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REACTION OF PHENACYLDIMETHYLSULFONIUM IODIDE WITH o-PHENYLENEDIAMINES

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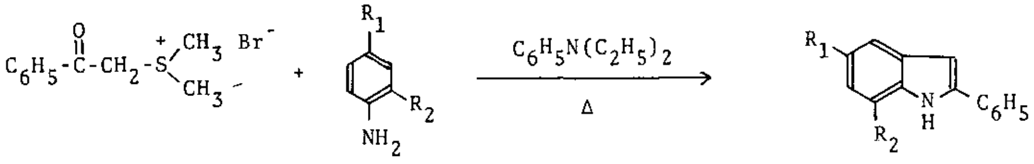
The reaction of o-phenylenediamine with phenacyldimethylsulfonium iodide gave 2-phenylquinoxaline. The same reaction by use of 3,4-diaminotoluene and 1,2-diamino-4-chlorobenzene instead of o-phenylenediamine afforded a mixture of the corresponding 6- and 7-substituted 2-phenylquinoxalines. In the case of 1,2-diamino-4-nitrobenzene, 6-nitro-2-phenylquinoxaline was obtained. On the other hand, the reaction of 1,2-diamino-4-methoxybenzene and phenacyldimethylsulfonium iodide gave 7-methoxy-2-phenylquinoxaline. Furthermore, condensation of maleonitrile with phenacyldimethylsulfonium iodide gave 2,3-dicyano-6-phenylpyrazine.

Sulfonium salts are widely used as one of significant and versatile intermediates in organic synthesis[1]. The reaction of phenacyldimethylsulfonium bromide with primary aromatic amines provides the useful method for the synthesis of 2-phenylindoles[2] (Scheme 1). We examined the similar reaction by use of o-phenylene-

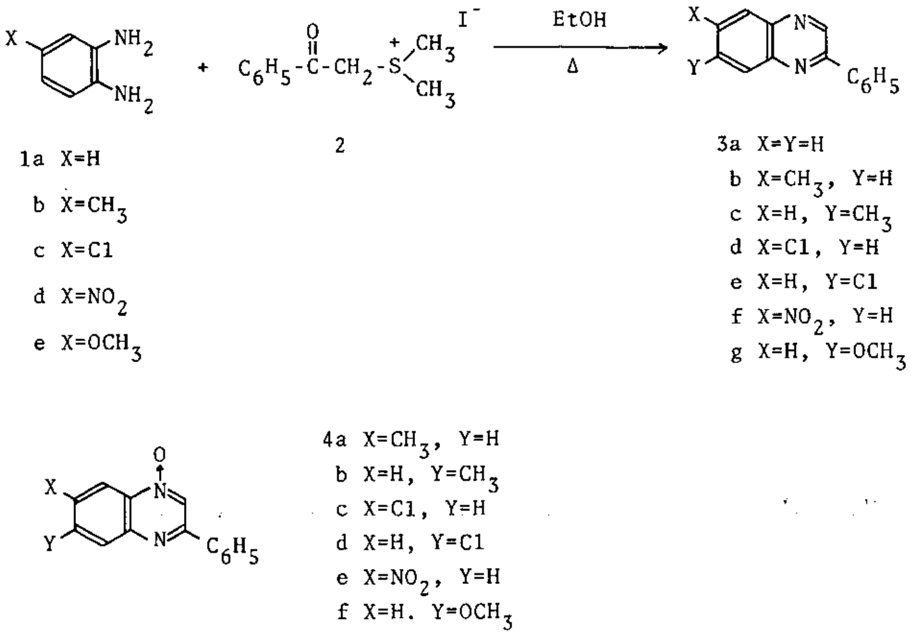


R_1=H, CH_3, F; R_2=H, CH_3

Scheme 1

diamine (R_2=NH_2 in Scheme 1) and phenacyldimethylsulfonium iodide in the expectation that 2-phenylquinoxaline would be formed instead of 7-aminoindole. We wish to report these results in this paper.

o-Phenylenediamine (1a) was heated in ethanol under reflux in the presence of one equiv. of phenacyldimethylsulfonium iodide (2)[3] for 2 hr to afford 2-phenylquinoxaline (3a) in 27 % yield, mp 75-77 °C (lit.[4] mp 77 °C) as expected, though in low yield. It is of interest to examine whether 6-substituted 2-phenylquinoxaline or the corresponding 7-isomer would be obtained on treatment of 4-substituted 1,2-diaminobenzene with 2. Treatment of 3,4-diaminotoluene (1b) with 2 in ethanol as above yielded a mixture of 6-methyl-2-phenylquinoxaline (3b; 14 %)[5,6], mp 77-79 °C (lit.[5] 79 °C) and 7-methyl-2-phenylquinoxaline (3c; 14 %), mp 133-136 °C (lit.[5] 136 °C) without positional selectivity. The structures of these products were confirmed by conversion to the corresponding N_4-oxides (4a) and (4b), respectively by oxidation with m-chloroperbenzoic acid (m-CPBA) as Mannore[7] and Kano[8] reported. These position isomers were easily distinguished by the observation of the aromatic proton signals in their ^{1}HNMR spectra[7,8]. The reaction of 1,2-diamino-4-chlorobenzene (1c) with 2 under the similar conditions gave a mixture of 6-chloro-2-phenylquinoxaline (3d)[6,7] and 7-chloro-2-phenylquinoxaline (3e)[6,7] in 27 % yield; this has led to a mixture of the corresponding N_4-oxides (4c) and (4d)[8] by oxidation with m-CPBA to determine the structures and the ratio of 3d and 3e, since it was difficult to distinguish the isomers of these parent bases from their ^{1}HNMR spectra. The ratio of 3d and 3e was easily confirmed as 1:2 by the observation of the aromatic proton signals in the ^{1}HNMR spectra of 4c and 4d as above. In the case of 1,2-diamino-4-nitrobenzene (1d) and 1,2-diamino-4-methoxybenzene (1e), the reaction proceeded with the positional selectivity. Condensation of 1d with 2 as above gave 6-nitro-2-phenylquinoxaline (3f)[8] in 30 % yield without formation of the corresponding 7-isomer, mp 208-210 °C (lit.[8] mp 209-210 °C). On the other hand, the reaction between 1e and 2 afforded 7-methoxy-2-phenylquinoxaline (3g)[8], mp 86-88 °C (lit.[8] mp 86-88 °C). These products were easily distinguished from alternative possible isomers by oxidation to N_4-oxides (4e) and (4f) with m-CPBA, respectively. The positionally selective synthesis of disubstituted quinoxaline derivatives (3f) and (3g) most probably proceeds by preferential reaction of the α-methylene carbon of the sulfonium salt with more basic amino group in 1d and 1e (Scheme 2).



1a X=H
b X=CH_3
c X=Cl
d X=NO_2
e X=OCH_3

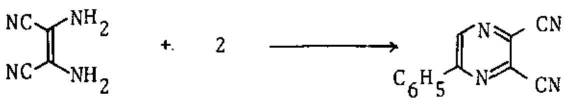
2

3a X=Y=H
b X=CH_3, Y=H
c X=H, Y=CH_3
d X=Cl, Y=H
e X=H, Y=Cl
f X=NO_2, Y=H
g X=H, Y=OCH_3

4a X=CH_3, Y=H
b X=H, Y=CH_3
c X=Cl, Y=H
d X=H, Y=Cl
e X=NO_2, Y=H
f X=H. Y=OCH_3

Scheme 2

Successively we examined the condensation of diaminomaleonitrile (5) with 2. Diaminomaleonitrile was heated with 2 in ethanol for 2 hr to yield 2,3-dicyano-6-phenylpyrazine (6) in 72 % yield, mp 168-169 °C (lit.[9] 170 °C) .(Scheme 3).



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Scheme 3

References and Notes

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3 Prepared by methylation of α-methylthioacetophenone with methyl iodide in methanol under mild reflux for 2 hr, mp 207-209 °C.

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