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SHORT STEP SYNTHESSES OF A NATURAL PRODUCT, 6-CYANO-5-METHOXY-12-METHYLINDOLO[2,3-*a*]CARBAZOLE AND NOVEL 6-AMINOINDOLO[2,3-*a*]THIAZOLO[5,4-*c*]CARBAZOLES¹

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Abstract ————— Starting from indigo, simple synthetic methods for 6-cyano-5-methoxy-12-methylindolo[2,3-*a*]carbazole and novel 6-aminoindolo[2,3-*a*]thiazolo[5,4-*c*]carbazoles are achieved using only conventional reagents.

Indolo[2,3-*a*]carbazole (**1**, Scheme 1) is a common skeleton of a class of compounds such as staurosporine,^{2a} ttipanazoles,^{2b} BE-13793C,^{2c} and so on. We have expected that manipulation of **1** is a promising method for finding a new biologically active compound. As a simple derivative of **1**, we have focused our attention to cytotoxic and antiviral 6-cyano-5-methoxy-12-methylindolo[2,3-*a*]carbazole (**6b**), isolated from blue-green alga *Nostoc sphaericum* (strain EX-5-1) by Moore and co-workers.³ Although we have established two synthetic routes to **6b** in the previous communications,⁴ their overall yields (13% and 5%, respectively) are still not satisfactory to carry out structure-activity relationship project. Now, we wish to report a satisfactory six step synthetic method for **6b** from indigo (**2**). In addition, simple preparation of novel 6-aminoindolo[2,3-*a*]thiazolo[5,4-*c*]carbazoles (**9a** and **9b**) is also developed.

First, 3-acetoxy-2,2'-biindolyl (**3**), prepared in one step from **2** in 88% yield,⁴ reacted with dichloroacetyl chloride in refluxing ethyl acetate to give 3-acetoxy-3'-dichloroacetyl-2,2'-biindolyl (**4**) in 85% yield. Treatment of **4** with aqueous 1.3% ammonia in MeOH-DMF at room temperature afforded *cis*-6-chloro-6a-hydroxy-5-oxo-5,6,6a,12-tetrahydroindolo[2,3-*a*]carbazole⁵ (**5a**) in 91% yield. Methylation of **5a** with dimethyl sulfate in the presence of K₂CO₃ produced 12-methyl compound (**5b**) in a quantitative yield. A novel reductive cyanation of **5b** was found to produce **6a** in a quantitative yield by the reaction with NaCN in DMF-H₂O. Finally methylation of **6a** with diazomethane afforded **6b** in 86% yield. Thus the natural product (**6b**) is available in six steps with an overall yield of 59% using only conventional reagents. The originality rate⁶ for **6b** from **2** is 57% based on our three reaction steps, **a**, **c**, and **e**.

C ring of **1**, since a chloroacetyl group of **7** is suitable for forming heterocycles.

With useful building blocks at hand such as **6a**, **9a**, and **6c** which is available from **5a** as reported previously,⁴ the structure-activity relationship project is in progress.

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REFERENCES AND NOTES

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