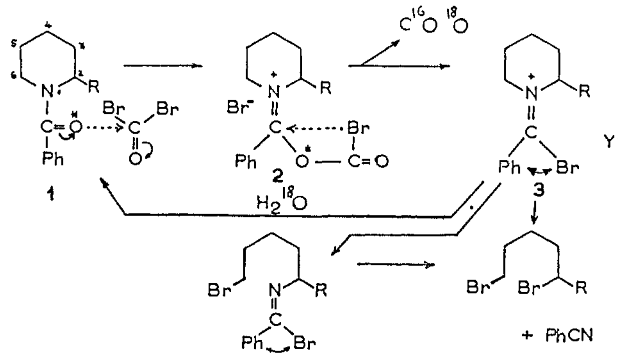
# Isolation of Iminium Bromides as Intermediates in the von Braun Reaction

*Sir:*

The von Braun reaction[1,2] of heterocyclic benzamides with phosphorus pentabromide has been applied in only a few cases in structure determination of alkaloids, *e.g.*, quinine,[3] sedridine,[4a,b] and conhydrine[5] have been correlated with well-known aliphatic compounds. This paucity of application exists despite the advantages the reaction offers over the repetitious Hofmann methylation procedure. The primary reasons for this are the rather harsh reaction conditions using phosphorus pentabromide and the lack of insight into the mechanism.

To overcome both these difficulties, we have applied carbonyl bromide as a new reagent in this reaction. Addition of this bromide to a benzene solution of benzoylconiine, **1a**, ir 1630 $cm^{-1}$ ($C{=}O$), gave, besides $CO_2$, an iminium bromide, **3a** ($Y = Br$), as a noncrysstalline red oil (60% yield), which in turn was converted with silver hexafluoroantimonate quantitatively into a crystalline salt, **3a** ($Y = SbF_6$), mp 150° (*Anal.* Calcd for $C_{15}H_{21}NBrSbF_6$: C, 33.93; H, 3.99; Br, 15.05; F, 21.47; N, 2.64. Found: C, 34.25; H, 3.92; Br, 15.80; F, 21.62; N, 2.63); ir (KBr) 1600 $cm^{-1}$ (C–Br); nmr (acetonitrile-$d_3$) $\delta$ 5.5 (m, 1, H-2), 3.4 (m, 2, H-6), 1.7 (m, 10, methylenes), 1.0 (t, 2, C-methyl), all in harmony with structure **3a** ($Y = SbF_6$). The bromide **3a** ($Y = Br$) showed in the mass spectrum peaks at *m/e* 295 and 297 indicative of the bromoiminium ion. Further *m/e* values of 273, 271, and 269 corresponded to 1,5-dibromooctane **4**, itself a von Braun reaction product.



a: R = $C_3H_7$ (coniine)

b: R = $CH_2CHOCOPhCH_3$ (sedridine)

Refluxing of the same iminium bromide **3a** ($Y = Br$) in dibromoethane (130°) afforded, after purification by column chromatography (silica gel–cyclohexane as solvent), in 25% yield, 1,5-dibromooctane **4** (nmr $\delta$ 1.1 (t, 3 H), 3.5 (t, 2 H, $CH_2Br$), 4.1 (s, 1 H, CHBr), as well as benzonitrile, *i.e.*, the end products of the von Braun reaction. Hydrolysis of the oil **3a** ($Y = Br$) in acetonitrile in the presence of triethylamine yielded benzoylconiine (**1a**) in 91% yield along with 2 mol of the base hydrobromide. Identical results have been achieved with N,O-dibenzoylsedridine (**1b**).

These results provide circumstantial evidence for a bromoiminium bromide as an intermediate in the von Braun reaction. Further support of this claim was given by the following isotope experiments. Labeled **1a** (60 atom % oxygen-18) when treated with carbonyl bromide produced carbon dioxide with peaks in the mass spectrum at *m/e* 46 (55%) and 44 (45%). This delineates the fate of the oxygen from the amide **1a** and is consistent with a cyclic four-center transition state **2**. When **3a** ($Y = Br$) was treated with oxygen-18-labeled water under the previous conditions, $^{18}O$-benzoylconiine, ir 1630 ($C{=}O$), 1610 $cm^{-1}$ ($C{=}^{18}O$), was isolated again in quantitative yield. The complete reversibility clearly indicates the intactness of the ring at this state—at variance with earlier postulates[6] as to ring opening prior to deoxygenation. It also shows that no halogenoimidoyl halide (**5**) was formed at this first step—unlike in the reaction of benzoylmonoalkylamides with thionyl chloride.[7] Further, the anionic exchange of Br for $SbF_6$ in crystal formation shows the anionic nature of one of the bromines and obviates the presence of a geminal covalent dibromide as an intermediate.[1]

Using N,O-dibenzoyl-$^{18}O$-sedridine (**1b**), the carbon dioxide which has formed showed the same isotopic composition as in case of **1a**. The iminium bromide, separated in a 60% yield, gave in the mass spectrum *m/e* 389.5, 391.5, and 393.5 corresponding to the final product **4b** of the von Braun reaction **4a** and also *m/e* 311 and 313 of an iminium bromide with the loss of benzoyl. This corroborates the conclusions reached with benzoylconiine.

As to whether imidoyl bromides[8] are indeed formed in the next stage from **3** prior to the dibromide **4** is now the focus of our current investigation.

We have already isolated two distillable bromoalkylimidoyl bromides (type **5**) as by-products in the von Braun reaction with dibenzoyl sedridine **4b** and conhydrine.[5] These probably have the alkyl group and bromine in *syn* position while their *anti* isomers should easily undergo *trans* elimination to dibromoalkanes. Attempts to determine the geometry of **3a** and **3b** are also in progress.

Experimentally, we would like to emphasize the value of carbonyl bromide, a low boiling liquid,[9] as a reagent in this and related reactions, *e.g.*, Vilsmeier–Haack synthesis.

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