DIRECT SYNTHESIS OF 3-ALKYLISOQUINOLINES WITH DIFFERENT ORIENTATIONS OF METHOXY GROUPS

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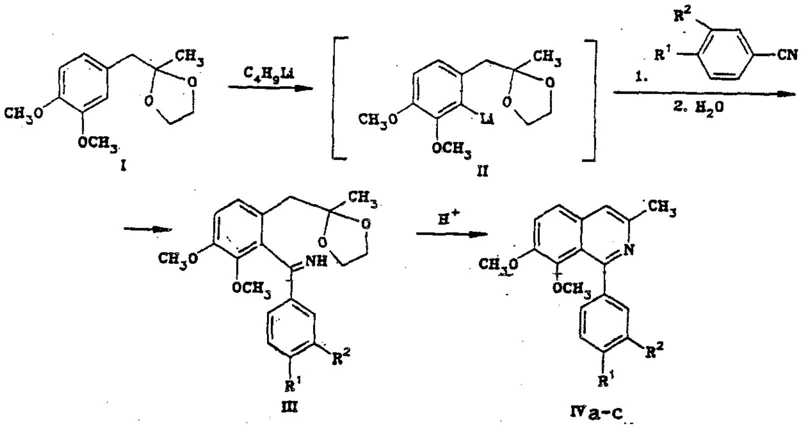
The problem of synthesizing 3-substituted isoquinolines with different orientations of alkoxy group substituents in the annelated benzene ring, which form the principal structural block of a variety of natural alkaloids [1], has been one of the most important problems in the synthetic chemistry of these compounds [2].



IV a $R^1=R^2=H$; b $R^1=OCH_3$, $R^2=H$; c $R^1—R^2=OCH_2O$

Utilizing the known reaction tendency of butyllithium to coordinate with alkoxy groups in aromatic compounds and thus to give products resulting from metallation at the ortho-position [3], we have devised a new one-pot synthesis of isoquinolines IVa-c via the reactions of the lithium derivative of veratrylacetone ketal II with aromatic nitriles, followed by acidic hydrolysis of the reaction mixtures.

Despite the relatively low yields of isoquinolines IV (20-35%) achieved in this manner, the preparative (ease) of this procedure makes it competitive with other known methods [1, 4].

Isoquinoline IVa. mp 66-68°C (from ethanol); 35% yield. IR spectrum: 1595, 1280, 1182 cm^{-1}. PMR spectrum (CF_3COOH): 2.37 (s, CH_3), 2.93 (s, OCH_3), 3.57 (s, OCH_3); 7.12 (s, 5H), 7.54 ppm (s, 3H).

Isoquinoline IVb. mp 92-94°C (from ethanol); 25% yield. IR spectrum: 1595, 1260, 1230 cm^{-1}. PMR spectrum (CF_3COOH): 2.38 (s, CH_3); 3.00 (s, OCH_3); 3.52 (s, OCH_3); 3.63 (s, OCH_3); 6.73 (d, 2H); 7.20 (d, 2H); 7.58 ppm (s, 3H).

Isoquinoline IVc. mp 114-115°C (from ethanol); 20% yield. IR spectrum: 1595, 1260, 1230, 1210 cm^{-1}. PMR spectrum ($CDCl_3$): 2.55 (s, CH_3); 3.18 (s, OCH_3); 3.80 (s, OCH_3); 5.83 (s, OCH_2O); 6.6-6.9 (m, 3H); 7.0-7.4 ppm (m, 3H).

Hydrolysis of the reaction mixture at pH $\geq$ 7 gave imine IIIa, which gave isoquinoline IVa in quantitative yield after acid treatment.

Imine IIIa. Colorless oil; 35% yield. IR spectrum: 3255, 1640, 1595, 1240, 780 cm^{-1}. PMR spectrum ($CDCl_3$): 1.12 (s, CH_3); 3.4-3.7 (m, $2OCH_3$, OCH_2CH_2O); 6.80 (d, 1H); 7.0-7.4 (m, 4H); 7.5-7.7 (m, 2H); 8.67 ppm (s, NH). M^+ 340.

The results of elemental analysis of all of these compounds were consistent with the calculated values.

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MACROHETEROCYCLES.

38.* SIMPLE SYNTHESIS OF AN UNSYMMETRICAL CYLINDRICAL TRICYCLIC CRYPTAND

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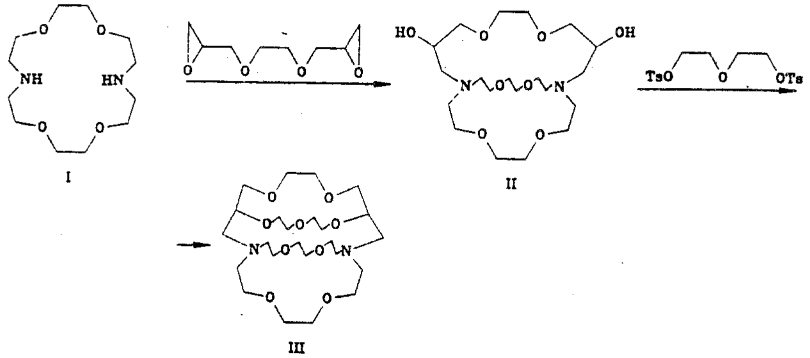
Cylindrical cryptands composed of two different crown ether rings as substructures are capable of the selective formation of binuclear inclusion complexes (cryptates) with two different metal ions or with organic dications; this opens up broad possibilities in terms of practical applications. Unfortunately, however, the synthesis of these types of cryptands is often multi-stage and complex [1, 2].

Using the synthesis of cryptand III as an example, we have demonstrated the feasibility of a relatively simple procedure for the preparation of cylindrical tricyclic cryptands, in which two different crown ether rings are bound via a methylene group.

Treatment of equimolar amounts of the diglycidic ether of ethylene glycol [3] and diaza-18-crown-6 [4] in a refluxing mixture of dry ethanol and tetrahydrofuran (1:1) resulted in the formation of the dihydroxycryptand II, which was isolated by column chromatography on neutral alumina. Condensation of dihydrocryptand II with diethylene glycol ditosylate in refluxing dioxane in the presence of sodium hydride gave the cylindrical tricyclic cryptand III.



3,10-Dihydroxy-5,8,15,18,23,26-hexaoxa-1,12-diazabicyclo[10.8.8]octacosane (II). Yield 69%, mp 82-83°C. Mass spectrum: m/e 436 (M^+). PMR spectrum ($CDCl_3$): 2.63 (m, 12H, NCH_2); 3.55 ppm (m, 28H, OCH_2, CH—O, OH).

4,7,13,16,19,24,27,31,34-Nonaoxa-1,10-diazatricyclo[18,17.1.1^{10,12}]pentatriacontane (III). Yield 19%, oil. Mass spectrum: m/e 506 (M^+). PMR spectrum ($CDCl_3$): 2.62 (m, 12H, NCH_2); 3.67 ppm (m, 34H, OCH_2, OCH).

The results of elemental analysis of compounds II and III corresponded to the calculated values.

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*For Communication 37, see [5].

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