Chinese Chemical Letters Vol. 15, No. 1, pp 26 – 28 , 2004
http://www.imm.ac.cn/journal/ccl.html

Synthesis of Surface-active Substituted *3H*-Indole Quaternary Ammonium Molecules

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Abstract: Two substituted *3H*-indole quaternary ammonium molecules were designed and synthesized using hexamethylphosphoramide (HMPA) as a solvent. The products were purified and characterized by IR, ^{1}H NMR, MS and elemental analysis.

Keywords: Substituted 3*H*-indole, quaternary ammonium, synthesis.

Rotaxanes are supramolecular structure in which the ring is threaded by a chain having bulky terminal cap groups so that the chain cannot be extruded from the ring[1-3]. It has been observed that substituted *3H*-indole molecules, *i.e*., iodomethyldioctadecyl 2-(*p*-hexylaminophenyl)-3, 3-dimethyl-5-carboethoxy-*3H*-indole ammonium and iodo-trimethyl-2-(*p*-hexylaminophenyl)-3, 3-dimethyl-5-carboethoxy-*3H*-indole ammonium, can form a new type of 1:3 (guest: host) rotaxane-like inclusion complex of cyclodextrin in aqueous solutions[4,5]. To further study whether the 1:4 rotaxane-like inclusion complex can be formed or not, we have designed and synthesized two substituted *3H*-indole quaternary ammonium molecules with longer main chain, namely, compounds **6** and **8**.

The alkylation of aromatic amines has been proven to be a particular challenge due to the delocalization of lone electron pair in the amino group, which dramatically decreases the reactivity of aromatic amines[6]. As a consequence, strict conditions are usually required for the direct alkylation of aromatic amines. Juaristi used HMPA as solvent in simple alkylation of aromatic amines such as anilines[6,7], since it can increase the nucleophilicity of carbanions and other electron rich species. Thus, HMPA was chosen as a solvent in this paper and good results were obtained. The routes for the synthesis of compound **6** are presented in **Scheme 1**.

The synthesis and purification of compound 5 have been carried out according to the methods of Skrabal *et al*.[8] and Popowycz[9]. Compound 2 was synthesized according to reference 10, and it reacted with compound 3 to afford compound 4 in CH_3CN under reflux for 18 hrs. Compound 6 was obtained from the reaction between compounds 4 and 5 in HMPA at 80°C for 24 hrs. All the syntheses were performed under nitrogen atmosphere. Compounds 4 and 6 were purified by column chromatography with mixed

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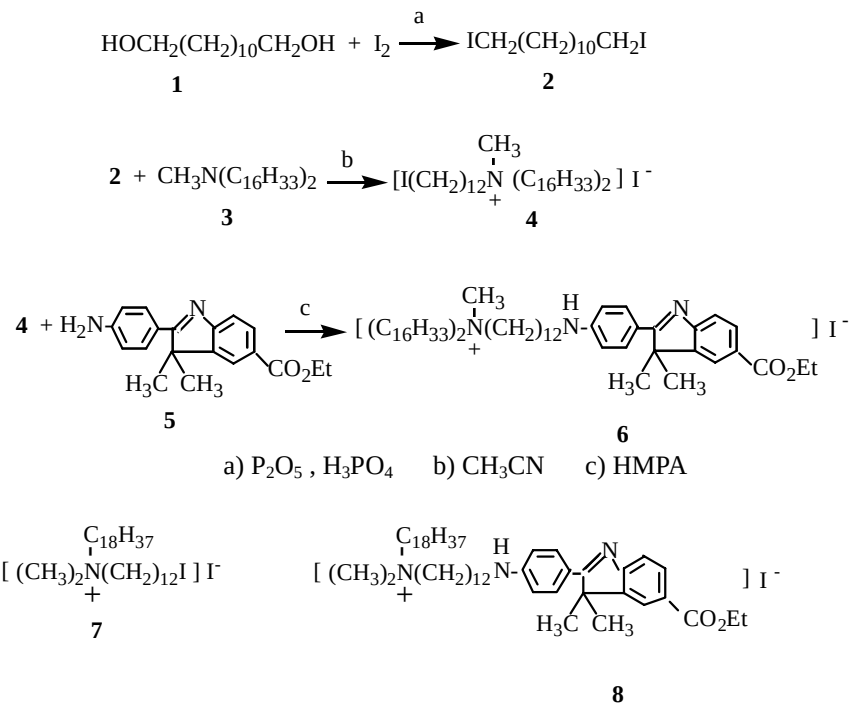
solvent and recrystallization.

Similar methods were used to the synthesis and purification of compound **8**.

Scheme 1



Acknowledgment

This work was supported by the National Natural Science Foundation of China (Grant No. 29901001) and the Doctoral Fund of Education Ministry of China (Grant No. 20010001003). We thank Professor Wen Ting Hua, Peking University, for the generous help in the synthesis and purification of the products.

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11. Compound **4**, white crystal, m.p. 59-62°C, 3.5 g (79.7%), IR (KBr) ν: 3451, 2917, 2849, 1470, 1165, 717 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ ppm: 0.881 (t, 6H, J=6.6 Hz, $-CH_3$), 1.240-2 (m, 76H, $-CH_2-$), 3.194 (t, 2H, J=7.0 Hz, ICH_2-), 3.316 (s, 3H, $-CH_3$), 3.461 (t, 6H, $-CH_2N$),

ppm. MS *m/z*: 774 (M^+-I+1). Compound **6,** yellow crystal, m.p. 39-42°C, 0.56 g (46.3%), IR (KBr) ν: 3462, 2919, 2851, 1711, 1605, 1467, 1232, 1167, 720 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ ppm: 0.877 (t, 9H, J=6.0 Hz, $-CH_3$), 1.252-2 (m, 82H, $-CH_2-$), 3.212-3.449 (m, 12H, $-CH_2N$), 4.351 (q, 2H, J=7.1 Hz, $-OCH_2-$), 6.687 (d, 2H, J=8.4 Hz, Ph-H), 7.782 (d, 1H, Ph-H), 8.051 (m, 3H, Ph-H), 8.359 (s, 1H, Ph-H). MS *m/z*: 955 (M^+-I+1). Elemental analysis calcd. for $C_{64}H_{112}N_3O_2I{\cdot}1.5H_2O$: C69.31, H10.38, N3.79, found: C69.25, H10.86, N3.53. Compound **7,** white crystal, m.p. 56-59°C, 4.2 g (66.9%), IR (KBr) ν: 3434, 2923, 2855, 1468, 1163, 721 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ ppm: 0.879 (t, 3H, J=6.6 Hz, $-CH_3$), 1.254-1.844 (m, 52H, $-CH_2-$), 3.193 (t, 2H, J=6.9 Hz, ICH_2-), 3.379 (s, 6H, $-CH_3$), 3.537 (t, 4H, J=7.8 Hz, $-CH_2N$). MS *m/z*: 592 (M^+-I+1). Compound **8,** yellow crystal, m.p. 42-45°C, 0.51 g (42.1%), IR (KBr) ν: 3434, 2921, 2852, 1710, 1604, 1465, 1232, 722 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ ppm: 0.876 (t, 6H, J=6.3 Hz, $-CH_3$), 1.252-2 (m, 58H, $-CH_2-$), 3.186-3.548 (m, 12H), 4.369 (q, 2H, J=6.9 Hz, $-OCH_2-$), 4.700 (s, 1H, NH), 6.694 (d, 2H, J=7.8 Hz, Ph-H), 7.500-8.052 (m, 4H, Ph-H), 8.366 (s, 1H, Ph-H). MS *m/z*: 773 (M^+-I+1). Elemental analysis calcd. for $C_{51}H_{86}N_3O_2I{\cdot}1H_2O$: C66.73, H9.38, N4.58, found: C66.52, H9.67, N4.22.

Received January 13, 2003