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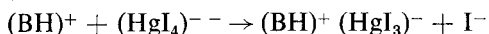
REFERENCES

- BAUMEL, I. P., ROBINSON, S. M. & BLATT, W. F. (1967). *J. pharm. Sci.*, **56**, 918-919.
 BAUMEL, I. P., SCHATZ, R., DEFEO, J. J. & LAL, H. (1969a). *J. Pharm. Pharmac.*, **21**, 119-120.
 BAUMEL, I., SCHATZ, R., DEFEO, J. J. & LAL, H. (1969b). *Ibid.*, **21**, 475-476.
 JOHNSON, W. L., GOLDRING, S. & O'LEARY, J. L. (1965). *Clin. Neurophysiol.*, **18**, 229-238.
 LAMAR, C., JR. & SELLINGER, O. Z. (1965). *Biochem. Pharmac.*, **14**, 489-506.
 PROLER, M. L. & KELLAWAY, P. (1962). *Epilepsia*, **3**, 117-130.
 ROBERTS, E. & FRANKEL, S. (1951). *J. biol. Chem.*, **190**, 505-512.
 WOOD, J. D., WATSON, W. J. & DUCKER, A. J. (1968). *J. Neurochem.*, **15**, 603-608.

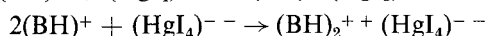
The nature of the products from the reaction between Mayer's reagent and tertiary amines

Mayer's reagent (an aqueous solution of potassium tetra-iodomercurate) gives precipitates with alkaloids and synthetic tertiary amines. This reaction forms the basis of a qualitative test for such compounds. Szász (1965; 1966) has reported, from a study of seventeen tertiary amines, that each amine is capable of forming two compounds with potassium iodomercurate, the nature of the compound formed being dependent upon the concentration ratio of the reactants. An excess of potassium tetra-iodomercurate yields coloured (yellow or brown) products, whereas when the amine is in excess the resultant compound is white or only faintly coloured.

Because the "amine-Mayer's reagent" products are formed only in acidic medium, it is reasonable to assume that they are simple salts with a protonated amine cation and either a tri-iodomercurate or tetra-iodomercurate anion. Microanalytical data support the stoichiometry of this proposal (Szász & Buda, 1969). The reactions may, therefore, be expressed by the following equations:



and



To confirm the salt-like character of the "amine-Mayer's reagent" products, a proton magnetic resonance (pmr) investigation of two representative tertiary amines, codeine and *NN*-dimethylaniline and their iodomercurates was undertaken (Table 1).

The pmr spectrum of dimethylaniline in acetone- D_6 shows a normal $-\text{N}-(\text{CH}_3)_2$ singlet at 7.20 τ and a complex AA'BB'C aromatic pattern centred on 3.08 τ . This spectrum differs only marginally from that recorded in deuteriochloroform (Ma & Warnoff, 1965; Anderson & Silverstein, 1965; Thompson, Warren & others, 1966). Protonation of the nitrogen, in the hydrochloride salt, results in the expected downfield shift of the *N*-methyl absorption to 6.59 τ and of the aromatic multiplet to 2.05 τ . The overall appearance of the aromatic multiplet is little changed. Dimethylaniline tri-iodomercurate and dimethylaniline tetra-iodomercurate exhibit their *N*-methyl signals at 6.36 and 6.42 τ respectively and both aromatic multiplets centre on 2.24 τ . Although these values correspond well with those of the simple hydrochloride and hydroiodide salts, the appearance of the aromatic multiplet is much changed in the iodomercurates.

Table 1. *Pmr* data on dimethylaniline, codeine and their derivatives. *Pmr* spectra (60 MHz) were determined in the solvent indicated with chemical shifts reported in ppm (τ) downfield from tetramethylsilane as an internal reference (Perkin-Elmer Model R-12).

Compound	$>N-CH_3$			$-O-CH_3$			Aromatic H		
	Acetone- D ₆	DMSO- D ₆	CDCl ₃	Acetone- D ₆	DMSO- D ₆	CDCl ₃	Acetone- D ₆	DMSO- D ₆	CDCl ₃
Dimethylaniline ..	7.20s	—	7.18s	—	—	—	3.08m	—	3.02m
Dimethylaniline hydrochloride*	6.59s	—	—	—	—	—	2.05m	—	—
Dimethylaniline hydroiodide ..	6.67s	—	—	—	—	—	2.10m	—	—
Dimethylaniline triiodomercurate	6.36s	—	—	—	—	—	2.24m	—	—
Dimethylaniline tetraiodomercurate ..	6.42s	—	—	—	—	—	2.24m	—	—
Codeine ..	7.60s	7.72s	7.54s	6.17s	6.30s	6.12s	3.37q	3.47q	3.17q
Codeine hydrochloride*	6.82s	7.05s	—	6.12s	6.20s	—	3.17q	3.28q	—
Codeine triiodomercurate ..	6.61s	—	—	6.11s	—	—	3.16q	—	—
Codeine tetraiodomercurate† ..	—	7.01s	—	—	6.22s	—	—	3.29q	—

s = singlet; q = quartet; m = multiplet.

* Hydrochloride salts were prepared *in situ* by passing dry hydrogen chloride through a solution of the base.

† Codeine tetra-iodomercurate is only sparingly soluble in acetone.

Similarly, codeine tri-iodomercurate and codeine tetra-iodomercurate exhibit *N*-methyl signals at values close to that of codeine hydrochloride. No significant variation in chemical shift or spectrum appearance was observed in either the aromatic AB quartet or the aromatic *O*-methyl signal of codeine and its derivatives.

These observations clearly indicate that the precipitates formed from the interaction of tertiary amines and potassium tetra-iodomercurate are tri- and tetra-iodomercurate salts. The change in the form of the aromatic pattern with the dimethylaniline iodomercurates may be attributed to the close proximity of the aromatic protons to the bulky mercury-complex anion.

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REFERENCES

- ANDERSON, W. R. & SILVERSTEIN, R. M. (1965). *Analyt. Chem.*, **37**, 1417-1418.
 MA, J. C. N. & WARNOFF, E. W. (1965). *Can. J. Chem.*, **43**, 1849-1869.
 SZÁSZ, G. (1965). *Acta pharm. hung.*, **35**, 256-258.
 SZÁSZ, G. (1966). *Ibid.*, **36**, 120-125.
 SZÁSZ, G. & BUDA, L. (1969). *Ibid.*, in the press.
 THOMPSON, W. E., WARREN, R. J., ZAREMBO, J. E. & EISDORFER, I. B. (1966). *J. pharm. Sci.*, **55**, 110-111.