Leandri G and Tundo A 1964 *J. Chem. Soc.* p. 3377
Mingoa Q 1930 *Gazz. Chim. Ital.* 60 509
Ramachandran L K and Witkop B 1964 *Biochemistry* 3 1603
Yudin L G, Kost A N and Pavlyuchenko A I 1971 *Khim. Geterotsikl. Soedin* 7 1517
Houlihan W J (ed.) 1972 *The chemistry of heterocyclic compounds* Part 1 (New York: Wiley Interscience) p. 21