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THE FACILE SYNTHESIS OF 2,6-DIAMINO-1,3,5,7-TETRAZACYCOPENT[f]AZULENE

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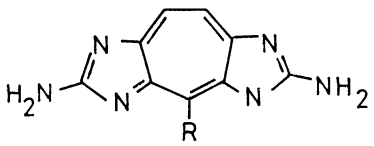
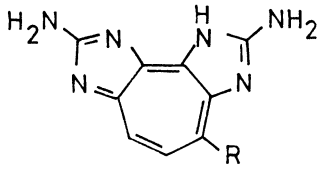
2,6-Diamino-1,3,5,7-tetrazacyclopent[f]azulene, a parent compound of zoanthoxanthins, was synthesized from 5,7-dibromo-2-methoxytropone by two step condensation with guanidine.

Zoanthoxanthins, the highly fluorescent marine natural products isolated from colonial anthozoans,[1,2] are found to contain a new aromatic ring system of tetrazacyclopentazulenes,[1,2] and are of interest in their biological activities.[3] The synthesis of the least substituted zoanthoxanthins (1 and 2) has been achieved by Büchi et al.[4] by means of the unique method of dimerization of 2-aminoimidazole



1 : R=Me 3 : R=H

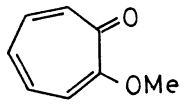


2 : R=Me, 4 : R=H

derivatives, based on the biogenetic hypothesis. This paper describes the sythesis of 2,6-diamino-1,3,5,7-tetrazacyclopent[f]azulene (3) (C-demethyl para-zoanthoxanthin), being a parent compound containing the zoanthoxanthin ring system, from tropolone.

2-Methoxytropone (5) is known to undergo the condensation reaction with guanidine or thiourea at the 1- and 2-positions to give the condensed compounds (6 : X=NH_2 or SH) having a 1,3-diazaazulene ring system.[5] On the other hand, halotropolones, such as 3-, 4-, and 5-bromotropolone, when treated with t-BuOK in DMSO in the presence of NaN_3, are found to give triazolotropolones (7 and 8) *via* dehydrotropolone intermediates.[6] Further, 3-halotropolone derivatives having the side-chain functionalized for intramolecular cyclization at the 5-position,

such as 3-bromo-5-thiocarbamidotropolone, are found to give tropolones condensed with five-membered heterocycles at the 4- and 5-positions, such as thiazolo[4,5-d]-tropolone, by addition-elimination reaction.[7] Such type reactions, especially



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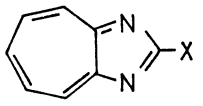
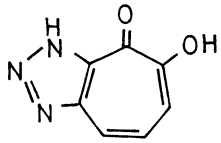


6 (X=NH_2, SH)



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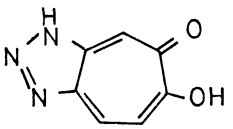

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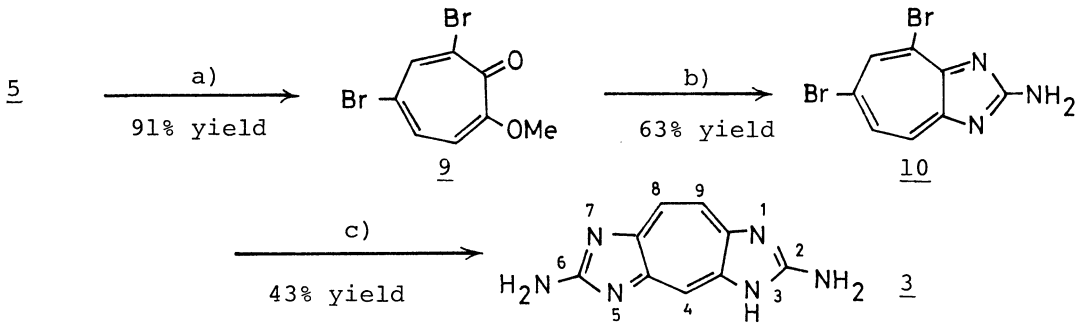
the reaction which proceeds *via* dehydro-intermediates, are applicable for synthesizing tetrazacyclopentazulene ring systems starting from polyhalotropolones or their methyl ethers.

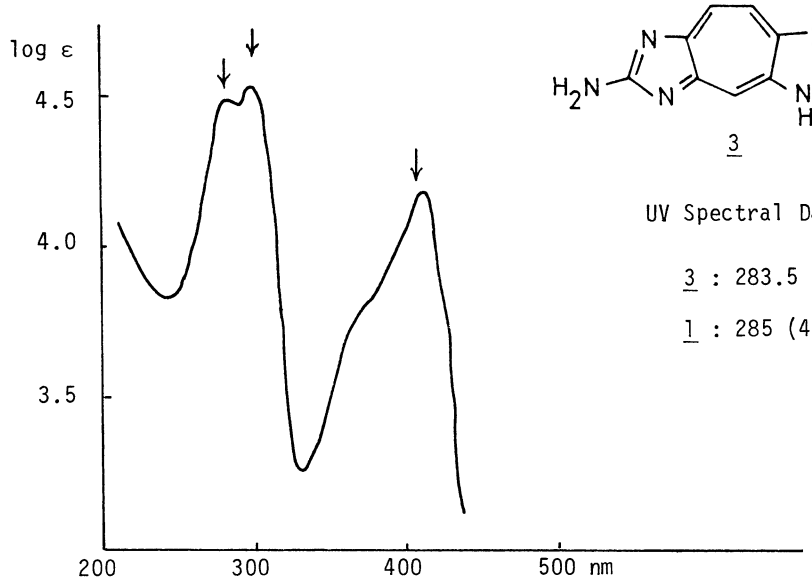
5,7-Dibromo-2-methoxytropone (9),[8] which was easily prepared from 5 by bromination with NBS in CCl_4 (91% yield), was used as the starting material for synthesizing 3. The condensation of 9 with guanidine took place in two steps,



Scheme 1. Synthetic scheme of 3 from 5. a) 3 molar eq. of NBS in CCl_4 under reflux; b) 2 molar eq. of guanidine hydrochloride and KOH in EtOH under reflux; c) 2 molar eq. of guanidine hydrochloride and 4 molar eq. of t-BuOK in DMSO at room temperature.

as shown in Scheme 1. It has been reported that 5 and its 5- and 7-bromo derivatives reacted with guanidine in the presence of NaOEt or a large excess of KOH to give 2-amino-1,3-diazaazulenes (6 : X=NH_2).[5] Under similar conditions, 9 gave no 1,3-diazaazulene derivative. However, in the presence of 1~2 molar equivalents of KOH, 9 reacted with guanidine to give 2-amino-4,6-dibromo-1,3-diazaazulene (10).[9] The product separated out during reflux as yellow microcrystals (from AcOH), mp over 300°C; UV: λ_{max} 260nm (log ε 4.58), 367(4.32) and 425(3.51); IR (KBr): 3350, 3120, 1640, 1503, 1360, 1340, 990 and 831 cm^{-1}; Pmr (CF_3CO_2H, 60 MHz): δ 8.45(1H, d, J=11.0 Hz, H-8), 8.85(1H, d, J=11.0 Hz, H-7), and 9.32 ppm (1H, s, H-5).

The second step condensation with guanidine did not take place under the



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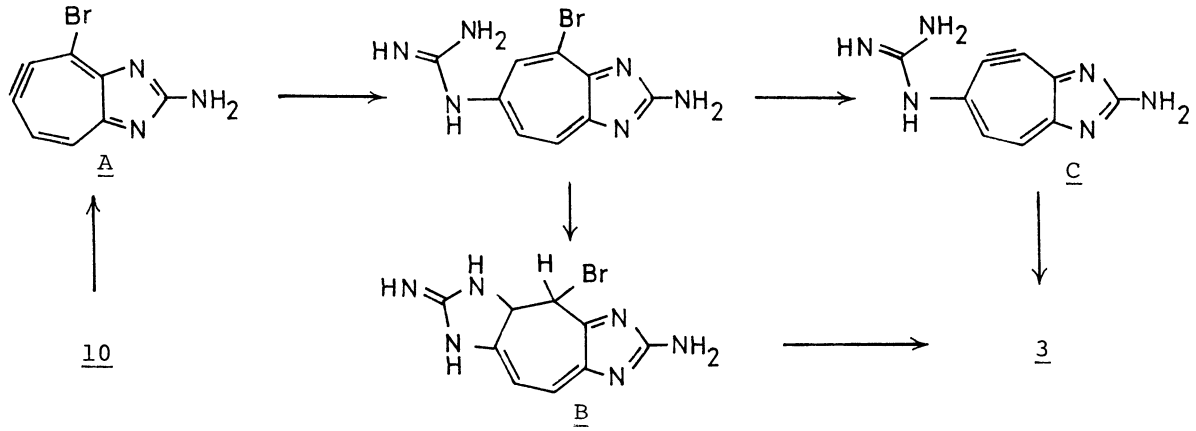
UV Spectral Data of 3 and 1 in MeOH

3 : 283.5 (4.37), 296 (4.40), 411 (4.07)

1 : 285 (4.50), 295 (4.57), 405 (4.18)[4]

Fig 1. UV Spectrum of 3 in MeOH. Arrows show λmax and log ε of Parazoanthoxanthin (1).

conditions similar to that employed in the first step. It proceeded, however, under the conditions that employed for the formation of dehydrotropolone intermediates.[6] The compounds, 10, reacted with guanidine in DMSO in the presence of t-BuOK to give the condensation products. The products were chromatographed over a silica-gel column and eluted with $CHCl_3$, $CHCl_3$-MeOH (4 : 1), and then $CHCl_3$-MeOH-aq.NH_3 (80 : 20 : 2). The third highly fluorescent fraction was chromatographed repeatedly to give 3.[10] The compound 3: yellow microcrystals (from AcOH), mp over 290°C; Mass: m/e 200 (M^+); UV (MeOH); λ_{max} 283.5 nm (log ε 4.37), 296(4.40), and 411(4.07); IR (KBr): 3270, 3025, 1655, 1550, 1400, 1278, 1170 and 690 cm^{-1}; Pmr (CF_3CO_2H): δ 8.64 (2H, s, H-8,9) and 8.23 ppm (1H, s, H-4). The UV spectrum of 3 is similar to that of parazoanthoxanthin (1) as shown in Fig. 1.[4]



Scheme 2. The possible reaction pathways for the formation of 3 from 10.

The condensation of 10 with guanidine to give 3 is assumed to proceed in the two-step reaction, involving the substitution *via* a dehydro-intermediate (A) and then the subsequent ring formation by the addition-elimination reaction *via* an intermediate (B) or the substitution *via* a dehydro-intermediate (C), as shown in Scheme 2.

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References and Notes

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8) The compound, 9, : Pale yellow needles (from MeOH), mp 206-207°C, S. Fujikura, M. Yasunami, K. Takase, and T. Nozoe, to be published.

9) The compounds, 3 and 10, gave satisfactory analyses in accord with the assigned structures.

10) Another fraction which also exhibited very strong fluorescence was obtained. The pmr spectrum of a crude product isolated from this fraction reveals a siglet at 8.20 ppm (CF_3CO_2H). From these findings and on consideration of the reaction mechanism, the formation of 4 is expected. The study of isolation of this compound is now progress.

11) Recently, the synthesis of 3 utilizing two step condensation of 2,4-dichloro-5-methoxytropone with guanidine was reported; H. Kondo, T. Minami, A. Mori, and H. Takeshita, The 12th Symposium on Nonbenzenoid Aromatic Compounds. September 1979 at Matsumoto, Abstracts p 85.

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