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NEW ONE STAGE SYNTHESIS OF 3,3'-BIS(2-METHYLINDOLYL)METHANE – A HOMOLOG OF THE MARINE ANTIBIOTIC VIBRIINDOLE

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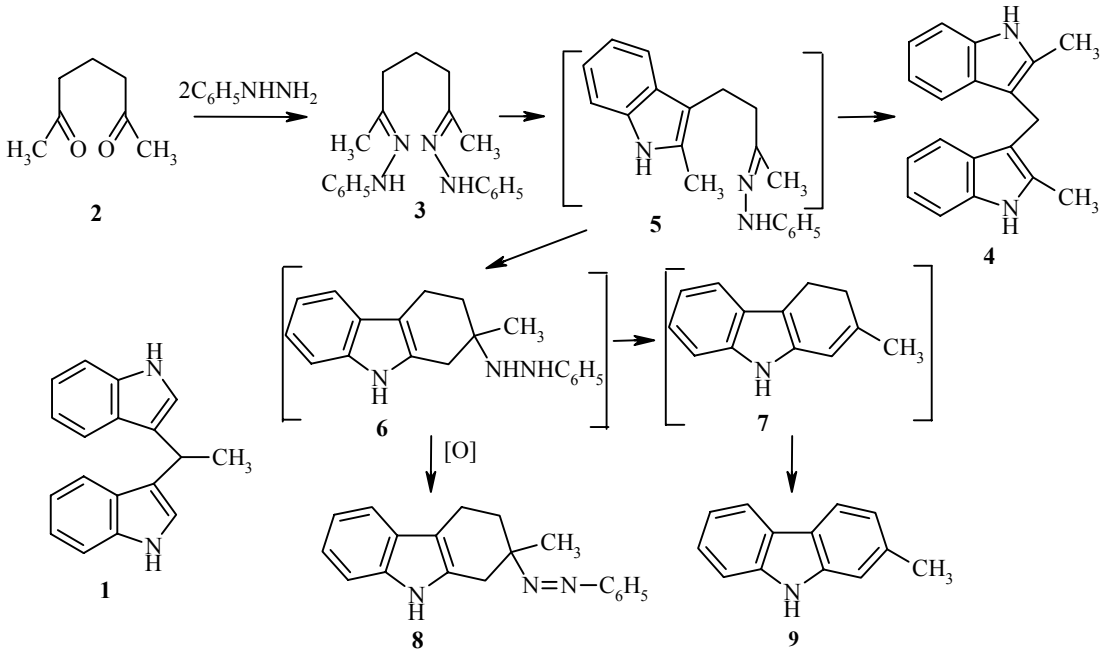
A group of antibiotics, derivatives of 3,3'-bisindolylmethane, have been found in marine bacteria. Vibriindole **1** and related compounds from various bacteria of the genus *Vibrio*, associated with marine organisms, are of this type [1-3].

We have shown that some 3,3'-bisindolylmethanes can be obtained by indolization of the easily obtained 1,5-diketones. For example, we obtained 3,3'-bis(2-methylindolyl)methane (**4**), a homolog of vibriindole, in 55% yield from the diketone **2** by thermal indolization of its diphenylhydrazone **3**. We found compound **4** to possess antimicrobial activity against the bacteria *Staphylococcus aureus*, *Enterococcus faecium*, and the microscopic fungus *Candida albicans*. Compound **4** has been synthesized previously in low yield by condensation of 2-methylindole with its 3-diethylamino derivative [4].



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Isolation from the reaction mixture of compounds **8** and **9** along with compound **4** shows that the intermediate hydrazone **5** not only underwent the Fischer indolization but was also cyclized to the intermediate **6,** which was transformed into the carbazoles **8** and **9** on oxidation and heating.

3,3'-Bis(2-methylindolyl)methane (4). A solution of bisphenylhydrazone **3** (1.54 g, 5.0 mmol), obtained by heating diketone **2** (10 mmol) with phenylhydrazine (20 mmol) in benzene with a Dean–Stark trap, in ethylene glycol (15 ml) was heated at 190°C for 5 h. The reaction mass was diluted with water, ether was added, the mixture was stirred, and the residue of **4** was separated (0.75 g, 55% yield); mp 234-236°C (ethanol). Lit. data: mp 236-237°C [4]. IR spectrum ($CHCl_3$), ν, cm^{-1}: 3450 (NH). Mass spectrum, *m/z*: 274 (M^+). ^1H NMR spectrum ($CDCl_3$), δ, ppm, *J* (Hz): 2.34 (6H, s, $2CH_3$); 4.1 (2H, A_2-system, s, CH_2); 6.96-7.38 (arom. H); 7.68 (2H, br. s, NH). Found, %: C 83.4; H 6.7; N 10.4. $C_{19}H_{18}N_2$. Calculated, %: C 83.2; H 6.5; N 10.2.

2-Methyl-2-phenylazo-1,2,3,4-tetrahydrocarbazole (8) was isolated by column chromatography on aluminum oxide from the ether extract of the mother liquor from the isolation of compound **4**. Yield 15%; mp 146-148°C (ethanol). IR spectrum ($CHCl_3$), ν, cm^{-1}: 3462 (NH), 1466 (Alk–N=N–Ph). Mass spectrum, *m/z*: 289 (M^+), 184 (M^+-PhN_2, 100%). ^1H NMR spectrum ($CDCl_3$), δ, ppm, *J* (Hz): 1.4 (3H, s, CH_3); 2.25 (1H, m); 2.36 (1H, m); 2.84 (1H, A part of AB system, d, *J* = 16.4); 3.45 (1H, B part of AB system, d, *J* = 16.4); 7.0-7.75 (arom. H); 7.75 (br. s, NH). Found, %: C 79.0; H 6.8; N 14.7. $C_{19}H_{19}N_3$. Calculated, %: C 78.9; H 6.6; N 14.5.

2-Methylcarbazole (9) was obtained in an analogous manner to compound **8**. Yield 11%; mp 246-248°C (ethanol), lit. data: mp 259°C [5]. IR spectrum, ν, cm^{-1}: 3462 (NH), 1610, 1489, 3051 (arom). Mass spectrum, *m/z*: 181 (M^+). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.5 (3H, s, CH_3); 6.9-7.3 (arom. H); 7.75 (br. s, NH). Found, %: C 86.3; H, 6.2; N 7.9. $C_{13}H_{11}N$. Calculated, %: C 86.2; H 6.0; N 7.7.

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