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A catalyst free synthesis of 8, 9, 11-trihalo-5*H*-benzofuro[3,2-*c*]carbazol-10-ols

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ABSTRACT

8, 9, 11-Trichloro-5*H*-benzofuro[3,2-*c*]carbazol-10-ol analogues have been synthesized by treating 2,3-dihydro-1*H*-carbazol-4(9*H*)-one with chloranil/fluoranil without any catalyst and is found to be applicable across a range of carbazolone substrates. A possible mechanism has been proposed.

The Nenitzescu reaction has been successfully employed for assembling fused ring heterocycles. The reaction involves treating 1,4-benzoquinone with β-aminocrotonic esters to afford 5-hydroxyindoles through the Michael addition followed by a nucleophilic addition. The scope of the Nenitzescu reaction has been extended in further by replacing the benzoquinone with tetrahalobezoquinones, methoxybenzoquinone, anthradiquinones, naphthoquinones, dialkyl quinone-2,3-dicarboxylates.[1–7] Similarly, in place of the *β*-aminocrotonic esters, compounds such as S, N-acetals and *N*,*N*-acetals,[8] ketene aminals,[6] heterocyclic ketene aminals,[1,2,5] 2-aminomethylene-1-indanones,[9] etc., have been studied. The reaction has also been studied in the presence[4,10,11] and absence of catalysts.

As a part of our effort to synthesize the novel fused heterocyclic ring scaffolds, we would like to explore the Nenitzescu reaction with 2,3-dihydro-1*H*-carbazol-4(9*H*)-one (**1a**) since it is having enaminone function as a part of a rigid ring system. Moreover the reaction of carbazolones with chloranil and fluoranil as electrophiles is also hither to unreported. On the other hand we aware that chloranil had been extensively used for the dehydrogenation of 1,2,3,4-tetrahydrocarbazoles into aromatic carbazoles[12] and so we were curious to find out whether this reagent would aromatize 1,2,3,4-tetrahydro-4-oxocarbazole to 4-hydroxycarbazole (a key intermediate for the well-known anti-hypertensive drug, carvedilol). In the event, our efforts led to the formation of interesting benzofurocarbazoles **7a–k** as a serendipitous product. The reaction was found to be general towards the reactants used and the results are presented here.

In the reaction of quinones with enaminones, several competitive pathways operate and the final outcome depends on the structure of the quinone, enaminone and the reaction conditions.[1,3,9] We envisaged that the reaction of **1a** with chloranil **2** may have three possibilities: path A, the Nenitzescu reaction path of Michael addition via aza-ene addition followed by nucleophilic addition by the carbazolone nitrogen to give compound **3** (or) path B, it may also be possible that the Michael addition could be followed by a nucleophilic addition of the carbazolone oxygen to form benzofuro-carbozole **4**. Both compounds **3** and **4** are novel scaffolds and hence were of interest (Scheme 1). The third possibility (path C) is dehydrogenation of the hydroaromatic ring to form 4-hydroxycarbazole **12**.

Initially the compound **1a** was treated with chloranil **2** (Table 1) in acetone without any catalyst[1] at room temperature. Though we were gratified to find the progress of the reaction (by TLC), we failed to observe the completion of the reaction. The same reaction with various solvents at room temperature even failed to proceed except in acetone and hence acetone was found to be the better solvent at the room temperature (Entries 1, 2 and 3). Further the raise in reaction temperature improved the yield in all the solvents studied (Entries 4, 5 and 6) and the isolated yield was found to be

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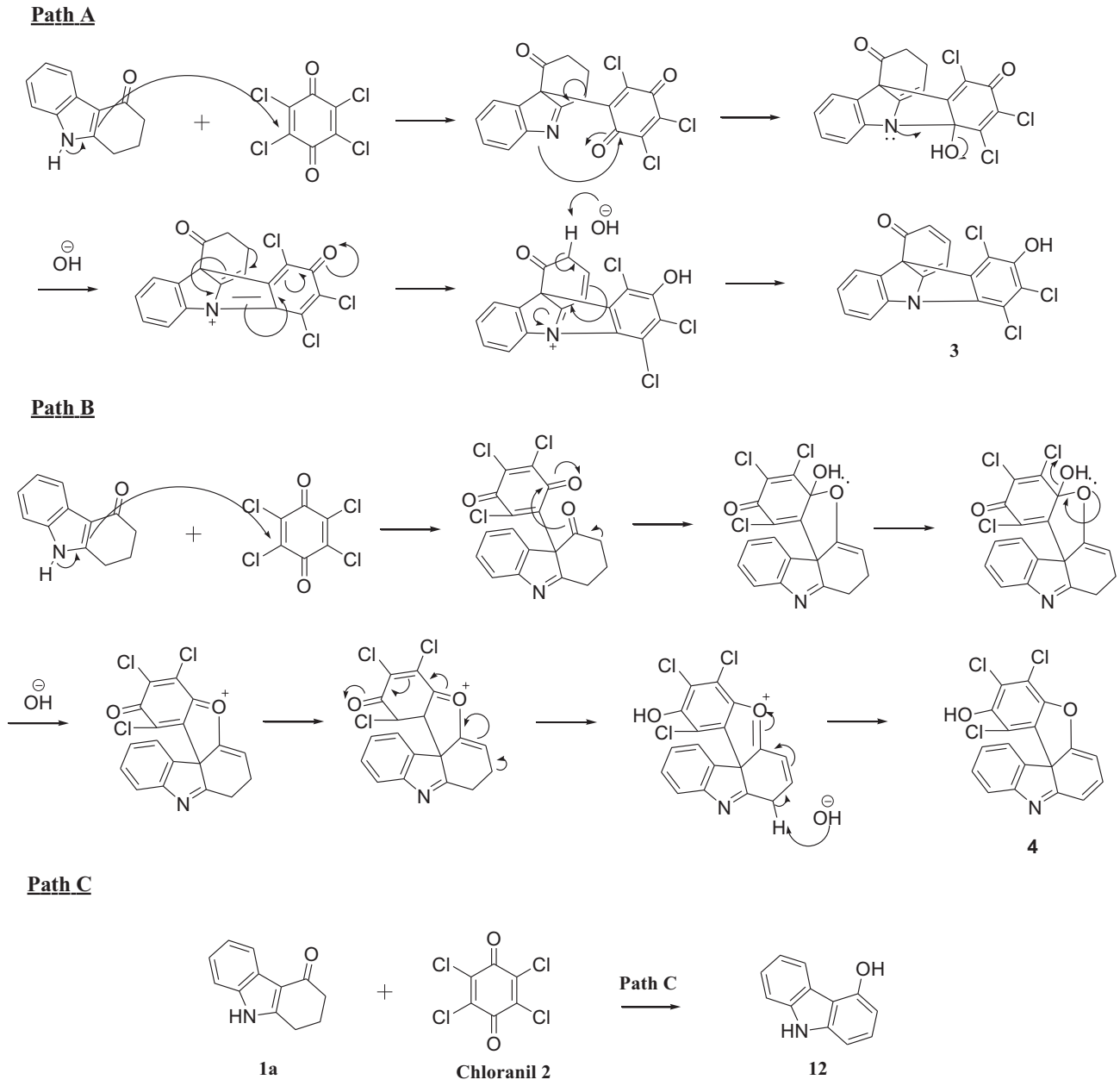

Scheme 1. Possible products from the reaction of **1a** and chloranil **2**.

Table 1
Reaction of carbazolone **1a** with chloranil **2** under various solvents.

Entry	Solvent	T (°C)	Time (h)	Yield (%)[a]
1	Acetone	RT	12	5
2	Dioxane	RT	12	No reaction
3	DMF	RT	12	No reaction
4	Acetone	55–60	12	39
5	Dioxane	85–90	12	38
6	DMF	115–120	5	44

[a] Isolated yield, RT: room temperature.

higher in DMF (Entry 6). The reaction was found be to clean on TLC even at the increased temperature.

The obtained product was characterized using spectral data. The examination of ^{13}C NMR spectrum of isolated solid product showed no signal up-field of 100 ppm (indicating the absence of the quaternary carbon) hence the possible formation of compound **3** through Nenitzescu mechanism was not considered. All signals in the ^{13}C NMR were found to be the downfield of 105 ppm. ^{1}H NMR exhibited only eight signals between δ11.88 and δ7.33 ppm revealed that the structure of product has to be completely

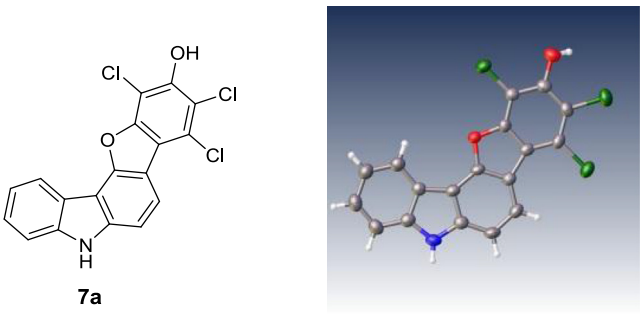

Fig. 1. Structure and ORTEP plot the compound **7a**.

aromatized one. Of the eight, only six signals showed cross peaks with carbon in the HSQC indicating a total of six aromatic protons. As four of the six aromatic protons were found to be contributed by the phenyl hydrazine moiety of the product, it was felt that the cyclohexanone portion of the molecule had aromatized and had only two aromatic protons indicating that one of the carbons of the cyclohexanone moiety was probably connected to chloranil. Two broad singlets observed at down field 10.86 and 11.89 were found to be D_2O exchangeable protons and hence considered as either NH/OH. The HR-MS spectrum exhibited *m/z* at 373.9 $(M-H)^-$ with multiple satellites differing by 2 mass units indicating the presence of chlorine atoms and a molecular formula of $C_{18}H_7Cl_3NO_2$ leading to the tentative structure **7a**. The point of ring fusion was best established with single crystal X-ray diffraction studies of **7a**. The crystallographic data was deposited with the Cambridge Crystallographic Data Centre (CCDC Number 1537477). The ORTEP of **7a** confirmed that the obtained compound is 8,9,11-trichloro-5*H*-benzofuro[3,2-*c*]carbazol-10-ol (Fig. 1). Thus, the reaction of **1a** with chloranil **2** in DMF led to the formation of 8, 9, 11-trichloro-5*H*-benzofuro[3,2-*c*]carbazol-10-*ol* (**7a**); surprisingly none of the expected compounds **3**, **4** or **12** were formed.

An attempt to improve the yield of the reaction under the acid catalysis at room temperature was failed (entry 1, entry 2 & entry 4, Table 2). The isolated yields under heating with or without acid catalyst also afforded the similar yield (Table 1 entry 4 vs. Table 2 entry 6, Table 1 entry 5 vs. Table 2 entry 3 and Table 1 entry 6 vs. Table 2 entry 5). The decomposition of the product under base catalysis in all solvents at room temperature (showed decomposition with multiple spots on the TLC) was observed and hence not pursued further (Entries 7, 8 and 9, Table 2). Thus, the reaction in DMF at 115–120 °C was regarded as an optimized condition and this was chosen as a standard reaction condition for further studies.

The literature survey revealed that the closely related benzofuro-carbazole compounds have drawn immense interest in the areas of organic field-effect transistors (OFETs)[13] and organic light emitting diodes (OLEDs).[14] Those compounds were reported to synthesise through the palladium catalyzed[14] pathway. The present work emphasizes an alternate and greener strategy to synthesize new benzofuro-carbazole derivatives without the use of any costlier catalyst. In this attempt we have synthesized a series of carbazolones **1a–j** and which in turn are treated with chloranil to afford benzofuro-carbazole **7a–j**.

The substituted carbazolone derivatives **1a–j** required for the study were prepared via Fischer Indole synthesis by condensing 1,3-cyclohexanedione (**5**) with different substituted phenyl hydrazine or their hydrochlorides **6a–j** in acetonitrile using one pot procedure.[15,16] After the formation of the hydrazones (Schiff's base), the reaction mass was concentrated and the product obtained was treated with acid under reflux to yield substituted carbazolone derivatives **1a–j** in low to moderate yields of 11–48% (Scheme 2 and Table 3). Although the reaction was done as a one pot reaction, the pure Schiff's base can be isolated just by filtering the reaction mixture, since the unreacted reactants and other impurities were

Table 2
Optimization of the reaction of carbazolone **1a** with chloranil **2** under various condition.

Entry	Solvent	Catalyst	Temp (°C)	Time (h)	Yield (%)[a]
1	Acetone	AcOH	RT	12	5% by TLC
2	Dioxane	AcOH	RT	12	No reaction
3	Dioxane	AcOH	85–90	12	38
4	DMF	AcOH	RT	12	No reaction
5	DMF	AcOH	RT	5	40
6	Acetone	AcOH	55–60	12	39
7	Acetone	K_2CO_3	RT	12	5
8	Dioxane	K_2CO_3	RT	12	No reaction
9	DMF	K_2CO_3	RT	12	No reaction

[a] Isolated yield, RT: room temperature.

Table 3
Synthesis of 2,3-dihydro-1*H*-carbazol-4(*H*)-ones **1a–j**.

Reactant	Products	R_1	R_2	R_3	R_4	Acid	Yield (%)[a]
6a	**1a**	H	H	H	H	conc. HCl	18
6b	**1b**	H	F	H	H	conc. HCl	48
6c	**1c**	H	Cl	H	H	conc. HCl	15
6d	**1d**	H	OCH_3	H	H	no acid	29
6e	**1e**	H	H	F	H	conc. HCl	19
6f	**1f**	H	H	H	Cl	conc. HCl	12
6g	**1g**	H	H	H	F	50% H_2SO_4	11
6h	**1h**	H	H	H	C_2H_5	conc. HCl	29
6i	**1i**	H	Cl	H	Cl	50% H_2SO_4	16
6j	**1j**	H	F	H	F	50% H_2SO_4	19

[a] : Isolated yields.

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getting retained in the mother liquor. The synthesis of carbazolones **1a–j** required variation in acidic conditions depending on the phenylhydrazines used (Table 3), hence the general procedure could not be employed for synthesis of **1a–j**.

In the case of methoxyphenyl hydrazine hydrochloride (**6d**), the carbazolone **(1d)** was obtained without any acid catalyst. All the synthesized carbazolones **1a–j** were characterized by their spectral data and included in the supplementary data. The compounds **1e**, **1h–j** are hither to unreported, whereas remaining compounds (their spectral data found to be in accord with the literature) in the series were available in the literature.[16–20]

Reagents and conditions: Carbazolone, chloranil/fluoranil in DMF, 115–120 °C, 4–5 h.

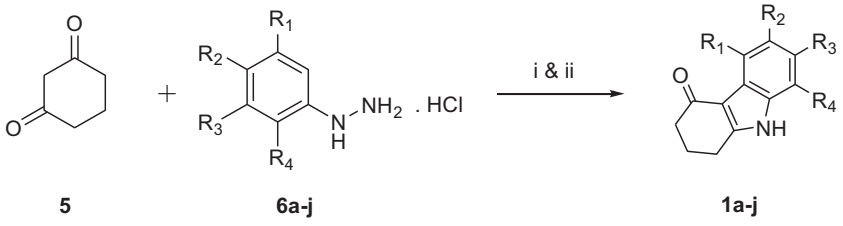
The synthesized carbazolones **1b–j** in turn were made to react with chloranil (**2**) under the optimized reaction condition in DMF at 115–120 °C (Table 4) which led to the formation of respective benzofuro-carbazoles **7b–j** in a reasonable yield (Scheme 3 and Table 4). Further, the carbazolone **1a** was made to react with fluoranil (**11**) in place of chloranil under the same reaction condition to afford the product **7k**. The product formation was confirmed using ^{1}H NMR, ^{13}C NMR and mass spectral data. All the benzofuro-carbazoles synthesized in this work are hither to unreported.

A probable mechanism for the formation of benzofuro-carbazole **7a** is shown in Scheme 4. As in Nenitzesu reaction, the lone pair of electron on the enamine nitrogen provides the driving force but the initial attack on the quinone moiety is via the extended conjugated system as shown in Scheme 4. The first step possibly involves nucleophilic attack by the extended conjugated form of the carbazolone **8a** on the quinone led to the intermediate **9a**. A subsequent dehydration followed by ring closure and aromatiza-

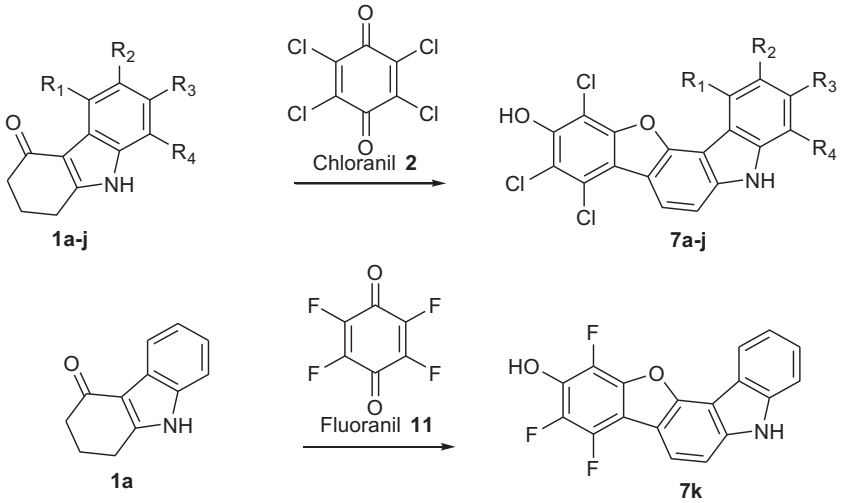
Table 4
Synthesis of 8, 9, 11-Trichloro-5*H*-benzofuro[3,2-*c*]carbazol-10-ols **7a–k**.

Entry	Product	R_1	R_2	R_3	R_4	X	Yield (%)[a]
1	**7a**	H	H	H	H	Cl	44
2	**7b**	H	F	H	H	Cl	28
3	**7c**	H	Cl	H	H	Cl	21
4	**7d**	H	OCH_3	H	H	Cl	42
5	**7e**	H	H	F	H	Cl	18
6	**7f**	H	H	H	Cl	Cl	21
7	**7g**	H	H	H	F	Cl	25
8	**7h**	H	H	H	C_2H_5	Cl	26
9	**7i**	H	Cl	H	Cl	Cl	52
10	**7j**	H	F	H	F	Cl	26
11	**7k**	H	H	H	H	F	30

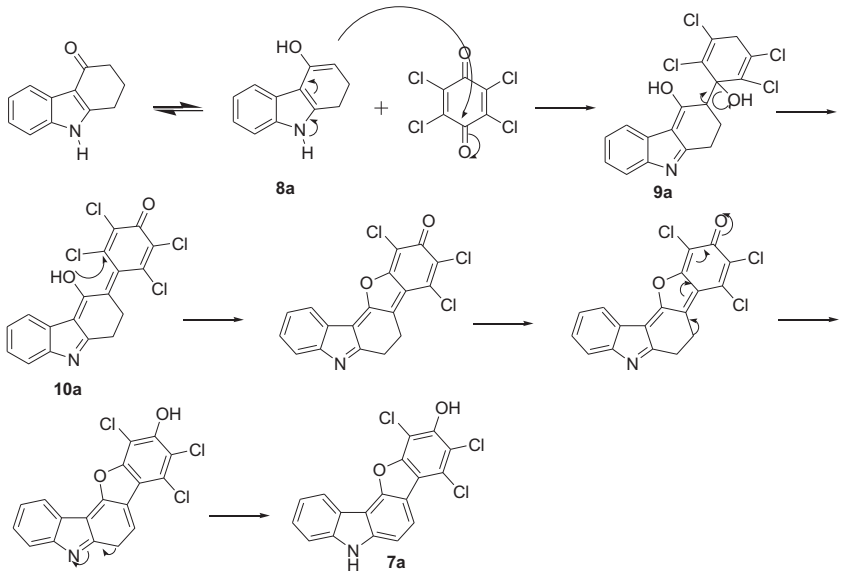
[a] Isolated yields.



Scheme 2. Synthesis of 2,3-dihydro-1*H*-carbazol-4(*H*)-ones **1a–j**.



Scheme 3. Synthesis of 8, 9, 11-trichloro-5*H*-benzofuro[3,2-*c*]carbazol-10-ol **7a–k**.



Scheme 4. Probable mechanism of 8, 9, 11-trihalo-5*H*-benzofuro[3,2-*c*]carbazol-10-ol **7a**.

tion yield the product **7a**. (The reaction is visualized as being ionic but an equivalent radical pathway can also be formulated). The fact that heating helped the reaction possibly indicates that formation of the five membered furan ring, which may be probable driving force. The expected initial attack by the β carbon of the enamine (by path A or B) on the electrophilic C-2 carbon of chloranil may not be favored due to steric constraints.

In summary, a novel, catalyst free method for the synthesis of halo substituted benzofuro-carbazoles has been developed by treating carbazolones with chloranil and fluoranil. The reaction is general and has a good scope. We believe that this transformation will serve as a useful method for the metal free synthesis of newer scaffolds for OLEDs materials. Work on further tuning the reaction conditions for improvement of yields and use of different kinds of quinones and carbazolones is in progress and the results will be reported elsewhere.

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A. Supplementary data

Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC 1537477. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.Uk).

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2017.09.009.

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