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A NEW METHOD FOR SYNTHESIZING A PYRROLE RING AND ITS APPLICATION TO THE DEVELOPMENT OF NEW p -SYSTEMS

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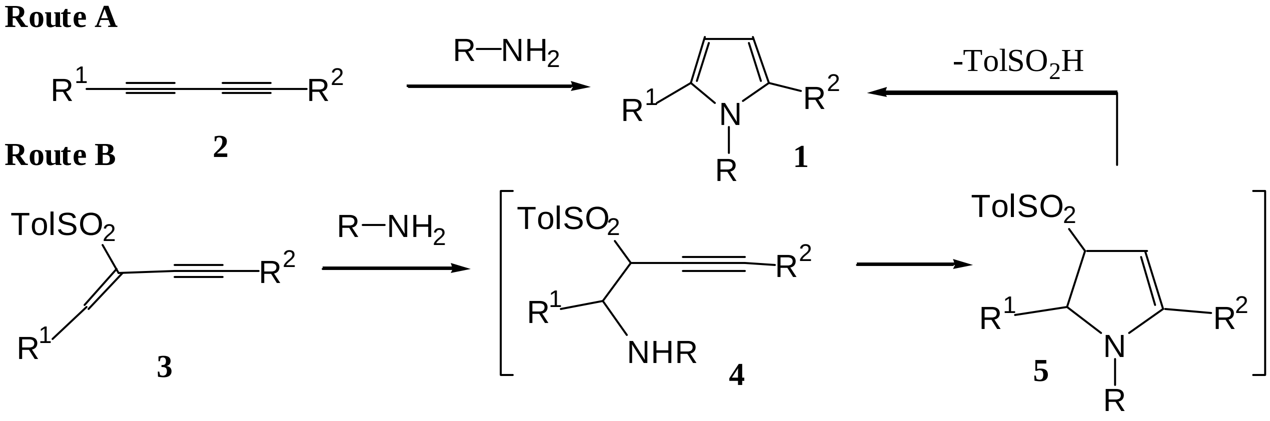
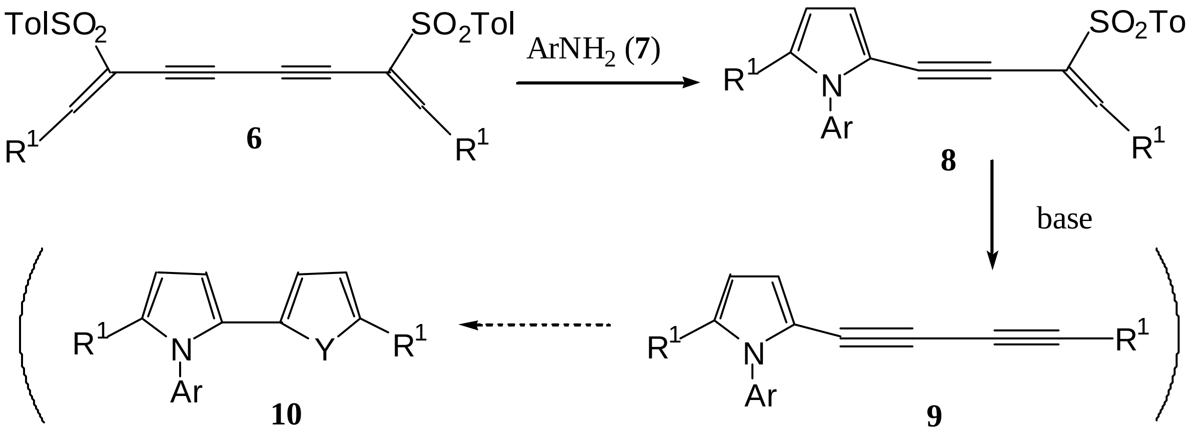
Abstract - A new type of reaction was developed for the construction of a pyrrole ring. When 1,8-disubstituted 2,7-bis(*p*-tolylsulfonyl)-1,7-octadiene-3,6-diynes (**6**) was treated with an aniline derivative (**7**) in the presence of CuCl (1.6 equiv.) and $CuCl_2$ (0.16 equiv.) in DMF (at 90 °C), one 2-sulfonyl-1-alken-3-yne part of **6** was converted to a 1-arylpyrrole skeleton in a reasonable yield.

A pyrrole ring (**1**) is known to be an important unit in many kinds of useful π-electron systems.[1] Among many methods for making this ring, the condensation of 1,4-diketones with an amine (the Paal-Knorr synthesis),[2] which is regarded as a [C4+N1]-type route, has been often utilized. A methodology from diacetylenes (**2**) leading to the pyrrole ring (route A in Scheme 1) is more straightforward for the [C4+N1]-type methodology, but has not been employed frequently. This is probably due to the forced conditions required for the reaction.[3] We were interested in Otera's recent paper[4] that vinyl sulfones can be easily led to the corresponding acetylenes by treatment with a base, suggesting to us the employment of 2-sulfonyl-1-alken-3-ynes (**3**) instead of **2** for constructing a pyrrole ring: the 2-sulfonyl-1-alkene part is considered to be a good Michael-type acceptor for an amine.[5] After the intramolecular addition of the resulting amino part to the C-C triple bond, the subsequent elimination of a sulfinic acid moiety gives the pyrrole derivative.



Scheme 1

We examined whether this proposed sequence was feasible with 2,7-bis(*p*-tolylsulfonyl)-1,7-alkadiene-3,6-diynes (**6**), which can be easily prepared from 2-propynyl *p*-tolyl sulfone.[6] If the reaction sequence is realized, a new type of π-system (**8**), a pyrrole ring having two substituents (Ar and R^1) at the 1- and 2-positions together with an acetylene bond at the 5-position, would be created. This is a useful precursor for various π-systems such as 1,2-diaryl-5-(4-arylbutadiynyl)pyrrole (**9**) and 1,2-diaryl-5-(2-thienyl or 2-pyrrolyl)pyrrole (**10**). Hence, our investigation started in order to determine the reaction conditions for transforming **6** into **8**. Now, we wish to report a preliminary result that this reaction sequence was realized in the addition of anilines (**7**) to **6**.[6]



Scheme 2

Since CuCl had been known to promote the reaction of aniline to a C-C triple bond,[9] we examined the reaction of **6** (R^1=Ph) with aniline (**7**; Ar=Ph) in the presence of CuCl: When a DMF solution of **6** (R^1=Ph) containing aniline (3.0 mol equiv.) and CuCl (1.0 mol equiv.) was heated at 90 °C for 1 h, the expected pyrrole derivative (**8**; Ar=R^1=Ph) was obtained in 30% yield along with the unreacted **6** (R^1=Ph). In this reaction, we observed no formation of a dipyrrole derivative (**10**; Ar=R^1=Ph, Y=PhN). In fact, this dipyrrole derivative was not formed on the treatment of **8** (Ar=R^1=Ph) with aniline under similar conditions. The yield of **8** (Ar=R^1=Ph) increased to 49% (the starting material: 29%) on pretreatment with CuCl in DMF at room temperature for 15 min and, after the addition of **6** (R^1=Ph), the resulting mixture was stirred at 90 °C for 6 h. To our surprise, this reaction became slower by bubbling nitrogen gas to give **8** (Ar=R^1=Ph) and **6** (R^1=Ph) in 23% and 49% yields, respectively (Entry 1 in Table 1). It is likely that the dissolved oxygen oxidizes Cu^+ partially to produce Cu^{2+} that promotes the reaction. Hence, we examined the additive effect of $CuCl_2$ in the present reaction system. Although $CuCl_2$ oxidizes aniline to form aniline black, a small amount of $CuCl_2$ was shown to be favored for the acceleration of the reaction. As the typical results summarized in Table 1 show, the best yield (62%) was attained when aniline (3.2 molar amount) was pretreated with CuCl (1.6 molar amount) and $CuCl_2$ (0.16 molar amount) in degassed DMF (15 min/room temperature) and then **6** (1.0 molar amount) was added (Entry 7 in Table 1). This procedure was applied to various derivatives of **6** to give the corresponding **8** in comparable yields, which are summarized in Table 2.

Table 1. The reaction of **6** (R^1=Ph) with aniline (**7**; Ar=Ph).[a]

Entry	**7** (equiv.)	CuCl (equiv.)	$CuCl_2$ (equiv.)	Time (h)	Yield (%)	
					8	**6**
1	2.0	1.0	---	6	23	49
2	2.0	1.0	0.10	6	52	8
3	2.0	1.0	0.20	6	39	43
4	2.0	1.0	0.10	6	22	59
5	3.2	1.6	0.16	6	55	13
6	4.0	2.0	0.20	6	58	--
7	3.2	1.6	0.16	8	62	1

[a] After aniline was stirred with CuCl and $CuCl_2$ in degassed DMF at room temperture for 15 min, **6** was added and the resulting mixture was further stirred at 90 °C.

Table 2. The reaction of **6** with anilines (**7**).[a]

Entry	R^1 of **6**	Ar of **7**	Yield (%) of **8**
1	Ph	Ph	62
2	Ph	p-$MeOC_6H_4$	47
3	Ph	p-MeC_6H_4	58
4	Ph	p-FC_6H_4	63
5[b]	2-naphthyl	Ph	54

[a] After **7** (3.2 equiv.) was stirred with CuCl (1.6 equiv.) and $CuCl_2$(0.16 equiv.) in degassed DMF at room temperture for 15 min, **6** (1.0 equiv.) was added and the resulting mixture was further stirred at 90 °C for 8 h.

[b] **7** (Ar=Ph) 4.3 equiv.; CuCl 2.2 equiv.; $CuCl_2$ 0.22 equiv.

The structure of **8** (Ar=R^1=Ph) was confirmed by single-crystal X-Ray crystallography.[7] Figure 1 shows its X-Ray structure. The distinct features of this structure are as follows: (i) a π-system spreads from the PhCH=C- double bond to the pyrrole ring *via* the triple bond; (ii) the terminal phenyl participates partially in the conjugation of the π-system; (iii) the phenyl at the 1-position stands almost perpendicular to the pyrrole ring; (iv) CH-π interaction was observed between the *N*-phenyl and the *ortho*-hydrogen of the terminal phenyl. This interaction was suggested by the short distance (2.70 Å) between the *ipso*-carbon of the *N*-phenyl and the *ortho*-hydrogen of the terminal phenyl. It should be noted that, in a solid state, **8** (Ar=R^1=aryl) exhibited a

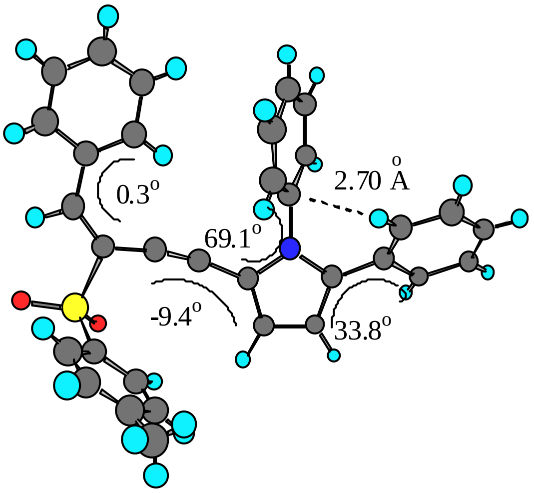
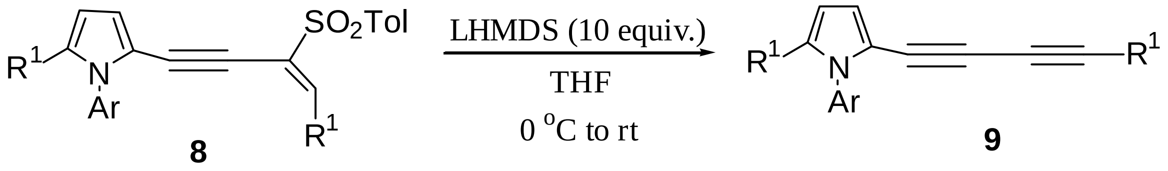


Figure 1. X-Ray Structure of **8** (Ar=R^1=Ph).

strong fluorescent light in the region of from 450 nm to 650 nm, suggesting that these compounds may be useful as a light-emitting material.

Thus, a new type of reaction was developed for the construction of a pyrrole ring, in which a 2,5-disubstituted 1-arylpyrrole was derived from a 1,4-disubstituted 2-sulfonyl-1-alken-3-yne and an aniline derivative (**7**) by the action of CuCl and $CuCl_2$. Further application of the present reaction to other 1,4-disubstituted 2-sulfonyl-1-alken-3-ynes is an on-going subject in our laboratory.

Finally, we would like to comment on the conversion of **8** to the diacetylene compound (**9**). Otera reported a vinyl sulfone could be transformed into the corresponding acetylene compound on treatment with a large excess amount (10 equiv.) of lithium hexamethyldisilazide (LHMDS).[4] When this reaction condition was applied to the compound (**8**), the expected **9** was given in good to excellent yields as summarized in the following equation.



Ar=Ph	R^1=Ph	80%	Ar=Ph	R^1=*p*-MeC_6H_4	63%
	R^1=*p*-$MeOC_6H_4$	93%	Ar=2-naphthyl	R^1=Ph	81%
	R^1=*p*-FC_6H_4	81%			

Scheme 3

In addition, we also found that treatment of the thus obtained **9** (R^1=Ph) with Na_2S in DMF at 100 °C gave 1,2-diphenyl-5-(5-phenylthien-2-yl)pyrrole (**10**; Ar=Ph, R^1=Ph, Y=S) in 97% yield. Therefore, the present reaction shows potential usefulness in the development of various new π-systems. The scope, mechanism, and synthetic application of thie novel reaction are under investigation.

ACKNOWLEDGMENT

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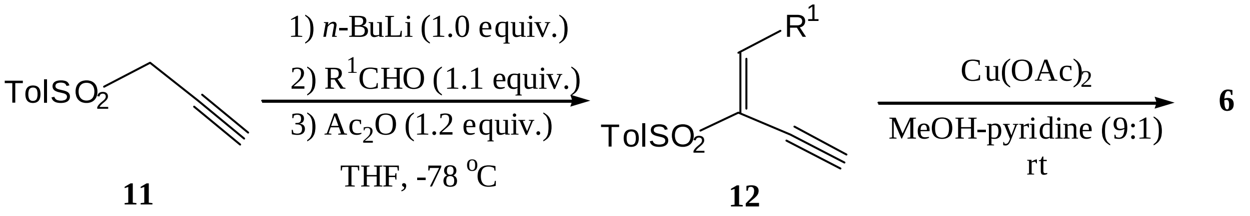
6. The compound (**6**) was prepared according to the following equation. The structure of the intermediary **12** (Ar=Ph) was determined by single-crystal X-Ray crystallography.[7]



11 **12** **6**

R^1=Ph	51%	R^1=Ph	89%
R^1=2-naphthyl	61%	R^1=2-naphthyl	95%

7. The data were collected with Cu Kα (λ=1.54178 Å) radiation on Mac Science MXC18 diffractometer. The structure was solved and refined by direct methods (SIR 92[8] on a computer program package: Crystan GM ver. 6.2.1 from MAC Science Co. Ltd.).

   8 (Ar=R^1=Ph): Orthorhombic, Pcba, a=16.208(7) Å, b=20.302(6) Å, c=16.061(4) Å, V=5285(3) Å^3, Z=8, *R*=0.058, *R*w=0.062, T=298 K.

   12 (R^1=Ph): Monoclinic, P2$_1$/n, a=11.178(2) Å, b=15.225(4) Å, c=8.792(2) Å, β=109.28(1)°, V=1412.3(6) Å^3, Z=4, *R*=0.059, *R*w=0.076, T=298 K.
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