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A facile synthesis of 2-[4′-dimethylaminophenyl]-3-aryl-β-carbolinium phenylsulfonates

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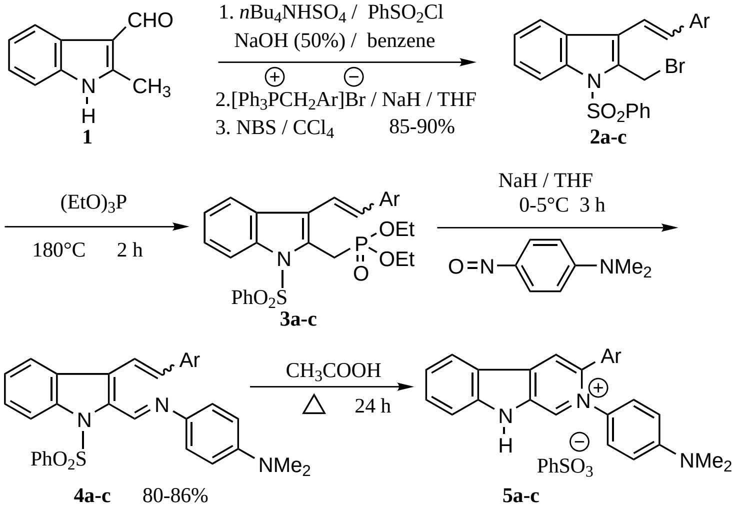
Abstract—A convenient method for the synthesis of 2-[4′-dimethylaminophenyl]-3-aryl-β-carbolinium phenylsulfonates from the corresponding 2-*N*′-aryliminomethylene-3-β-arylvinylindoles by thermal oxidative cyclization is reported. © 2002 Published by Elsevier Science Ltd.

The synthesis of various substituted β-carbolines continues to be a goal due to the wide variety of natural products containing this structural unit. It is known that 3,4-disubstituted-β-carboline derivatives block benzodiazepam receptors of the central nervous system (CNS).[1] Due to the biological importance of these compounds there has been much interest in their synthesis through different routes. β-Carboline alkaloids are usually synthesized from tryptamine derivatives either through Pictet–Spengler[2] or Bischler–Napieralski reactions.[3] To the best of our knowledge there is no report on the synthesis of 2,3-diaryl-β-carbolines. In continuation of our studies[4] on the synthesis of β-carbolines through a non-tryptamine pathway, we report here a synthesis of 2-[4′-dimethylaminophenyl]-3-aryl-β-carbolinium phenylsulfonates **5a**–**c** by an oxidative thermal cyclization of 2-*N*′-aryliminomethylene-3-β-arylvinylindoles **4a**–**c**.

2-Methylindole-3-carbaldehyde **1** was converted to the corresponding 1-phenylsulfonyl-3-(β-arylvinyl)-2-bromomethylindoles **2a**–**c** by the conventional procedure (Scheme 1).[4c] An Arbuzov reaction of **2a**–**c** with triethyl phosphite afforded the diethyl [1-phenylsulfonyl-3-(β-arylvinyl)indol-2-yl]methyl phosphonates **3a**–**c** in 85–91% yields. The structures of these compounds were



Scheme 1.

Keywords: β-carbolinium phenylsulfonates; oxidative thermal cyclization.

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Table 1.

Entry	Ar	3		5	
		Mp (°C)	Yield (%)	Mp (°C)	Yield (%)
a	2,4-Dichlorophenyl	168	90	192	40
b	4-Bromophenyl	150	85	185	45
c	2-Bromophenyl	154	91	188	42

confirmed by spectral data and in some cases by XRD studies.[5] An aza Wittig–Horner reaction[6] of the phosphonate esters **3a**–**c** with 4-nitroso-*N*,*N*-dimethylaniline afforded 2-*N*′-aryliminomethylene-3-β-arylvinylindoles **4a**–**c** in 80–86% yields. The structures of compounds **4a**–**c** were confirmed by IR and ^{1}H NMR spectra only. An oxidative cyclization of compounds **4a**–**c** in boiling acetic acid gave the corresponding quaternary salts of β-carboline, namely 2-[4′-dimethylaminophenyl]-3-aryl-β-carbolinium phenylsulfonates **5a**–**c** in 40–45% yields (silica gel column EtOAc:MeOH, 95:5). The formation of β-carbolinium salts probably involves an electrocyclization followed by oxidation and hydrolysis of the *N*-phenylsulfonyl group. The structures of compounds **5a**–**c** were confirmed by spectral studies,[7] elemental analysis and XRD in the case of **5a** (Table 1).[5]

These compounds may be medicinally interesting in the light of an observation that quaternary salts of β-carboline derivatives such as fascaplysin, etc. have shown interesting medicinal properties.[8] In conclusion we have developed a new route for 2,3-diaryl-β-carbolinium salts via thermal oxidative cyclization of the corresponding imines. Further work on the same line is in progress.

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7. Spectral data for compound **5a**: IR: 3423 (NH), 1383 and 1182 cm^{-1} (SO$_2$).
   ^{1}H NMR (CDCl$_3$) 300 MHz: δ 2.91 (s, 6H, N(C$\underline{H}_3$)$_2$), 6.46 (d, 2H, $J=8.2$ Hz, 3′ and 5′-H of dimethylaminophenyl ring), 7.09 (d, 2H, $J=8.2$ Hz, 2′ and 6′-H), 7.25–7.90 (m, 11H, Ar-H), 8.13 (d, 1H, $J=7.9$ Hz, carboline-8-H), 8.26 (s, 1H, carboline-4-H), 9.49 (s, 1H, carboline-1-H), 13.50 (bs, 1H, NH). ^{13}C NMR (CDCl$_3$) 75 MHz: δ 40.03, 111.40, 114.08, 119.13, 121.96, 122.63, 125.96, 126.61, 127.51, 127.97, 129.49, 129.64, 130.23, 131.41, 132.33, 132.53, 132.96, 133.29, 134.38, 135.39, 136.73, 138.71, 145.70, 150.84. Mass (*m*/*z*, %): 432 (*M*+, 41), 434 (*M*+2, 21), 433 (69), 431 (100), 416 (10), 77 (13).
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