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A Serendipitous C−C Bond Formation Reaction between Michael Donors and Diiminoquinoid Ring Assisted by Quaternary Ammonium Fluoride

Vijaykumar V. Paike, R. Balakumar, Hsin-Yu Chen, Hong-Pin Shih, and Chien-Chung Han*

Department of Chemistry, National Tsing Hua University, Hsinchu, Taiwan, ROC

cchan@mx.nthu.edu.tw

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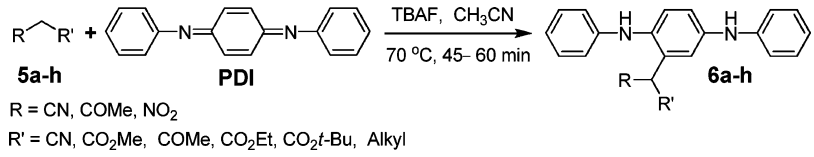
ABSTRACT



An efficient C−C bond formation reaction assisted by a fluoride ion has been identified for *N,N*′-diphenyl-1,4-phenylenediimine with the compounds having an active methylene group. The reaction follows the typical Michael addition fashion and proceeds to completion within 1 h at 70 °C in acetonitrile in the presence of tetrabutylammonium fluoride (TBAF), while the same reaction failed to proceed in the absence of a fluoride anion. The new finding reported herein also offers an unprecedented method for a direct functionalization of polyaniline backbone with versatile functional alkyl groups.

The Michael addition reaction is one of the most useful carbon−carbon bond forming reactions, which are of general synthetic interest in organic synthesis. Enolates or stabilized carbanions could be regarded as proper nucleophiles for a conjugate addition reaction to the α,β-unsaturated carbonyl moieties.[1,2] Various types of catalysts such as metal complexes,[3] chiral ionic liquid,[4] phase transfer catalyst,[5] organocatalyst,[6] L-proline salt,[7] and TBAF are used to facilitate the reaction.[8] Similar types of reactions for the α,β-unsaturated imino compounds or diiminoquionoid rings have, however, rarely been reported.[9] Polyaniline (Pan) represents

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a very interesting class of conducting polymers, which is renown for its fairly large number of redox states. The backbone structure of polyaniline, as illustrated in Figure 1,

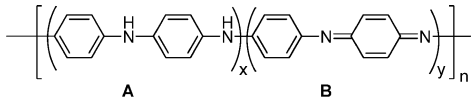


Figure 1. Representative structure of polyaniline.

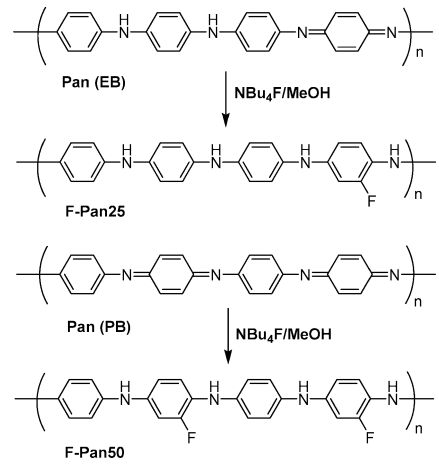
can be regarded as consisting of various ratios of the reduced repeat units A (containing the diaminobenzenoid rings) and the oxidized repeat units B (containing the diiminoquinoid rings). Like other classes of conducting polymers, the application of polyaniline has been greatly hindered by its poor solution-processability.

Although the solubility of substituted-polyanilines (S-Pans) prepared from the alkyl- and alkoxy-substituted aniline monomers are higher, their conductivities are ~3−5 orders of magnitude lower than the unsubstituted Pan. Such conductivity reductions are believed to be caused by the increased extent of the nonconjugated defect backbone structures that was induced to form during the growth of the polymer chain due to the competing electronic directing placement effect of the substituent's. Such a problem has been alleviated by utilizing the concurrent reduction and substitution (CRS) reaction method to introduce the substituent group after the formation of a polyaniline backbone. For example, highly conductive and processable functionalized polyanilines with various alkylthio and dialkylamino groups have been prepared via the CRS method by reacting the preformed Pan of a desirable redox state with nucleophiles, like thiols and amines.[9] The reactions were believed to occur at the diiminoquinoid sites and follow a typical Michael addition fashion, which converted the unsubstituted diiminoquinoid ring into the substitituted diaminobenzenoid rings. The efforts in extending the same reaction to the oxygen and carbon-based nucleophiles have however proved to be futile, up to now.

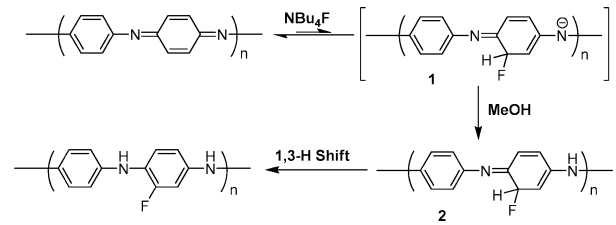
Recently, such CRS reaction was found to be a useful synthetic method for making highly conductive and electroactive fluorinated-polyanilines (F-Pans) having a controlled extent of fluorination (ranging from 25 to 130 mol %),[10] by reacting Pan with a fluoride anion, as illustrated in Scheme 1. Most interestingly, the fluoriation reaction did not go in the typical aprotic solvent media (i.e., NMP, DMF, CH_3CN), but it worked effectively (though slowly) in some selected protic solvent media (i.e., MeOH and EtOH). The plausible mechanism was proposed as the one illustrated in Scheme 2.

We rationalized that although the nucleophilicity of the fluoride anion has been weakened in these protic solvents, it is still sufficient to make an effective nucleophilic attack at the diiminoquinoid rings of Pan, as facilitated by the high polarizability of the highly conjugated π-electron

Scheme 1. Fluorination of Emeraldine Base (EB) and Pernigraniline Base (PB) Forms of Polyaniline (Pan) via the CRS Reaction



Scheme 2. Plausible Mechanism for the Fluorination of Pan



cloud system. The equilbrium concentration of the fluorinated intermediate **1** may not be high, but the basicity of the intermediate is high enough to seize the proton from the employed protic solvents to form the protonated and fluorinated intermediate **2** (Scheme 2), which would ultimately result in the fluorinated-polyaniline leucoemeraldine base as driven by the extra energy gain from the resonance energy of the newly formed aromatic ring. To further evaluate the fundamental properties of the F-Pans and understand the reaction mechanism of such fluorination, similar reactions between the fluoride anion and the model compound *N*,*N*′-diphenyl-1,4-phenylenediimine (PDI) was investigated. Surprisingly, there was no reaction in the aprotic solvents (e.g., CH_3CN, CH_2Cl_2, DMSO, DMF, NMP, and THF) as well as in the protic solvents (e.g., MeOH and EtOH), even with excess amounts of fluoride anion. We thought that maybe in this much less conjugated PDI system, the much reduced polarizability of the π-electron cloud system is no longer sufficient to suppport the fluoride to make an effective nucleophilic attack at the diiminoquinoid rings of PDI. Thus, an the alternative way to facilitate the above reaction is to activate the PDI counterpart through the protonation of the imino sites by a much more efficient proton source than ROH.

Therefore, one drop of acetic acid was added to provide such an essential ingredient, but the reaction failed, which

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we rationalized that the presence of the free acid may significantly further reduce the nucleophilicity of the fluoride and thus result in no reaction. Apparently, what we actually needed is a latent proton source, which should not be a free proton but could serve as an effective proton source as needed by the reaction intermediate. For this purpose we chose nitromethane, because it is a polar aprotic solvent and contains a proton source which is more acidic than MeOH but not as free as acetic acid.

Interestingly, when the reaction was conducted in nitromethane in the presence of 4 equiv of TBAF at ambient temperature, all starting material PDI was consumed within 15 h. During the reaction course, the color of the reaction solution changed gradually from orange to pale yellow, indicating the gradual disappearance of the starting material PDI. At higher reaction temperature (70 °C), the same reaction proceeded much faster and finished within 45 min (Table 1). The ^{1}H NMR spectrum of the obtained product

Table 1. Nitromethylation of PDI Assisted by Fluoride Anion

entry[a]	TBAF (equiv)	solvent	yield[c] (%)
1	4	MeOH	N.R.
2	4	CH_3CN	N.R.
3	4	CH_2Cl_2	N.R.
4	4	DMSO	N.R.
5	4	DMF	N.R.
6	4	THF	N.R.
7	4	CH_3NO_2	71
8	0	CH_3NO_2	N.R.
9	4	CH_3NO_2	73
10	4	CH_3CN[b]	72
11	2	CH_3CN[b]	70
12	1	CH_3CN[b]	68
13	0.5	CH_3CN[b]	65

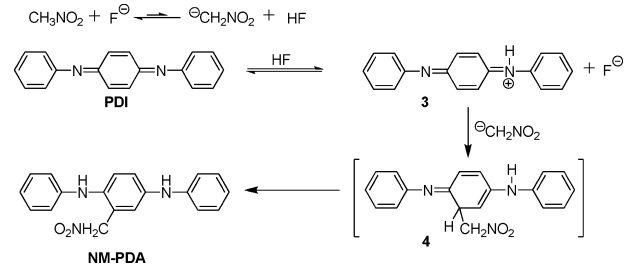
[a] Reaction conditions: entries 1−8: at rt for 15 h; entries 9−13: at 70 °C for 45 min. [b] Containing 1 vol % of CH_3NO_2. [c] Yield of isolated product after column chromatography. N.R. - no reaction.

indeed showed the typical spectrum for the monosubstituted *N*,*N*′-diphenyl-1,4-phenylene-diamine (mono-PDA) with the substituent appearing at the center ring.[9a] However, both of its ^{1}H and ^{13}C NMR spectra did not show the expected ^{1}H−^{19}F splitting pattern, instead, the ^{1}H NMR of the isolated compound showed the presence of an additional singlet peak at ∼δ 5.5, which did not undergo H-D exchange as D_2O was added. The peak integration indicated that the new singlet accounts for methylene protons, which was further confirmed by ^{13}C DEPT and 2D NMR (e.g., HMBC, HSQC) study. The HRMS data indicated that it is a PDA being monosubstituted by a moiety having a mass of 60, possibly corresponding to a $-CH_2NO_2$ group instead of a fluorine.

The control experiment indicated that no reaction occurred between PDI and nitromethane in the absence of TBAF. It was clear that TBAF is mediating the reaction. Most interestingly, we found that the same reaction can proceed under similar conditions even with nitromethane as low as 1 vol % in other solvent mediums such as CH_3CN, as well as with a lesser amount of TBAF (0.5−4 equivalents), giving quite similar yields (entries 10−13, Table 1). The significance of this reaction was shown by the fact that when the CRS reaction was tried between PDI and n-BuLi, there was no sign for the formation of expected butyl-substituted PDA, even when CH_3NO_2 was used as the solvent medium. Other bases (e.g., KOH, NaOH, NEt_3, and DBU) in CH_3NO_2 have also failed to promote the reaction. The tetrabutylammonium salts with a counteranion of stronger nucleophilicity, like chloride and bromide, also failed.

Hence, it is evident that it is the fluoride anion of TBAF mediating the substitution reaction to yield substituted PDA's. Based on all the above results, we proposed a plausible mechanism for the nitromethylation of PDI in Scheme 3.

Scheme 3. Plausible Mechanism for the Nitromethylation of PDI



When the fluoride encounters the nitromethane molecule, small equilibrium amounts of HF and nitromethane anion may form as driven by the unusually strong bonding energy of H−F (i.e., 136 kcal/mol)[11] and the relatively low pK_a value of nitromethane (10.2).[11]

The released HF is acidic enough (unlike MeOH) to protonate the imino N of PDI and renders the diiminoquinoid ring **3** reactive enough to be nucleophilically attacked by the nitromethane anion. The resultant nitromethylated intermediate **4** then could undergo either a 1,3-H shift or a deprotonation and successively protonation process with the aid of fluoride as a base to yield the final nitromethylated-PDA (NM-PDA). The fluoride anion released from the above reaction cycle and then could induce another cycle of reactions, which accounts for the catalytic nature of this reaction. The same mechanism can also explain the ineffectiveness of tetrabutylammonium chloride or tetrabutylammonium bromide, because the initial deprotonation of the nitromethane by Cl^- or Br^- are much unlikely due to the much weaker bonding strength of HCl (103 kcal/mol)[11] and HBr (88 kcal/mol)[11] than HF.

Interestingly, we found that this reaction could serve as an efficient way to introduce a C−C bond, if it worked with an appropriate compound having a suitable latent proton source. We have systematically screened the scope of the reaction for a variety of diketones, keto esters, dicyano and

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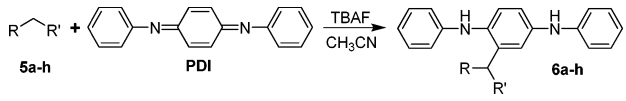
cyano esters having an active methylene group and we found that the reaction worked very well and delivered desired compounds in good to excellent isolated yield, as summarized in Table 2. From Table 2, it was also observed that the CRS

Table 2. Reaction of PDI with Various Michael Donors Assisted by TBAF



entry[a]	Michael donors	time (min)	product	yield[b] (%)
1	CH_3NO_2 **5a**	45	**6a**	72
2	NO_2 **5b**	50	**6b**	70
3	NO_2 **5c**	60	**6c**	68
4	**5d**	50	**6d**	74
5	NC CN **5e**	45	**6e**	80
6	**5f**	50	**6f**	76
7	**5g**	55	**6g**	77
8	**5h**	55	**6h**	73

[a] All reactions were carried out at 70 °C in CH_3CN containing 1 vol % of Michael donor and 4 equiv of TBAF. [b] Yield of isolated product after column chromatography.

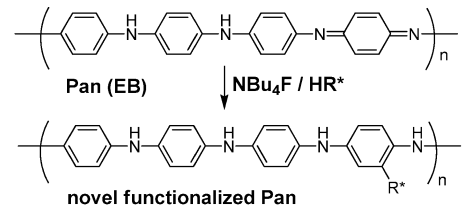
reaction between the PDI and Michael donors can tolerate both the electron-donating (entries 1−3, Table 2) as well as the electron-withdrawing groups (entries 4−8, Table 2) that appeared on the Michael donors and give excellent isolated yield (68−80%) in a short span of reaction time (40−55 min) at 70 °C in acetonitrile. Interestingly, the ^{1}H NMR spectra (in DMSO-d_6) of those compounds having a CN substituent (entries 5−8, Table 2) at the benzylic position however showed no peaks corresponding to the benzylic C−H moiety. In addition, their ^{1}H NMR spectra all showed two different NH peaks, with one peak at ~δ5.9−6.6 accounting for two protons and another peak at ~δ6.5−7.9 for one proton (as confirmed by running H-D exchange experiments). Furthermore, their ^{13}C NMR spectra and their corresponding 2D NMR (e.g., HMBC, HSQC) studies confirmed that they all have a quarternary, but not a tertiary benzylic carbon.

We rationalized that these compounds might have undergone further enolization due to the high acidity of the resultant benzylic protons and the basic nature of the NH group of the PDA backbone system, as driven by the energy gains from their enlarged conjugation extent and the additional H-bonding (or Coulombic) interaction.

Similar enolization has also occurred to the acetylacetonated-PDA (entry 4, Table 2), as evidenced by the missing benzylic proton and the formation of two different methyl groups. Interestingly, in the case of 2-nitropropane it was found that the original nitro group at the benzylic position seems to undergo further elimination to yield a diamino-substituted α-methylstyrene. In the case of nitroethane, the product **6b** is stable in its solid form at low temperature, but in solution state it gradually lost its HNO_2 group, forming a diamino-substituted styrene that readily underwent further polymerization, possibly being catalyzed by the released HNO_2 acid. Regarding these low pK_a Michael donor systems, the same reaction mechanism as illustrated in Scheme 3 might be applied.

Most interestingly, these novel Michael addition reactions have also been successfully expanded to the polymer system, providing the first feasible synthetic method for a direct addition of a C-based substituent to the benzene rings of Pan and rendering the possible syntheses of various novel functionalized polyanilines (Scheme 4) for the first time.

Scheme 4. Preparation of Novel Functionalized Alkylated Pans



Further studies on these new Pans are under progress and their application on dye-sensitized solar cell is currently explored in our Lab.

In conclusion, we have demonstrated a fluoride-assisted serendipitous C−C bond formation reaction between diiminoquionoid ring and a Michael donor in CH_3CN. The reaction proceeds well at 70 °C within 1 h to give moderate yields (70−80%) and can tolerate both the electron-donating and electron-withdrawing substituents on the substrate. Control experiments demonstrated that other stronger nucleophilic halides or stronger bases however failed to promote the same reaction. A plausible mechanism is also proposed to account for all the observations.

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Supporting Information Available: Typical experimental procedure with the spectral data of all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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