

Short Communications

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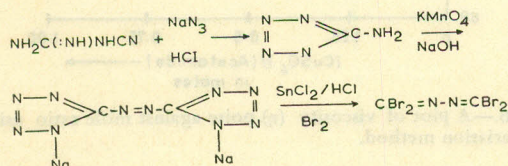
ISOCYANATE TETRABROMIDE AND ITS REACTIONS

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The structure of isocyanate tetrabromide suggested that, it might be used as a source of dibromocarbene. The synthesis of this compound from guanidine nitrate has been reported.¹ The method was long and the yields were poor. The compound was prepared in high yield from dicyandiamide as shown in scheme 1.



A mixture of dicyandiamide (41 g) water (100 ml) and sodium azide (58.5 g) was heated in presence of hydrochloric acid (75 ml) at 60–70° for 7 hr. Work up in the usual manner gave 5-aminotetrazole, m.p. 216–17° (from aqueous ethanol) as colourless plates (65g, 75%). Calcd. for CH_3N_5 : C, 14.1; H, 3.5; N, 28.35. Found: C, 14.4; H, 3.8; N, 28.6%.

5-Aminotetrazole was then converted to isocyanate tetrabromide as described by Thiele.¹ The product crystallised from petroleum ether (b.p. 40–60°) as colourless needles, m.p. 39–40°, IR spectrum (CH_2Cl_2); 1590 and 860 cm^{-1} .

Reactions

(a) *With Cyclohexene.*—On heating isocyanate tetrabromide (8 g) with cyclohexene (20 g) at 90–95° for 8 hr the reactants were recovered unchanged.

(b) *With Maleic Anhydride.*—On mixing isocyanate tetrabromide (136 mg) with a solution of maleic anhydride (49 mg) in dry toluene (6 ml), no charge transfer complex was isolated, but instead, on heating for 3 hr fumaric acid (24 mg, 40%), m.p. and mixed m.p. 265–68°, was isolated. This suggested a structure resembling to those of vinyl halides, where a C–Br bond acquires a double bond character.

(c) *With Acetylene Dicarboxylate.*—A solution of acetylene dicarboxylate (3.72 g) and isocyanate tetrabromide (1.7 g) was heated at 40° for 4 hr in the hope that an adduct might be obtained, which on further heating would break up to give dibromocarbene, but the starting materials were recovered unchanged.

(d) *With Methanolic Potassium Hydroxide.*—Tetramethoxy isocyanate was isolated, which crystallised from petroleum ether (b.p. 60–80°) as colourless needles, m.p. 111–12° (lit.¹ m.p. 111–12°), IR spectrum (Nujol): 1650, 1295, 1200, 1180, 1080, 1030, 850 and 750 cm^{-1} , UV spectrum (95% ethanol) ϵ_{max} 272 $\text{m}\mu$ (\log_e 3.61).

On adding a solution of tetramethoxy isocyanate (176 mg) to a solution of maleic anhydride (98 mg) in toluene (6 ml), a deep yellow colour was obtained. This solution on cooling deposited a colourless solid m.p. 130–31° (from alcohol), IR spectrum included bands at 1725, 1685, 1630 and 1590 cm^{-1} ; UV spectrum (95% ethanol): ϵ_{max} 3.2 (\log_e 3.92). Calcd. for $\text{C}_{10}\text{H}_{14}\text{N}_2\text{O}_7$: C, 47.4; H, 5.1; N, 10.2. Found: C, 47.0; H, 4.9; N, 10.0%.

Acknowledgement.—The author is grateful to Dr. E. J. Forbes for suggesting the problem and to the Birmingham University for providing the facilities to carry out this work.

Reference

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THE ACTION OF A BASE ON α,α -DIBROMOACETANILIDE

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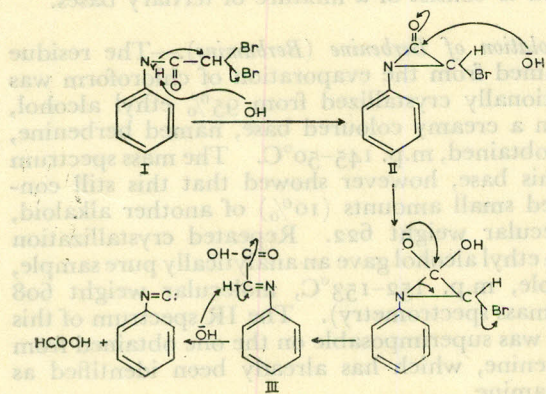
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α,α -Dibromoacetanilide was prepared by heating a mixture of aniline (15 g), dibromoacetyl bromide (6 ml), potassium carbonate (15 g) and benzene (150 ml) for 1 hr at 50–60°. Work up in the usual manner followed by crystallisation from ethanol gave colourless plates, m.p. 138–39°, yield 30 g, 64%.

Compound I (2 g) was heated with methanolic solution of potassium hydroxide (2.5 g in 25 ml methanol). Phenyl isocyanide was detected and on burning the gasses no blue flame was detected.

The gasses evolved in the above reaction were passed through a solution of palladous chloride. No precipitate was formed, thus indicating the absence of carbon monoxide. These results are in contradiction to those of Flim.¹

A mixture of α,α -dibromoacetanilide (10 g) and alcoholic potassium hydroxide (2.5 g in 25 ml methanol) was heated for 30 min. The flask was cooled and hydrochloric acid (20 ml) was added. The reaction flask was set for the steam distillation (500 ml). To the distillate was added mercuric chloride (20 g) and the mixture heated for 10 hr on a steam bath. The precipitated mercurous chloride was filtered, washed with warm water and dried (14 g). Thus the yield of formic acid formed on the basis of the above reaction was 1.2 g, 70%. The presence of formic acid was further confirmed by the formation of its sodium salt. The formation of the products could be rationalized by the following mechanism.



The above mechanism postulates the formation of an intermediate II through Favorskii rearrangement followed by an attack of the base on the carbonyl to give compound III which, reacts further with the base to give the observed products.

Acknowledgement.—The author is grateful to Dr. E. J. Forbes for his helpful discussion and to the Birmingham University for providing the facilities.

Reference

1. Flim, Ber., 23, 60.

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THE ALKALOIDS OF BERBERIS PETIOLARIS WALL

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Berberis petiolaris Wall is abundantly available in Murree Hills.¹ Huq and Ikram,² in a recent communication, have reported the isolation of and compared chromatographically the alkaloids of this species with those of *Berberis lycium* Royle.³ Since the alkaloids berbenine, berbericine and berbericinine iodide of both the species were reported to be new, we were interested to work on their identification and structure elucidation.

The concentrated methanolic extract of the powdered roots of *B. petiolaris* Wall was macerated with 5% acetic acid. The filtered, acidic aqueous extract was basified with ammonium hydroxide solution and extracted with chloroform to remove the tertiary bases. The water soluble, quaternary bases were then isolated as chloride, iodide and picrates.

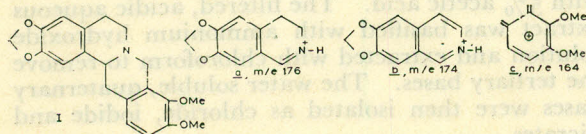
TLC showed that the tertiary base fraction was a mixture of several components. Repeated crystallization of this fraction gave a white base, m.p. 152-53°C. The mass spectrum of the white base disclosed that it was still a mixture of two bases: the major fraction (about 90% of the mixture) had a molecular ion peak at m/e 608 and the other at m/e 622. The white base on further purification, by repeated crystallization from ethanol as well as chromatographically, finally gave a white, crystalline base, corresponding to berbenine of Ikram and his coworkers,³ which had already been identified by us⁴ to be berbamine by spectral analyses. Work is in progress on the isolation, purification and identification of other tertiary bases. It may be pertinent to mention here that the alkaloid having molecular ion peak at m/e 622 may be tetrandrine or isotetrandrine, but so far we have not been able to isolate sufficient material for complete identification.

The quaternary alkaloids were isolated as berbericinechloride, berbericinine iodide and basepicrate. Berbericinine iodide, was found to be a mixture of two components. The purification and identification of berbericinine iodide as palmatine iodide has already been reported.⁵ Berbericine chloride on recrystallization from water gave yellow crystals,

$\text{C}_{20}\text{H}_{18}\text{NO}_4^+\text{Cl}^-$ m.p. 205°C (dec.)

The UV spectrum of berbericine chloride in ethanol showed λ_{\max} at 231, 265, 349 and 428 m μ ($\log \epsilon$ 3.45, 4.34, 4.36 and 3.68), which is characteristic⁶ of 2,3-9,10-tetrasubstituted protoberberines. The base is nonphenolic because addition of 10% NaOH does not show any shift of the absorption maxima.

Sodium borohydride reduction of berbericine iodide gave a tetrahydro base, m.p. 167°C. The mass spectrum of the tetrahydro base showed peaks at m/e 339 (M⁺) 176 (a) 174 (b) and 164 (c). The NMR spectrum (CDCl₃) of the tetrahydro base showed the presence of a methylenedioxy group (singlet, 4.15 τ), two methoxyl groups (two singlets, 6.15 and 6.16 τ), four aromatic protons (3.29 and 3.24 τ) and 9 aliphatic protons. On the basis of mass and NMR spectra, the tetrahydro base is suggested to be identical with tetrahydroberberine (I), which was confirmed by mixed m.ps. and TLC of an authentic sample of tetrahydroberberine.



Since the tetrahydro base is identified to be tetrahydroberberine, the original base must be berberine (II). This was, in turn, unequivocally established by the comparison of IR and NMR spectrum of berbericine chloride with berberine chloride which resembled very closely and showed the following peaks in the NMR spectrum (trifluoroacetic acid): 0.41 (C₈-H), 1.53 (C₁₃-H), 1.98 (2H at C₁₁ and C₁₂), 2.53 (C₁₂-H), 3.11 (C₄-H) 3.92 (O-CH₂-O) 5.72 and 5.85 (2 OCH₃), a triplet at 5.09 with J=6.0 c/s, (C₆-H₂) and another triplet at 6.71 τ with J=6.0 c/s (C₅-H₂), which accounts for almost all the protons of berberine chloride.

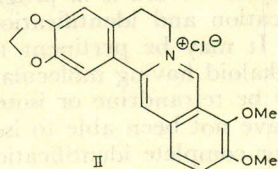


TABLE I.—COMPARISON OF UMBELLATINE AND BERBERICINE.

Compound	Salt, m.p.				
	Cl	I	SO ₄	Picrate	NO ₃
Berbericine	199-200°(dec.)	268-70°(dec.)	274-75°(dec.)	227-228°(dec.)	263-64°(dec.)
Umbellatine	200°(dec.)		274°(dec.)	231°(dec.)	265-67°(dec.)

It is suggested that berbericine hydrochloride is identical with berberine chloride. A comparison (Table I) of various salts of berbericine and umbellatine, an alkaloid isolated from a number of Indian *Berberis*⁷ species, shows that both the alkaloids may be identical. The IR, UV, NMR and mass spectra of both the bases were indeed identical in all respects. Hence, in view of this, it is confirmed that umbellatine chloride is identical with berberine chloride.⁸

Experimental

The powdered, dried roots (5 kg) were soxhleted with methanol (10 l.) The methanolic extract was concentrated to a thick residue, which was then macerated with 5% acetic acid (2 l.), and filtered. The acidic aqueous extract was basified with sufficient ammonium hydroxide, and extracted with chloroform to give tertiary bases.

Purification of Tertiary Bases.—The chloroform extract was dried (Na₂SO₄) and evaporated to dryness. The residue was taken up in 5% acetic acid, and filtered. The acidic extract was made alkaline and extracted with chloroform. The chloroform solution was subjected to TLC and found to consist of a mixture of tertiary bases.

Isolation of Berberine (Berbamine).—The residue obtained from the evaporation of chloroform was fractionally crystallized from 95% ethyl alcohol, when a creamy coloured base, named berberine, was obtained, m.p. 145-50°C. The mass spectrum of this base, however showed that this still contained small amounts (10%) of another alkaloid, molecular weight 622. Repeated crystallization from ethyl alcohol gave an analytically pure sample, sample, m.p. 152-153°C, molecular weight 608 (by mass spectrometry). The IR spectrum of this base was superimposable on the one obtained from berberine, which has already been identified as berbamine.

Fractionation of Quaternary Bases.—The basified aqueous extract left after the extraction of tertiary bases showed a strong test for alkaloids. This was then fractionated according to the procedure of Ikram and his coworkers.³

Berbericine Iodide (Palmatine Iodide).—The crystalline mass was found to be a mixture of two alkaloids, which were separated by column chromatography.⁵ The bases so obtained were then found to be identical with authentic samples of berberine iodide and palmatine iodide in terms of m.ps., mixed m.ps., superimposable IR (KBr pellet and Nujol mull), NMR (in trifluoroacetic acid) and UV spectra. TLC confirmed the identity of the isolated iodides with authentic material.

Berbericine Chloride (Berberine Chloride).—Recrystallization from water gave yellow silky needles, m.p. 205°C (lit. m.p. 205°),⁸ mixed m.p. 205°. The isolated berbericine chloride had superimposable IR, NMR and UV spectra with an authentic sample of berberine chloride.

Preparation of Berbericine Acetone (Berberine Acetone).—To a hot solution of berbericine chloride in aqueous acetone, an excess of 10% NaOH solution was added. The solution was left overnight when a brownish mass was obtained. Recrystallization from ethyl acetate gave light brown needles, m.p. 162–163°C (lit. m.p. 163°).⁹

Reduction of Berbericine Iodide.—The reduction of berbericine iodide with sodium borohydride, followed by usual work up, gave a tetrahydro base, m.p. 167°C (lit. m.p. 167°).¹⁰ The tetrahydro base had superimposable UV, IR, NMR and mass spectra with an authentic sample of tetrahydro berberine. TLC (in ether) showed identical *R_f* values for both the tetrahydro base and an authentic sample.

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THE ALKALOIDS OF DELPHINIUM VESTITUM WALL: ISOLATION AND CHARACTERIZATION OF LYCOCTONINE

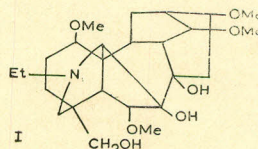
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Delphinium vestitum Wall (locally known as Juhi) is available in the hilly regions of Murree, Azad Kashmir and Kaghan.¹ The leaves of the plant are known² to be poisonous to goats. As the plant has not been previously examined chemically, and in view of the continued interest on the diterpenoid alkaloids^{3,4,5} of *Delphinium* and *Aconitum* species, we have now studied the alkaloids of *D. vestitum* Wall. The dried ground root was extracted with ethyl alcohol, and the crude bases were isolated from the extract. These were freed from the acid and neutral components and separated into weak and strong bases.

From the weak bases, two alkaloids could be isolated. Alkaloid A, an amorphous solid, m.p. 110°C and alkaloid B, a syrupy base. The IR spectrum of the alkaloid A showed bands indicative of OH (3450 cm⁻¹), amide and/or ester carbonyl (1700 cm⁻¹), an aromatic ring (1600 and 1500 cm⁻¹), and ester (1250 cm⁻¹). Its NMR spectrum contained signal attributable to an *N*-ethyl group (triplet at 8.96τ) four methoxyls (τ 5.75 (3H), 6.68 (6H) and 6.6 (3H) and an



aromatic ring (τ 2.0, 2.4, 2.7 (4H). On saponification, the alkaloid A gave rise to a crystalline basic substance, $C_{25}H_{41}NO_7$ (by mass spectrometry), m.p. 90–92°C which showed a single spot on TLC and no longer contained carbonyl, aromatic and ester absorption in the IR. Its NMR spectrum contained signals attributable to an N-methyl group (triplet at 8.97 τ) and four methoxyls (τ 6.75 (3H), 4.67 (3H), 4.60 (3H), 4.54 (3H). From this data, it was clear to us that the hydrolyzed base might be lycoctonine (I). However, the m.p. of our substance, i.e. 90–92°C, was too low as compared with those reported for lycoctonine, viz. 120–139°C in the literature.⁶ While this manuscript was under preparation, we came across a reference in which the m.p. of lycoctonine is given as 90–92°C. Finally, the identity of the two bases was established by comparison of IR spectra which were superimposable.

Studies are in progress to characterize the original alkaloids A and B.

Experimental

M.ps. are uncorrected. IR spectra are of KBr discs and were taken on a Perkin Elmer 337 grating spectrometer, PMR spectra were measured at 60 M/c in deuteriochloroform with TMS as external standard ($\tau=10$), UV light absorption are of solution in 95% (v/v) ethanol.

Isolation of Lycoctonine (Hydrolysis of Alkaloid A).—Alkaloid A (2.5 g), which was obtained by the column chromatography of the weak base fraction on alumina was dissolved in methanol (50 ml) containing sodium hydroxide (250 mg) and water (10 ml). The solution was refluxed for 1 hr and then bulk of the methanol was removed under reduced pressure. The residual solution was diluted with water (50 ml) and extracted with

chloroform (5×40 ml). The chloroform extracts after drying (Na_2SO_4) were evaporated under reduced pressure to yield a white glass material. This was recrystallized from acetone–petroleum ether to give colourless needles of lycoctonine, m.p. 90–92°C (lit. m.p. 90–92°C⁷, 120–139°C⁶). The IR spectrum of the isolated alkaloid was identical with that of an authentic specimen of lycoctonine.

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