

# A Convenient and One-pot Synthesis of 9-Substituted Carbazoles from Primary Amine Hydrochlorides and 2,5-Dimethoxytetrahydrofuran

Choji Kashima\*, Shigeki Hibi, Tatsuya Maruyama,  
Kazuo Harada and Yoshimori Omote

Department of Chemistry, University of Tsukuba, Sakura-mura, Niihari-gun,  
Ibaraki 305, Japan

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Carbazoles are the very important compounds in material science, nevertheless conventional syntheses required severe and complicated reaction conditions. In the process of preparation of pyrrole derivatives, we found that a primary amine hydrochloride **1** and 2,5-dimethoxytetrahydrofuran **2** were refluxed in a benzene-water (100:4 (v/v)) mixture to be obtained 9-substituted carbazole **5** in a high yield. This method is the one-pot synthesis of 9-substituted carbazoles **5** under mild and convenient conditions.

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Carbazoles, which were isolated for the first time from anthracene oil of coal tar, are the typical heterocyclic compounds. Recently carbazole derivatives have received much attention as the materials for semiconductors [1], photoconductive compounds [2], and so on. For example, 9-vinylcarbazole polymerizes easily in the presence of dilute aqueous perchloric acid [3] to form plastics which have been extensively investigated as a thermal- and photo-conducting polymer [2].

Conventional methods for syntheses of carbazoles such as the Grabe-Ullmann method [4] and the Tauber method [5] have been known. Also, carbazoles were recently synthesized from 2-nitrobiphenyl [6] or diphenylamine [7] by reductive cyclization. But these methods required severe and complicated conditions and the preparations of 2-nitrobiphenyl and diphenylamine were considerably difficult. In the course of the investigation of pyrrole derivatives [8], we found that 9-substituted carbazoles **5**

could be synthesized by a mild and convenient one-pot reaction (Scheme I).

### Results and Discussion.

According to the method of Pittet *et al.* [10], 1-substituted pyrroles **3** were prepared by heating the corresponding primary amine with 2,5-dimethoxytetrahydrofuran **2** in acetic acid. However the reaction of **2** with a primary amine hydrochloride **1** afforded a small amount of 9-substituted carbazole **5** in benzene instead of acetic acid. In order to optimize the formation of carbazoles, commercially available methylamine hydrochloride **1a** and **2** were refluxed under argon atmosphere in various solvents, protic or aprotic, or two phase system (Table I).

First, various kinds of organic solvents were used in this reaction, however the yield of the carbazoles could not be raised. For example, when the solution of primary amine hydrochloride **1** in alcohol or tetrahydrofuran was heated,

Scheme I

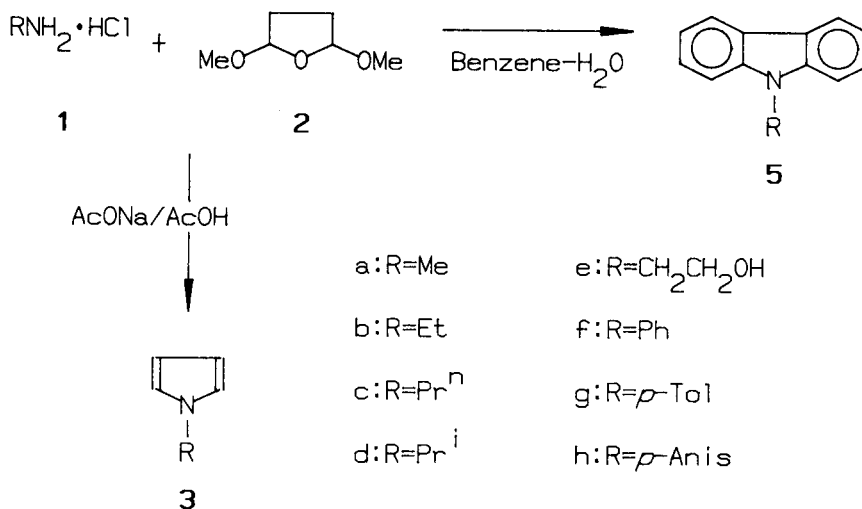


Table I

The Formation of 9-Substituted Carbazole **5a** in Various Solvents by treatment with **1a** and **2**

entry	Solvent system (v/v)	% Yield <b>5a</b> [a]
1	methanol	0
2	tetrahydrofuran	0
3	benzene	7
4	benzene-water (100:1)	14
5	benzene-water (100:2)	22
6	benzene-water (100:4)	39
7	benzene-water (100:6)	20
8	benzene-water (100:8)	15
9	toluene-water (100:4)	35
10	<i>n</i> -hexane-water (100:4)	10
11	tetrahydrofuran-water (100:4)	16
12	diethylether-water (100:4)	trace
13	benzene-water-SDS(cat) [b] (100:4)	11
14	benzene-water-SDS(cat) [b] (1:1)	10

[a] Determined by gc. [b] Catalytic amount of sodium dodecyl sulfate was added.

Table II

Yield of 9-Substituted Carbazole **5** and Solvent System

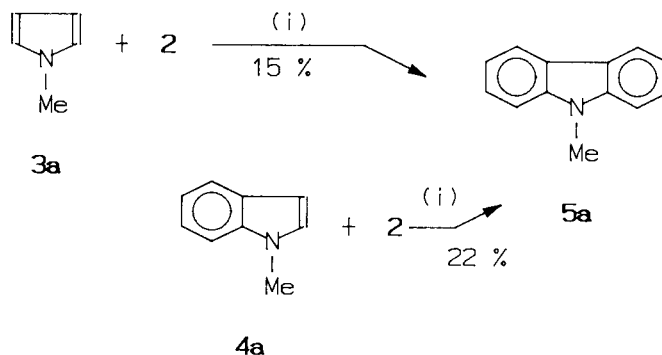
R	Solvent system (v/v)	% Yield	ref [a]	
<b>a</b>	Me	benzene-water (100:4)	39	11
<b>b</b>	Et	benzene-water (100:4)	34	11
<b>c</b>	<i>n</i> -Pr	benzene-water (100:4)	59	11
<b>d</b>	<i>i</i> -Pr	benzene-water (100:4)	69	11
<b>e</b>	CH <sub>2</sub> CH <sub>2</sub> OH	benzene-water (100:4)	60	13
<b>f</b>	Ph	benzene	0 [b]	—
<b>g</b>	<i>p</i> -Tol	benzene	0 [b]	—
<b>h</b>	<i>p</i> -Anis	benzene	30	12

[a] Literature references to authentic 9-substituted carbazoles. [b] 1-Substituted pyrroles were quantitatively obtained.

carbazole could not be obtained and **2** was recovered. Even in the presence of a phase transfer catalyst (sodium dodecyl sulfate), the formation of a carbazole was unsuccessful. Second, in order to dissolve **1**, a small amount of water was added to benzene. The yield of carbazole was dependent on the amount of the water. After all, carbazole was obtained in the highest yield in a benzene-water (100:4 (v/v)) mixture. Furthermore, since **2** is easily polymerized by acid, the primary amine hydrochloride was required in excess amount. For example, an equimolar mixture of isopropylamine hydrochloride **1d** and **2** was refluxed in a water-benzene (100:4 (v/v)) mixture under argon atmosphere overnight to afford 9-isopropylcarbazole **5d** in 69% yield based on **2**. Similarly, 9-substituted carbazoles **5** having a variety of substituent group were obtained in the yields summarized in Table II.

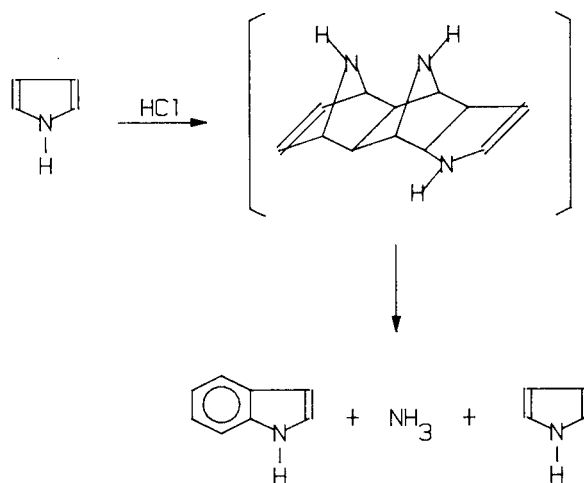
Meanwhile, 9-(2-hydroxyethyl)carbazole **5e** is a precursor of 9-vinylcarbazole, which has received attention in the material sciences. Compound **5e** has been prepared from carbazole, ethylene oxide and powdered potassium

Scheme II [a]



[a] (i) HCl/Benzene-H<sub>2</sub>O (100:4 (v/v)).

Scheme III



hydroxide in 2-butanone [13]. Under these situations, we attempted to prepare **5e** according to this new convenient preparative method. The mixture of commercially available monoethanolamine hydrochloride **1e** and **2** was refluxed in a benzene-water (100:4 (v/v)) mixture to obtain **5e** in 60% yield by the one pot reaction.

In the case of aniline hydrochloride **1f**, 1-phenylpyrrole **3f** was obtained in quantitative yield. But by the introduction of an electron donating group on the benzene ring, 9-(substituted phenyl)carbazole was formed. For example, a mixture of *p*-anisidine hydrochloride **1h** and **2** was refluxed in benzene to afford 9-(4-methoxyphenyl)carbazole **1h** in 30% yield.

For the confirmation of the origin of the benzene ring in 9-substituted carbazole, methylamine hydrochloride **1a** was treated with **2** in a water-toluene mixture instead of a benzene-water mixture. As a result, the solvent was not incorporated into the product and the benzene ring of carbazole was concluded to be formed from **2**. In addition,

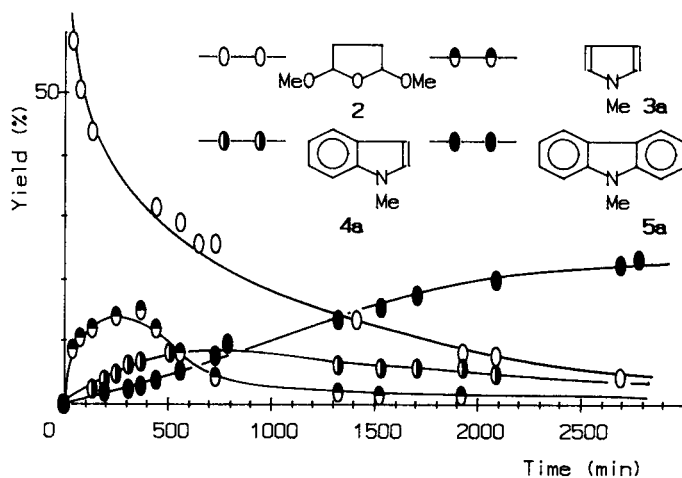
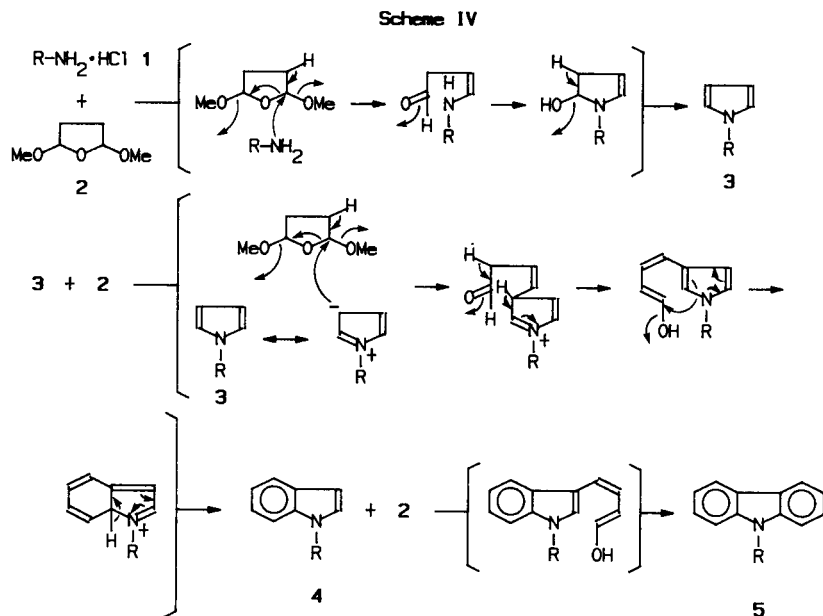


Figure 1. Decrease of 2,5-dimethoxytetrahydrofuran **2** and yields of 1-methyl pyrrole **3a**, 1-methyl indole **4a** and 9-methyl carbazole **5a**, monitored by GC.

when the products in the reaction mixture were monitored with time by gas chromatography, 1-methylpyrrole **3a** and 1-methylindole **4a** were detected. From the fact that maximal yields of **3a** and **4a** appeared in Figure 1, 9-methylcarbazole **5a** was supposed to be formed by the consecutive reaction through **3a** and **4a**. Actually, **5a** was obtained from either **3a** or **4a** by treatment with **2** in a benzene-water mixture in the presence of hydrochloric acid (Scheme II). Here, some chemical reactions were carried out to infer the formation mechanism of **4a** and **5a**. In the reaction of **3a** with furan which should be easily derived from **2**, a Diels Alder reaction did not proceed and neither **4a** nor **5a** could be detected. On the other hand, Dennstedt reported that 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 (Scheme III) [14]. However **3a** did not give any trace of **5a** under refluxing in a benzene-water mixture even in the presence of acid. From these facts, the reaction mechanism was temporarily speculated as shown in Scheme IV.

#### EXPERIMENTAL

Melting points were measured on a Yanagimoto Micro Melting Point Apparatus, and uncorrected. The  $^1\text{H}$ -nmr spectra were measured on a Hitachi R-24 (60 MHz) Spectrometer in deuteriochloroform using tetramethylsilane as an internal standard. The gas chromatography was carried out on a Shimadzu GC-4CM gas chromatograph by using SE-30 (2

m) column. Flash column chromatography was carried out on a column of silica gel (230-400 mesh, Merck).

#### General Procedure for the Preparation of 9-Substituted Carbazoles 5.

To a solution of primary amine hydrochloride **1** (5 mmoles) in 1.6 ml of water, 2,5-dimethoxytetrahydrofuran **2** (5 mmoles) dissolved in 40 ml of benzene was added and refluxed under an argon atmosphere overnight. The reactive mixture was filtered with celite and washed with water twice. The organic layer was dried over anhydrous magnesium sulfate and the solvent was removed *in vacuo*. Chromatography on silica gel with chloroform-acetone-ethanol mixture (100:5:1 (v/v)) gave the 9-substituted carbazole **5**, which was identified by comparison of the melting point with an authentic sample. The yield of **5** was calculated based on **2**.

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