

THE CORRECT STRUCTURE OF THE SUPPOSED "1,2,4-TRIAZACYCLOOCTATETRAENES"

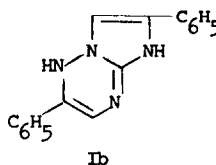
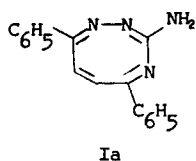
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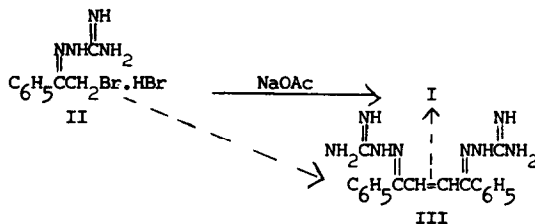
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In 1957 Beyer and Pyl(1) reported that phenacyl bromide guanyldiazone hydrobromide (II), on treatment with a weak base, gave a product (I) to which they assigned a triazocine



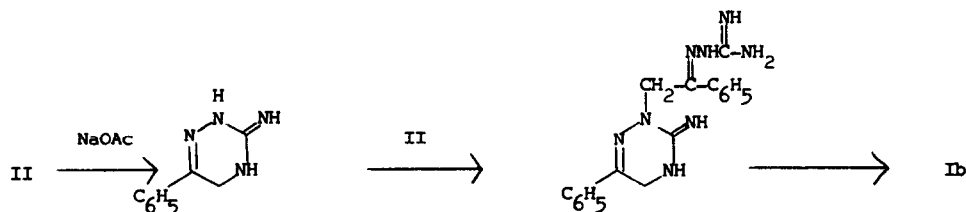
structure, Ia (3-amino-5,8-diphenyl-1,2,4-triazacyclooctatetraene). We have found the correct structure of this product to be an imidazotriazine, Ib (2,6-diphenyl-1,5-dihydroimidazo[1,2b]-s-triazine) (2). The structure has been confirmed by an independent synthesis.

The conclusion that I contained an eight-membered ring was based on the assumption that II was initially converted to a dibenzoyl ethylene bis-guanyldiazone (4) (III), which then



cyclized to Ia. (These authors recognized that the difficulty with this sequence was that dibenzoyl ethylene guanyldiazone fails to undergo this reaction.) No other evidence was given to support the proposed eight-membered ring structure.

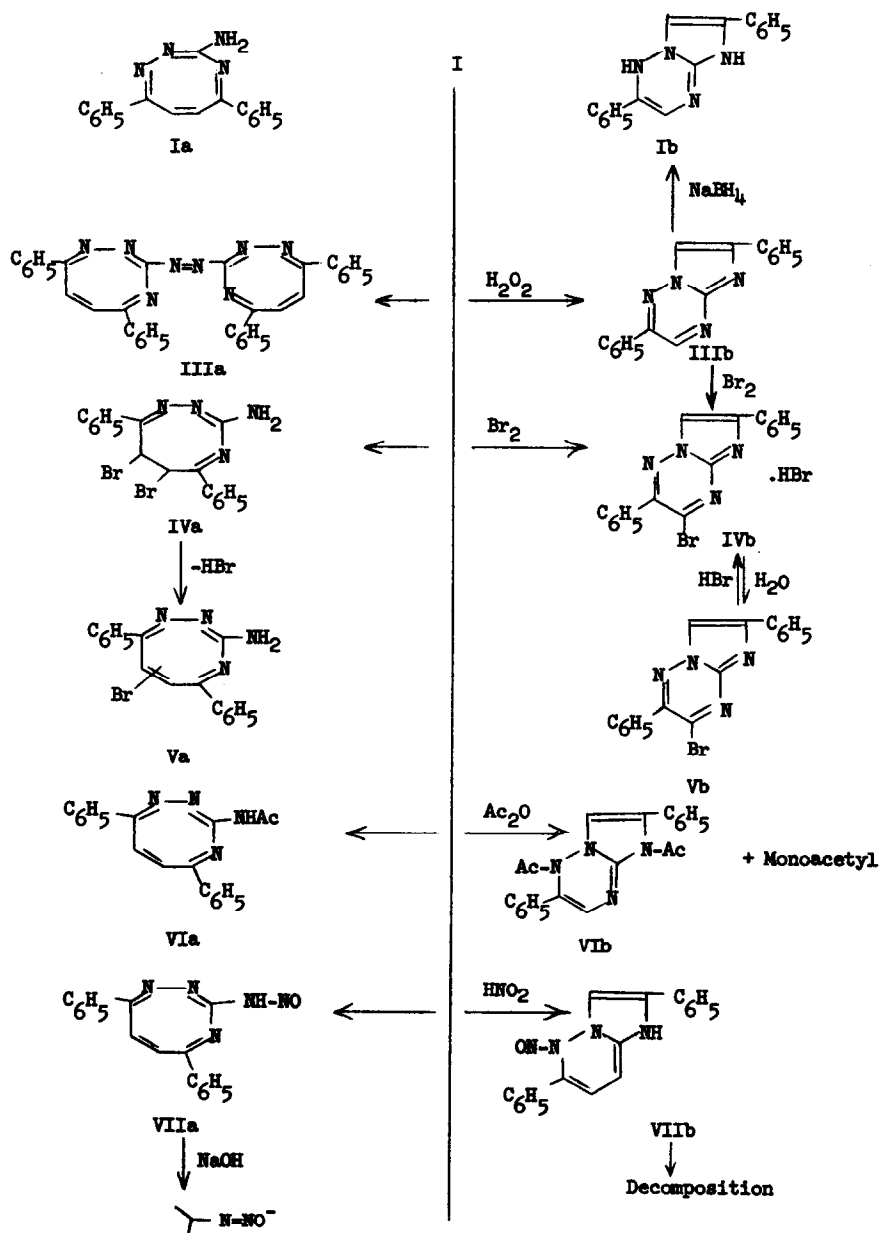
The structure which we propose could be formed by the reaction sequence shown below:



I was readily converted to another compound on oxidation. On the basis of its yellow color and elemental analysis, the oxidation product was assumed to be an azo compound, Va, and this was used as evidence of a primary amino group on an "aromatic" ring system (although it is unlikely that a triazocine would be aromatic). A molecular weight determination (by mass spectrum) of the oxidation product shows that it has a molecular weight of 272, corresponding to a loss of 2 hydrogen atoms from the original structure; the azo compound would have a m/e 544. Therefore, the original compound must contain an oxidizable ring system. The elemental analyses for the "azo" and the "dehydro" structures are the same. The properties and method of synthesis are consistent with structure IIb. The structures Ib and IIIb have been confirmed by independent syntheses (below).

Other evidence presented (1) in confirmation of the presence of a primary amino group was the formation of a mono-acetyl derivative, VIa. On repetition of this experiment both a mono- and di-acetyl derivative, VIIb mp 204-208°C, were isolated, as would be predicted by structure Ib (5). The IIIb, as expected, was recovered unchanged from attempted acylation.

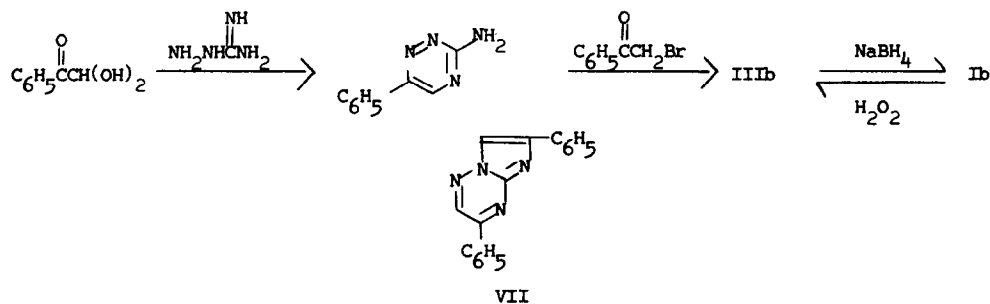
The final evidence for the presence of a primary aromatic type amine was that on treatment with nitrite, I "gives an orange-yellow nitroso compound, which is soluble in alkali giving a blood red color (therefore it was considered to be a primary nitrosamine) and couples with  $\beta$ -naphthol to give an azo dye" (1). No experimental details, analytical data, or melting point was given for this "azo dye". On repetition of this experiment, a nitroso compound was obtained, which analyzed correctly but melted at 162° rather than at 144° as reported (1). This nitroso compound was insoluble in aqueous sodium hydroxide but dissolved in acetone-sodium hydroxide giving a red color. However, dissolution in acetone alone also gave a red color. The same color was observed using other solvents. An azo dye could not be isolated and the original nitrosation product could not be recovered from these solvents. Nitrosation apparently forms an N-nitroso derivative of Ib, which then evidently undergoes rearrangement or ring opening with formation of the red color. The oxidized material (IIIb) does not



react with nitrite.

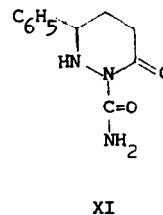
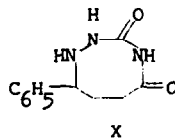
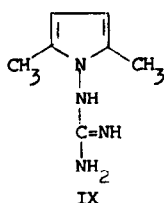
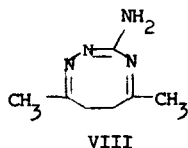
Another reaction was described which required elucidation. It was reported (1) that, on bromination, a "dibromo-adduct" is formed (i.e., a 5,6-, 6,7-, or 7,8- dibromo compound such as IVa), which rapidly and spontaneously loses hydrogen bromide to give the 6- or 7- bromo derivative of Ia. The bromination reaction can now be interpreted as follows: On bromination, Ib is first oxidized, in situ, to IIIb, which is then brominated giving Vb, which is isolated as the hydrobromide, IVb; on stirring with methanol, the salt is hydrolyzed giving the free base, Vb (6). These structures have been confirmed by treating preformed IIIb with bromine to give IVb and Vb, and by mass spectral examination which shows m/e 351 for the monobromide. Structure Va would require a molecular weight of 353.

The structures of I and of IIIb were confirmed by the following independent synthesis: Reaction of phenylglyoxal with aminoguanidine gave a mixture of 3-amino-6-(and-5)-phenyl-1,



2,4-triazines (7); these were separated and each was treated with phenacyl bromide. The 5-phenyltriazine gave the known compound, VII (8); the 6-phenyltriazine gave IIIb (9), identical in all respects to the material obtained on oxidation of I. Reduction of IIIb with sodium borohydride in methanol gave a 91% yield of Ib.

Two other "triazocines" have been reported in the literature, VIII (10) and X (11). The assigned structure, VIII, was used by Beyer and Pyl (1) in support of structure Ia. These authors subsequently showed (12) that structure VIII was incorrect, and that the correct structure for this compound was IX (13).



Cyclization of 4-(carbamoylhydrazino)-4-phenylbutyric acid gave a compound for which the two structures X and XI were proposed (14). In a subsequent publication (11) structure X was arbitrarily used although no evidence in its support was presented.

It now appears that no authenticated report of a compound containing the 1,2,4-triazacyclooctatetraene (triazocine) ring system has yet appeared.

#### References

1. H. Beyer and T. Pyl, Ann. **605**, 50(1957).
2. The reported failure (3) of I to undergo condensations characteristic of compounds containing the  $\text{-N}=\overset{\text{NH}_2}{\text{C}}\text{-Y}$  group is now clear.
3. L. M. Werbel and M. L. Zamora, J. Heterocyclic Chem. **2**, 287(1965).
4. By analogy with the conversion of phenacyl bromide to dibenzoyl ethylene, B. M. Bogoslovskii, J. Gen. Chem. (Russ.) **14**, 993(1944), [C.A. **39**, 4600(1945)]; N. Campbell and N. M. Khanna, J. Chem. Soc. S33(1949).
5. All compounds analyzed correctly for C,H,N and Br. The molecular weights of all compounds were determined by mass spectral means. The structures of N,N<sup>1</sup>- and N,N- diacetyl compounds are readily differentiated in the carbonyl region of the infra-red (the former gives a sharp peak at 6.0  $\mu$ , the latter a broad bond at 5.83  $\mu$ ).
6. The bromine is arbitrarily shown as being at position 3 but may be at 7. X-ray studies are being initiated in an attempt to determine the location of the bromine atom in Vb, and of the double bonds in Ib.
7. J. A. Elvidge, G. T. Newbold, I. R. Senciall, and T. G. Symes, J. Chem. Soc., 4157(1964); J. B. Ekeley, R. E. Carlson, and A. R. Ronzio, Rec. trav. chim. **59**, 496(1940).
8. R. Fusco and S. Rossi, Rend. Ist. lombardo. sci., Pt. I. Classe sci mat. e. nat., **88**, 194(1955); C.A. **50**, 10743d (1956).

9. Although the isomeric structures 2,7-diphenyl-1,5-dihydroimidazo-[1,2b]-as-triazine and 3,6(or 5)-diphenyl-1,7-dihydroimidazo-[2,1c']-as-triazine cannot be rigorously excluded, the assigned direction of ring closure to give IIIb is consistent with all reports of related ring closures. See for example: W. L. Mosby, Heterocyclic Systems with Bridge-head Nitrogen Atoms. Part II, p. 903, Interscience Publishers, Inc., N.Y. (1961); T. Pyl, S. Melde, and H. Beyer, Ann. 663, 108(1963); S. Rossi and R. Trave, Chimica e l'industria (Milano), 40, 827(1958); also refs. 3 and 8.
10. J. Thiele and E. Dralle, Ann. 302, 275(1898).
11. J. Bougault and P. Chabrier, Compt. Rend. 228, 1952(1949).
12. H. Beyer, T. Pyl, and C.-E. Völcker, Ann. 638, 150(1960).
13. A standard method of synthesis of pyrroles is reaction of 1,4-diketones with NH<sub>2</sub>-containing reagents.
14. J. Bougault, E. Cattelain, and P. Chabrier, Compt. Rend., 225, 876(1947).