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THE CONVENIENT AND ONE-POT SYNTHESIS OF N-SUBSTITUTED CARBAZOLES

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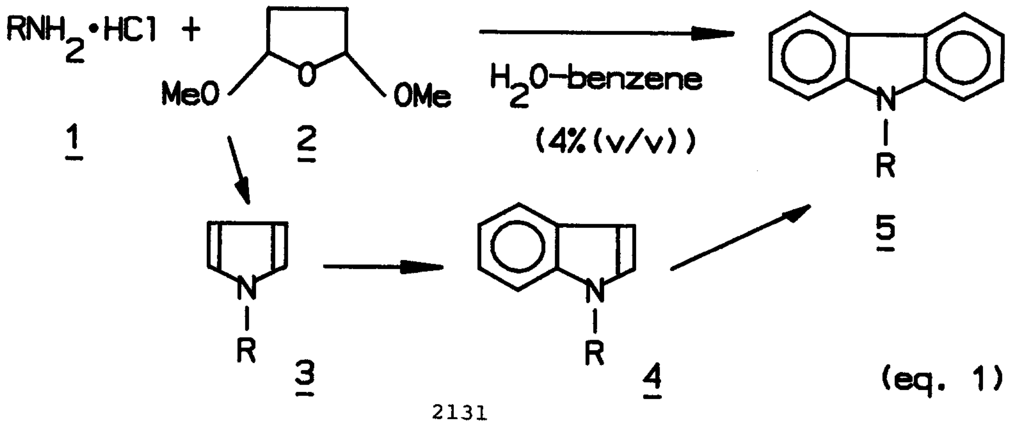
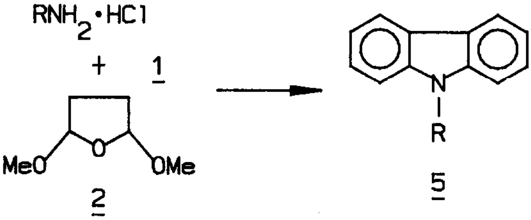
SUMMARY: In spite of the very important compounds in the material sciences, conventional syntheses of carbazoles required severe and complicated reaction conditions. We can now report the convenient and one-pot synthesis of N-substituted carbazoles under mild conditions.

Carbazoles were discovered in anthracene oil of coal tar, and are the parent structure of typical heterocyclic compounds. Recently carbazole derivatives were paid much attention to as the materials for semiconductors,1) photoconductive compounds2), and so on. Conventional methods for synthesis of carbazoles were known by the Grabe-Ullmann method3) and the Tauber method,4) and carbazoles were recently synthesized from 2-nitrobiphenyl or biphenylhydroxylamine by reductive cyclization. But these methods required severe and complicated conditions and the preparations of 2-nitrobiphenyl and the biphenylhydroxylamine were relatively difficult. In the course of the investigation concerning pyrrole derivatives,5) we found the convenient and one-pot synthesis of N-substituted carbazoles under mild conditions.



(eq. 1)

Commercially available alkylamine hydrochloride and 2,5-dimethoxytetrahydrofuran were reacted under reflux in water-benzene (4%(v/v)) mixture to give N-alkyl carbazole in good yield. In order to dissolve alkylamine hydrochloride, a small amount of water was necessary. For example, a mixture of isopropylamine hydrochloride (5 mmol) and 2,5-dimethoxytetrahydrofuran (5 mmol) was refluxed in water(1.6 ml)-benzene(40 ml) (4%(v/v)) mixture under argon atmosphere overnight to afford 9-isopropylcarbazole in a 69% yield based on 2,5-dimethoxytetrahydrofuran. Isopropylamine hydrochloride was required in excess amount, because 2,5-dimethoxytetrahydrofuran is easily polymerized by acid. A case of aromatic amine hydrochloride, N-substituted pyrrole was obtained in quantitative yield. But by the introduction of electron donating group on the benzene ring, N-substituted carbazole was formed. For example a mixture of p-anisidine hydrochloride (5 mmol) and 2,5-dimethoxytetrahydrofuran (5 mmol) were refluxed in benzene(40 ml) to afford 9-(4-methoxyphenyl)carbazole in a 30% yield.

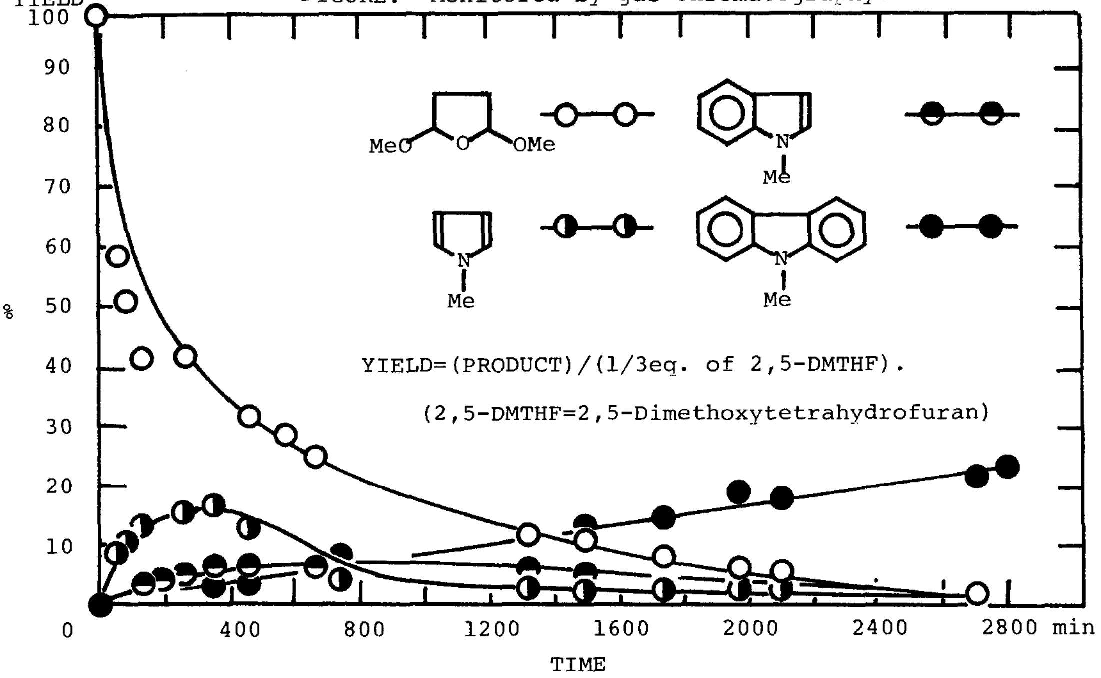


R	Yield (%)
Me	42
Et	34
n-Pr	59
i-Pr	69
p-Anis	30

(Table)

Similarly a mixture of methylamine hydrochloride and 2,5-dimethoxytetrahydrofuran were refluxed to afford 9-methylcarbazole in a 42% yield. In order to investigate the mechanism, the products in the reaction mixture were monitored with time by gas chromatography. N-Substituted pyrrole and indole were detected by gas chromatography, comparing with the authentic samples. From the figure, the following reaction mechanism was speculated. 2,5-Dimethoxytetrahydrofuran reacts with alkylamine hydrochloride to give N-alkyl pyrrole via the cleavage reaction of furan ring by hydrochloric acid. Further 2,5-dimethoxytetrahydrofuran reacts with N-alkyl pyrrole to give N-alkyl indole. N-Alkyl carbazole may be obtained via the similar reaction. Dennstedt reported that N-unsubstituted pyrroles dimerized in the presence of dry mineral acids, and that a subsequent treatment with dilute sulfuric acid brought about the loss of ammonia with the formation of indole.6) But N-substituted pyrrole did not dimerize under our conditions. Furthermore 9-methylcarbazole was obtained from either 1-methylpyrrole or 1-methylindole by the treatment with 2,5-dimethoxytetrahydrofuran in water-benzene (added hydrochloric acid) under reflux condition. From these facts, these reactions may proceed consecutively, and the rate determining step may be the reaction of pyrrole with 2,5-dimethoxytetrahydrofuran.

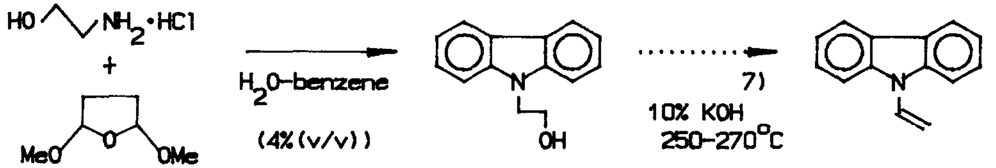
FIGURE. Monitored by gas chromatography.



YIELD=(PRODUCT)/(1/3eq. of 2,5-DMTHF).

(2,5-DMTHF=2,5-Dimethoxytetrahydrofuran)

9-Vinylcarbazole polymerizes easily in the presence of dilute aqueous perchloric acid[9] to form plastics which has been extensively investigated as a thermal and photoconducting polymer.[2] Meanwhile, 9-(2-hydroxyethyl)carbazole is a precursor of noteworthy 9-vinylcarbazole, which is an industrial material. The dehydration of 9-(2-hydroxyethyl)carbazole with 10% potassium hydroxide at 250-270°C was realized as a convenient method.[7] 9-(2-Hydroxyethyl)carbazole may be obtained from carbazole, ethylene oxide and powdered potassium hydroxide in ethyl methyl ketone.[8] Under these situation, we attempted to prepare 9-(2-hydroxyethyl)carbazole according to this new convenient preparative method of 9-substituted carbazoles. The mixture of commercially available monoethanolamine hydrochloride and 2,5-dimethoxytetrahydrofuran was refluxed for 15 hr in water-benzene (4%(v/v)). The expected 9-(2-hydroxyethyl)carbazole was obtained in a 60% yield by the one pot reaction.



9-(2-Hydroxyethyl)carbazole

9-Vinylcarbazole

(eq. 2)

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