Tetrahedron Letters,Vol.26,No.47,pp 5841-5842,1985 0040-4039/85 $3.00 + .00
Printed in Great Britain

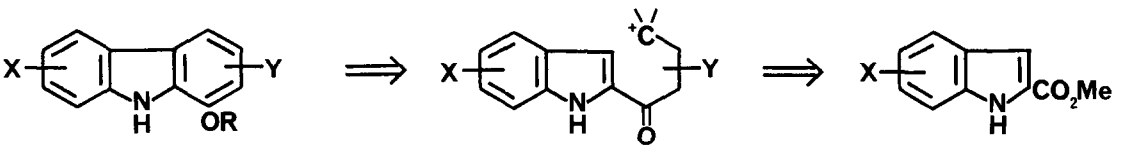
A NEW ROUTE TO 1-OXYGENATED CARBAZOLES. SYNTHESIS OF MURRAYAFOLINE-A

Tracey Martin and Christopher J. Moody*

Department of Chemistry, Imperial College of Science and Technology
London SW7 2AY, U.K.

Summary. 1-Oxygenated carbazoles are prepared in four steps from indole-2-carboxylates by Claisen condensation with butyrolactones, followed by hydrolysis with concomitant decarboxylation, oxidation, and ring closure (Scheme 2); the route is applied to the synthesis of the carbazole alkaloid, murrayafoline-A.

There are now some fifty carbazole alkaloids known,[1] and several of these contain an oxygen substituent at the 1-position.[2] Although many carbazole alkaloids have been synthesised by classical Fischer-Borsche cyclisation of the appropriate cyclohexanone arylhydrazones,[1] the vigorous conditions required for the subsequent dehydrogenation step render the method inappropriate when sensitive substituents are present. We now report a new synthesis of 1-oxygenated carbazoles based on the strategy shown in Scheme 1. This approach which involves ring closure of a 2-substituted indole bearing a four carbon chain, in which the terminal carbon atom is electrophilic, to the nucleophilic indole 3-position, has surprisingly found little use in carbazole synthesis to date.[3]

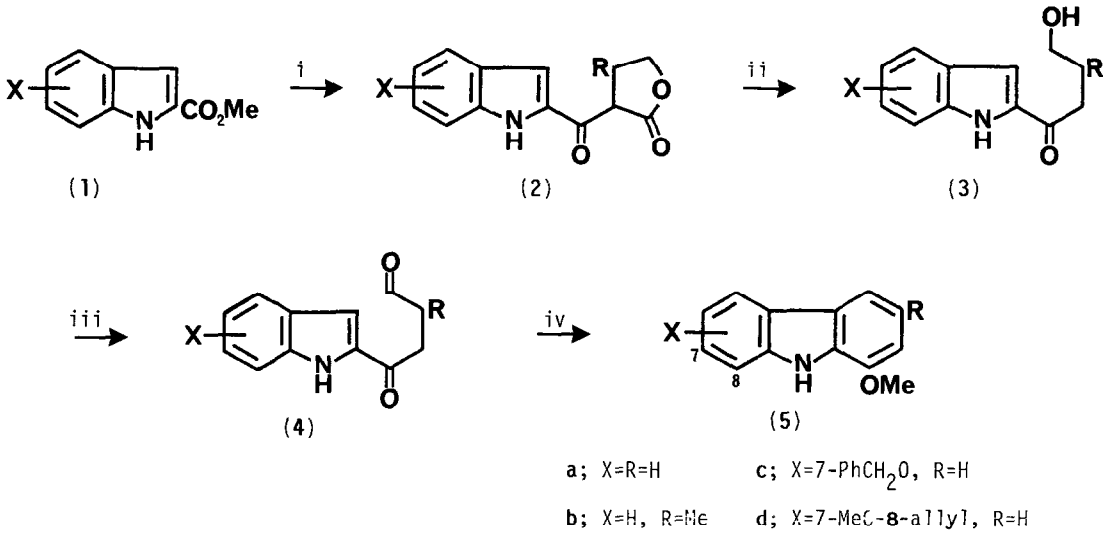


(1)

Scheme 1.

The starting indole-2-carboxylates (**1**) are readily available either by a Reissert synthesis,[4] or in two steps from the corresponding benzaldehydes *via* azidocinnamates,[5] a method which we have used extensively.[6] The indole esters are converted into carbazoles as shown in Scheme 2, the key step being the initial Claisen condensation[7] with butyrolactone or 4-methylbutyrolactone to give the lactones (**2**) (51-73%). On heating in aqueous dioxane containing sodium hydroxide the lactones (**2**) underwent hydrolysis and concomitant decarboxylation to give the alcohols (**3**) (73-98%). Oxidation of the alcohols (**3**) with pyridinium chlorochromate (PCC) gave the corresponding aldehydes (**4**)(61-83%) which were cyclised to give the 1-methoxy-

carbazoles (**5**) (40-59%) simply by stirring in boron trifluoride-methanol complex at room temperature. The cyclisation step could also be effected using hydrogen chloride in methanol or ethanol [56% for (**5a**), 46% for the corresponding 1-ethoxycarbazole].



(1) (2) (3) (4) (5)

a; X=R=H **c**; X=7-$PhCH_2O$, R=H

b; X=H, R=Me **d**; X=7-MeC-**8**-allyl, R=H

Scheme 2. Reagents: i, 4-R-butyrolactone, NaOMe, dioxane; ii, H_2O, NaOH, dioxane; iii, PCC, CH_2Cl_2; iv, MeOH-BF_3, room temp.

1-Methoxy-3-methyl-9H-carbazole (**5b**) (murrayafoline-A) has recently been isolated from Murraya euchrestifolia Hayata,[2a] and the sample prepared by the above route was identical to material obtained from natural sources.

We thank the S.E.R.C. for a studentship (to T.M.), and Professor H. Furukawa for an authentic specimen of murrayafoline-A picrate.

References

1. D.P. Chakraborty, Fortschr. Chem. Org. Naturst., 1977, **34**, 299.

2. For some more recent examples see (a) T.-S. Wu, T. Ohta, H. Furukawa, and C.-S. Kuoh, Heterocycles, 1983, **20**, 1267; (b) H. Furukawa, T.-S. Wu, and T. Ohta, Chem. Pharm. Bull., 1983, **31**, 4202; (c) H. Furukawa, M. Yogo, C. Ito, T.-S. Wu, and C.-S. Kuoh, ibid., 1985, **33**, 1320; (d) P. Bhattacharyya and B.K. Chowdhury, Chem. Ind. (London), 1984, 301.

3. J.A. Joule, Adv. Heterocycl. Chem., 1984, **35**, 83.

4. R.J. Sundberg, 'The Chemistry of Indoles,' Academic Press, New York, 1970.

5. H. Hemetsberger, D. Knittel, and H. Weidmann, Monatsh. Chem., 1970, **101**, 161.

6. E.g. A.R. MacKenzie, C.J. Moody, and C.W. Rees, J. Chem. Soc., Chem. Commun., 1983, 1372; C.J. Moody, J. Chem. Soc., Perkin Trans. 1, 1984, 1333.

7. cf. M. Sato, H. Tagawa, A. Kosasayama, F. Uchimaru, H. Kojima, T. Yamasaki, and T. Sakurai, Chem. Pharm. Bull., 1978, **26**, 3296.

(Received in UK 19 September 1985)