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Microwave promoted one-pot preparation of fluorinated propargylamines and their chemical transformation

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This paper is dedicated to Professor Wei-Yuan Huang on the occasion of his 90th birthday.

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ABSTRACT

A series of fluorinated propargylamines have been synthesized from the one-pot three-component reaction of fluorobenzaldehyde, aniline and phenylacetylene under solvent-free and microwave irradiation. The fluorinated propargylamines were then further transformed to chalcones or quinoline derivatives respectively depending on the different structures of propargylamines.

1. Introduction

It is known that propargylamines are prepared in one-pot reaction of benzaldehyde, aniline and phenylacetylene under the conventional thermal conditions or microwave irradiation conditions. Alternatively addition reactions of phenylacetylenes to imines also provide the propargylamines and their enantioselective versions are the recent topic [1]. In general, thermal conditions require long reaction time [2] and the use of poisonous organic solvents [3]. We have recently reported the procedure under the solvent free and short reaction time conditions [4].

There are many literature reports about the synthesis of quinoline derivatives, such as hafnium (IV)-catalyzed one-pot synthesis of substituted quinolines in fluorous media [5], iron-catalyzed tandem reactions of aldehydes, terminal alkynes, and primary amines [6], one-pot coupling-addition-cyclocondensation-sulfur extrusion sequence [7], nickel-catalyzed cyclization of 2-iodoanilines with aroylalkynes [8], and the reaction of 2-aminobenzophenone and ethyl acetoacetate in the presence of phosphotungstic acid [9]. In 2004, microwave promoted solvent-free one-pot three-component reaction to 2-pentauorophenylquinoline derivatives was reported by our group [10].

According to previous reports, corresponding quinoline derivatives were formed after chemical transformation of propargylamines [11]. However, it was noticed that propargylamines obtained from anilines with electron withdrawing groups have not been studied. Thus, in this paper we investigated the chemical transformation of fluorinated propargylamines with different substituent groups.

2. Results and discussion

A series of fluorinated propargylamines were prepared by one-pot three-component condensation reaction of fluorobenzaldehyde, aniline and phenylacetylene, using CuCl as catalyst, in N_2 atmosphere, under microwave irradiation (750 W) (Scheme 1 and Table 1) [4].

Different type of products were obtained when the fluorinated propargylamines **4** were further irradiated by microwave in air, in the presence of montmorillonite doped with CuCl. That is, it was found that N-phenyl propargylamines **4ba** and **4ca** gave the corresponding quinoline derivatives **6** in 72% and 75% yield respectively, while all of the other N-nitrophenyl propargylamines gave two products, fluorinated chalcones **5** and the nitroanilines **2**. (Scheme 2 and Table 2)

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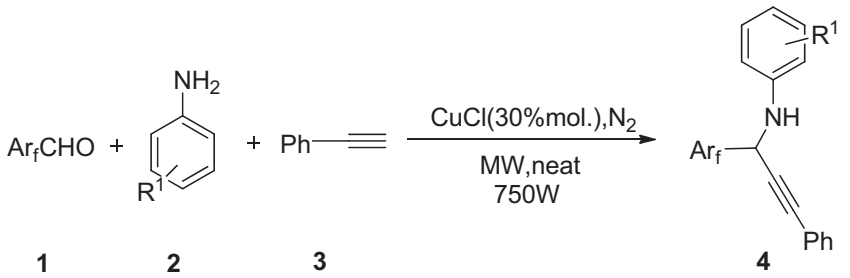
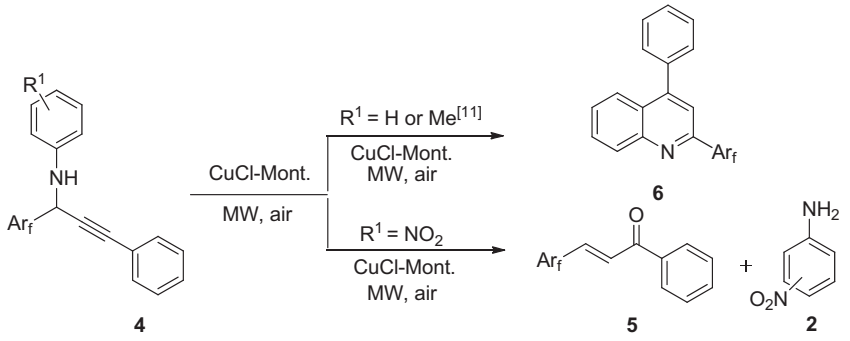


Ar_f=2-FC_6H_4 **1a**; 3-FC_6H_4 **1b**; 4-FC_6H_4 **1c**; 2,3-$F_2C_6H_3$ **1d**; 2,4-$F_2C_6H_3$ **1e**; 2,5-$F_2C_6H_3$ **1f**; 3,4-$F_2C_6H_3$ **1g**

R^1=H **2a**; m-NO_2 **2b**; p-NO_2 **2c**

Scheme 1. Synthesis of fluorinated propargylamines **4**.



Scheme 2. Chemical transformation of **4** to **5** or **6**.

As shown in entries 4–14, yields of fluorinated chalcones and nitroanilines were moderate to good. In addition, the same results were obtained when unpurified fluorinated propargylamines were used.

Next, we examined the direct synthesis of the quinoline derivative **6** by the one-pot three-component reactions. Under the atmospheric, microwave irradiation and solvent-free conditions, quinoline derivative **6** was obtained, when fluorobenzaldehyde **1a–1g**, aniline **2a–2c** and phenylacetylene **3** were mixed with montmorillonite doped with CuCl. (Scheme 3)

First, the effect of irradiation power was briefly investigated. As a model reaction, formation of **6cc** was chosen. It was observed that yield of **6cc** was gradually increased by increasing the irradiation power up to 300 W, but it became lower when the microwave power exceeded 300 W. Thus, 300 W was chosen as the optimum irradiation power for **6cc**. Then the effect of microwave irradiation time was studied, and 3 min was found to be the optimized reaction time for the formation of **6cc**. On the basis of these optimized conditions, various combinations of fluorobenzaldehydes and anilines were employed for the three-component

Table 1
One-pot synthesis of propargylamines **4** under microwave irradiation condition[a].

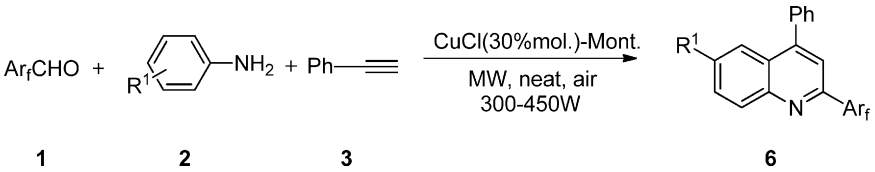
Entry	Aldehyde 1	Amine 2	Time (min)	Product	Yield (%)[b]
1	**1b**	**2a**	4	**4ba**	45
2	**1c**	**2a**	4	**4ca**	46
3	**1a**	**2c**	4	**4ac**	41
4	**1b**	**2c**	2	**4bc**	89
5	**1c**	**2c**	2	**4cc**	50
6	**1d**	**2c**	5	**4dc**	45
7	**1e**	**2c**	4	**4ec**	66
8	**1f**	**2c**	4	**4fc**	34
9	**1g**	**2c**	4	**4gc**	35
10	**1a**	**2b**	2	**4ab**	43
11	**1b**	**2b**	2	**4bb**	78
12	**1c**	**2b**	2	**4cb**	53

[a] Using CuCl as catalyst, in N_2 atmosphere, power 750 W, and the molar ratio of 1/2/3/CuCl = 1:1.2:1.5:0.3.
[b] Isolated yield based on **1**.

Table 2
Chemical transformation of **4** under microwave irradiation condition[a].

Entry	**4**	Power (W)	Time (min)	Product and yield (%)[b]	
1	**4ba**	450	6	**6ba** (72)	–
2	**4ca**	450	6	**6ca** (75)	–
3	**4ac**	600	6	**5a** (41)	**2c** (30)
4	**4bc**	600	6	**5b** (50)	**2c** (34)
5	**4cc**	450	10	**5c** (78)	**2c** (70)
6	**4dc**	750	3	**5d** (67)	**2c** (63)
7	**4ec**	750	3	**5e** (52)	**2c** (48)
8	**4fc**	750	3	**5f** (37)	**2c** (20)
9	**4gc**	750	5	**5g** (55)	**2c** (29)
10	**4ab**	600	6	**5a** (40)	**2b** (34)
11	**4bb**	600	6	**5b** (47)	**2b** (46)
12	**4cb**	450	10	**5c** (73)	**2b** (68)

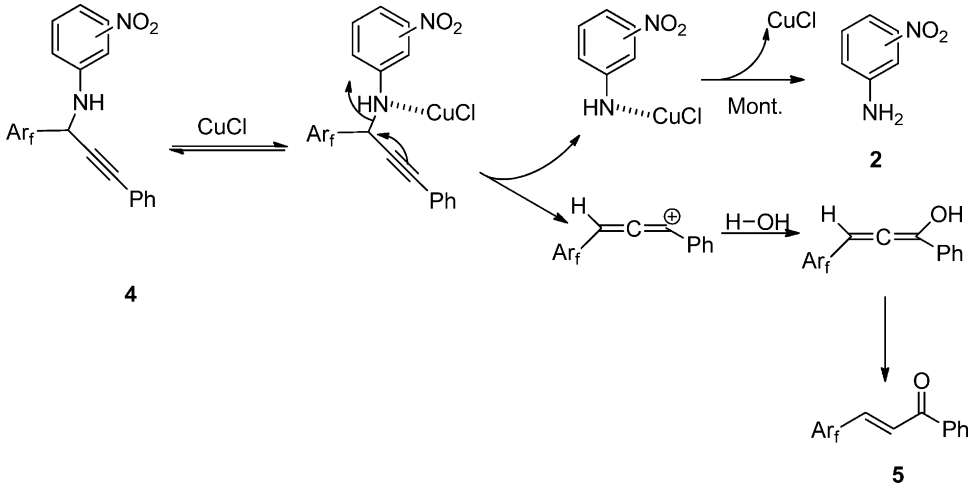
[a] Montmorillonite clay (about 0.7 g based on 1 mmol propargylamine) doped with CuCl, open in air.
[b] Isolated yield based on **4**.



1 2 3 6

Ar_f=2-FC_6H_4	**1a**	R^1=H	**2a**
3-FC_6H_4	**1b**	m-NO_2	**2b**
4-FC_6H_4	**1c**	p-NO_2	**2c**
2,3-$F_2C_6H_3$	**1d**		
2,4-$F_2C_6H_3$	**1e**		
2,5-$F_2C_6H_3$	**1f**		
3,4-$F_2C_6H_3$	**1g**		

Scheme 3. Synthesis of quinoline derivatives **6**.



4 **2** **5**

Scheme 4. Possible mechanism for the chemical transformation of **4** to **5**.

reactions with phenylacetylene. Results are summarized in Table 3.

The formation of chalcone derivative and the nitroaniline from the N-nitrophenylated propargylamine would possibly be explained by considering that nitroaniline would act as a good leaving group which contributed to the generation of the allenic cation species. The subsequent reaction with water proceeded quickly to yield chalcone. Montmorillonite doped with CuCl played an important role for the activation of the nitroaniline by the coordination as shown in Scheme 4.

The mechanism of transformation of N-phenylpropargylamine **4ba** and **4ca** into quinoline derivative **6** is involving the air oxidation step shown in Scheme 5 as previous reported [11].

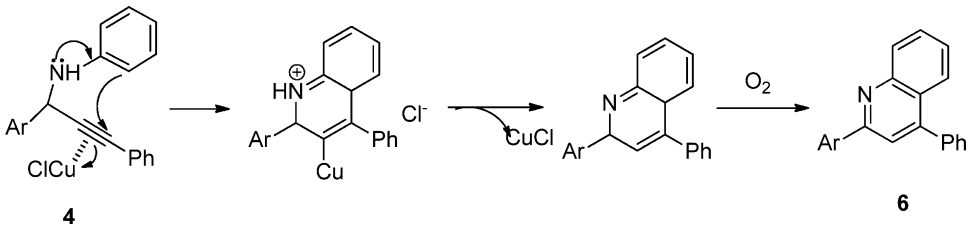
The preparation of N-arylated propargylamines and their transformation into quinoline derivatives or chalcone derivatives are summarized in Scheme 6.

When R^1 is CH_3 or H, the following cyclization reaction of propargylamines gave quinoline derivatives; however, when R^1 is an electron drawing NO_2 group, it afforded chalcones and anilines. The results demonstrated that catalyst and nitrogen atmosphere

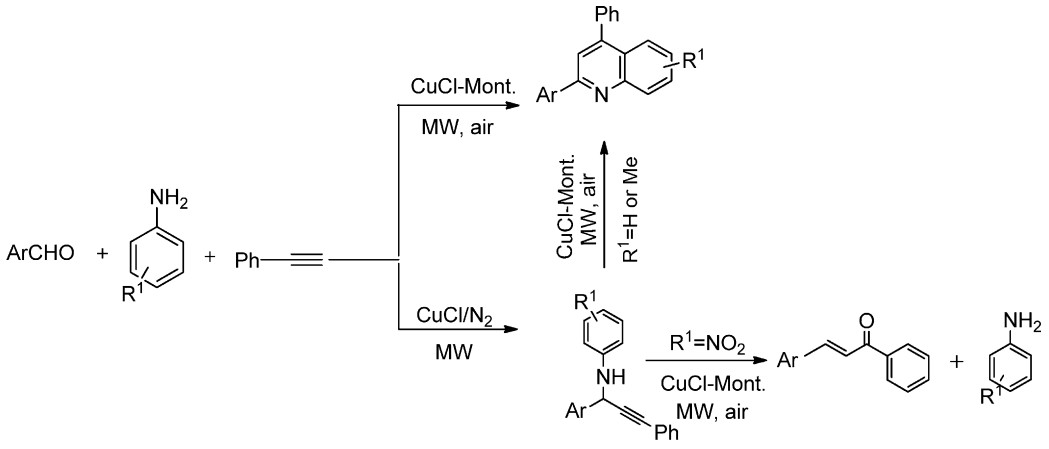
Table 3
One-pot reaction to prepare quinoline derivatives[a].

Entry	Aldehyde 1	Aniline 2	Power (W)	Time (min)	Product	Yield (%)[b]
1	**1b**	**2a**	300	5	**6ba**	61
2	**1c**	**2a**	300	4	**6ca**	64
3	**1a**	**2c**	300	5	**6ac**	78
4	**1b**	**2c**	300	4	**6bc**	80
5	**1c**	**2c**	300	3	**6cc**	86
6	**1d**	**2c**	300	3	**6dc**	75
7	**1e**	**2c**	300	3	**6ec**	80
8	**1f**	**2c**	300	3	**6fc**	78
9	**1g**	**2c**	300	3	**6gc**	76
10	**1a**	**2b**	450	8	**6ab**	68
11	**1b**	**2b**	450	6	**6bb**	72
12	**1c**	**2b**	450	6	**6cb**	74

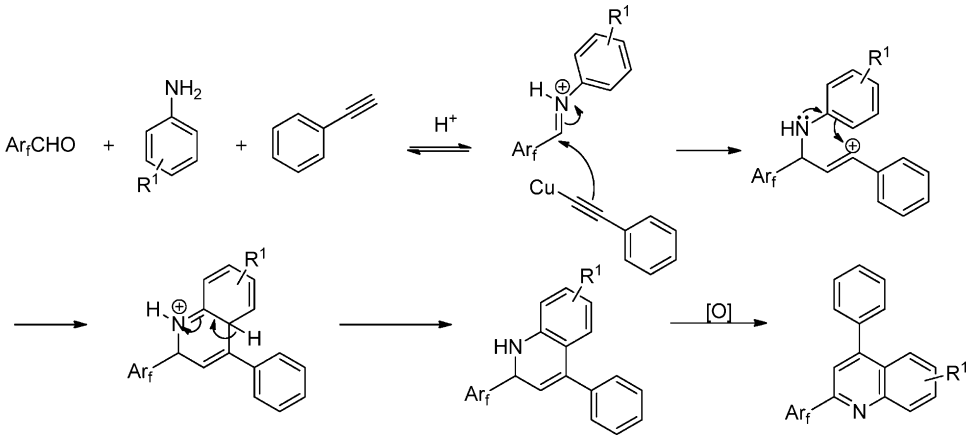
[a] Montmorillonite clay (about 1.2 g based on 1 mmol benzaldehyde) doped with CuCl, open air, and the molar ratio of 1/2/3/CuCl = 1:1:2:0.3.
[b] Isolated yield based on aldehyde **1**.



Scheme 5.



Scheme 6.



Scheme 7. Possible mechanism of one-pot synthesis of quinoline derivatives.

are necessary and essential for the synthesis of propargylamine. But the transformation of propargylamines proceeded in the presence of catalyst under atmospheric conditions, and the reaction could be prevented when exposed to nitrogen atmosphere. It could be inferred that in our investigation, the one-pot three-component preparation of quinolines did not proceed via propragylamines intermediate. A possible mechanism is proposed in Scheme 7. Proton provided by montmorillonite preferentially interacts with amino nitrogen to promote an iminium ion, and subsequently it reacts with the triple bond of **3** activated by CuCl to generate a vinylic intermediate. A final oxidation by O_2 in air affords the quinoline product **6**. [11]

3. Conclusion

Employing fluorobenzaldehyde, aniline and phenylacetylene as the reagents, CuCl as the catalyst, in N_2 atmosphere, a series of fluorinated propargylamines were prepared under solvent-free microwave irradiation condition. Further microwave irradiation in the presence of CuCl catalyst under atmospheric condition, the propargylamines transformed to quinoline derivatives or decomposed to chalcones and anilines, depending on the substituent on aniline ring. In the meantime, quinoline derivatives were obtained from the one-pot three-component reaction in the presence of montmorillonite doped with CuCl under microwave irradiation and solvent-free conditions.

4. Experimental

4.1. General

All reactions were performed in an improved domestic Sanyo, EM-208-EB1, microwave oven (2450 MHz, 80–750 W). TLC was performed on precoated silica gel HSGF-254 plates (0.15–0.2 mm;

Huanghai), and products and starting materials were detected by viewing under UV light. Column chromatography was performed on silica gel (200–300 mesh). Infrared spectra were recorded on an AVATAR370 FT spectrophotometer (PerkinElmer, USA). NMR spectra were determined with DRX500 MHz spectrometer (Bruker, USA), using solutions in deuterated chloroform with tetramethylsilane as the internal standard for ^{1}H, ^{19}F and ^{13}C nuclei, respectively. Low resolution mass spectrum or high resolution mass spectra were obtained on Finnigan MAT-8430 instrument using the electron impact ionization technique (70 eV).

4.2. Preparation of fluorinated propargylamines

4.2.1. General procedure

Fluorobenzaldehyde **1a**–**1g** (1 mmol), amine **2a**–**2c** (1.2 mmol), and phenylacetylene **3** (1.5 mmol) were mixed with CuCl (0.3 mmol) and ground into a fine, homogeneous mixture; then the mixture was put in a 25-mL round bottomed ask and exposed to microwave irradiation at proper power using a microwave oven for an appropriate time under nitrogen. After completion of the reaction (as monitored by TLC), the reaction mixture was diluted with ethyl acetate, and the catalyst was ltered out. After removal of the solvent under vacuum, the crude material was purified by silica gel column (using petroleum ether:ethyl acetate = 10:1 as elute) to afford pure product **4**.

4.2.2. N-(4-Nitrophenyl)-3-amino-3-(2-uorophenyl)-1-phenylprop-1-yne **4ac**

Yellow solid, mp 57.3–58.9 °C. IR (KBr) ν: 3375, 3078, 2922, 1601, 1325, 1303, 1265, 1110, 754, 690 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.09 (d, J = 15 Hz, 2H), 7.76 (t, J = 15.5 Hz, 1H), 7.47–7.33 (m, 6H), 7.20 (t, J = 10 Hz, 1H), 7.13 (t, J = 15 Hz, 1H), 6.73 (d, J = 15 Hz, 2H), 5.81 (d, J = 13.5 Hz, 1H), 5.27 (brs, 1H). ^{19}F NMR ($CDCl_3$, 470 MHz): δ = −117.99 to −118.02 (m, 1F). MS (EI) m/z: 346 (M^+). HRMS (EI) m/z calcd. for $C_{21}H_{15}FN_2O_2$: 346.1118; Found: 346.1122.

4.2.3. N-(4-Nitrophenyl)-3-amino-3-(4-uorophenyl)-1-phenylprop-1-yne **4cc**

Yellow solid, mp 55.3–56.6 °C. IR (KBr) ν: 3414, 3402, 3068, 2922, 1596, 1506, 1304, 1110, 832, 758 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.10 (d, J = 9 Hz, 2H), 7.62 (dd, J = 9, 5.5 Hz, 2H), 7.44 (dd, J = 7.5, 2 Hz, 2H), 7.35–7.29 (m, 3H), 7.11 (t, J = 8.5 Hz, 2H), 6.73 (d, J = 9 Hz, 2H), 5.59 (d, J = 5 Hz, 1H), 5.16 (brs, 1H). ^{19}F NMR ($CDCl_3$, 470 MHz): δ = −108.94 (s, 1F). MS (EI) m/z: 346 (M^+). HRMS (EI) m/z calcd. for $C_{21}H_{15}FN_2O_2$: 346.1118; Found: 346.1120.

4.2.4. N-(4-Nitrophenyl)-3-amino-3-(2,3-diuorophenyl)-1-phenylprop-1-yne **4dc**

Yellow solid, mp 86.8–87.6 °C. IR (KBr) ν: 3362, 3056, 2924, 1602, 1526, 1488, 1325, 1303, 1267, 1112, 835, 754 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.10 (d, J = 9.5 Hz, 2H), 7.46 (t, J = 7.5 Hz, 1H), 7.42 (d, J = 6.5 Hz, 2H), 7.36–7.29 (m, 3H), 7.22–7.13 (m, 2H), 6.71 (d, J = 9.5 Hz, 2H), 5.86 (s, 1H), 5.32 (brs, 1H). ^{19}F NMR ($CDCl_3$, 470 MHz): δ = −136.78 to −136.85 (m, 1F), −142.73 to −142.81 (m, 1F). MS (EI) m/z: 364 (M^+). HRMS (EI) m/z calcd. for $C_{21}H_{14}F_2N_2O_2$: 364.1023; Found: 364.1024.

4.2.5. N-(4-Nitrophenyl)-3-amino-3-(2,4-diuorophenyl)-1-phenylprop-1-yne **4ec**

Brown liquid, IR (KBr) ν: 3400, 3079, 2925, 1620, 1599, 1527, 1348, 1315, 1111, 835, 756 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.69–7.61 (m, 3H), 7.43 (d, J = 5 Hz, 2H), 7.33–7.28 (m, 4H), 7.12 (tt, J = 8.5, 2 Hz, 2H), 7.04–7.01 (m, 1H), 5.53 (d, J = 13 Hz, 1H), 4.57 (brs, 1H). ^{19}F NMR ($CDCl_3$, 470 MHz): δ = −113.33 to −113.39 (m, 1F), −114.71 to −114.80 (m, 1F). MS (EI) m/z: 364 (M^+). HRMS (EI) m/z calcd. for $C_{21}H_{14}F_2N_2O_2$: 364.1023; Found: 364.1027.

4.2.6. N-(4-Nitrophenyl)-3-amino-3-(2,5-diuorophenyl)-1-phenylprop-1-yne **4fc**

Brown liquid, IR (KBr) ν: 3374, 3081, 2925, 1598, 1493, 1445, 1310, 1264, 1111, 833, 755 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.10 (d, J = 10.5 Hz, 2H), 7.45–7.41 (m, 3H), 7.40–7.33 (m, 3H), 7.13–7.01 (m, 2H), 6.71 (d, J = 10.5 Hz, 2H), 5.82 (d, J = 7 Hz, 1H), 5.20 (brs, 1H). ^{19}F NMR ($CDCl_3$, 470 MHz): δ = −116.78 to −116.86 (m, 1F), −123.81 to −123.89 (m, 1F). MS (EI) m/z: 364 (M^+). HRMS (EI) m/z calcd. for $C_{21}H_{14}F_2N_2O_2$: 364.1023; Found: 364.1020.

4.2.7. N-(4-Nitrophenyl)-3-amino-3-(3,4-diuorophenyl)-1-phenylprop-1-yne **4gc**

Yellow solid, mp 84.9–85.8 °C. IR (KBr) ν: 3351, 3058, 2224, 1602, 1519, 1471, 1326, 1310, 1112, 834, 750 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.12 (d, J = 9 Hz, 2H), 7.72–7.68 (m, 1H), 7.43–7.41 (m, 2H), 7.36–7.29 (m, 3H), 6.96 (td, J = 8, 2 Hz, 1H), 6.91 (td, J = 8.5, 2 Hz, 1H), 6.71 (d, J = 9 Hz, 2H), 5.80 (d, J = 6.5 Hz, 1H), 4.94 (brs, 1H). ^{19}F NMR ($CDCl_3$, 470 MHz): δ = −108.45 to −108.52 (m, 1F), −113.66 (q, 1F). MS (EI) m/z: 364 (M^+). HRMS (EI) m/z calcd. for $C_{21}H_{14}F_2N_2O_2$: 364.1023; Found: 364.1018.

4.2.8. N-(3-Nitrophenyl)-3-amino-3-(2-uorophenyl)-1-phenylprop-1-yne **4ab**

Reddish brown liquid, IR (KBr) ν: 3407, 3065, 2962, 1617, 1527, 1487, 1349, 1248, 756, 734, 691 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.76 (td, J = 7.5, 2 Hz, 1H), 7.66 (t, J = 2.5 Hz, 1H), 7.61 (d, J = 3 Hz, 1H), 7.48–7.43 (m, 3H), 7.34–7.28 (m, 4H), 7.22 (t, J = 6.5 Hz, 1H), 7.14 (t, J = 8 Hz, 1H), 7.04 (dd, J = 8 Hz, 1H), 5.83 (s, 1H), 4.65 (brs, 1H). ^{19}F NMR ($CDCl_3$, 470 MHz): δ = −118.06 to −118.11 (m, 1F). MS (EI) m/z: 346 (M^+). HRMS (EI) m/z calcd. for $C_{21}H_{15}FN_2O_2$: 346.1118; Found: 346.1114.

4.2.9. N-(3-Nitrophenyl)-3-amino-3-(3-uorophenyl)-1-phenylprop-1-yne **4bb**

Reddish brown liquid, IR (KBr) ν: 3405, 3065, 2927, 1617, 1592, 1527, 1349, 1248, 757, 735, 691 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.62 (d, J = 6 Hz, 2H), 7.46–7.38 (m, 5H), 7.19 (t, J = 8 Hz, 4H), 7.07 (td, J = 8 Hz, 1H), 7.02 (d, J = 7.5 Hz, 1H), 5.57 (s, 1H), 4.65 (brs, 1H). ^{19}F NMR ($CDCl_3$, 470 MHz): δ = −111.65 to −111.66 (m, 1F). MS (EI) m/z: 346 (M^+). HRMS (EI) m/z calcd. for $C_{21}H_{15}FN_2O_2$: 346.1118; Found: 346.1116.

4.2.10. N-(3-Nitrophenyl)-3-amino-3-(4-uorophenyl)-1-phenylprop-1-yne **4cb**

Reddish brown liquid, IR (KBr) ν: 3406, 3068, 2962, 1621, 1602, 1527, 1349, 1226, 757, 735, 691 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.63 (t, J = 8.5 Hz, 4H), 7.43 (d, J = 6 Hz, 2H), 7.34–7.28 (m, 4H), 7.12 (t, J = 8.5 Hz, 2H), 7.03 (dd, J = 8, 2 Hz, 1H), 5.55 (s, 1H), 4.60 (brs, 1H). ^{19}F NMR ($CDCl_3$, 470 MHz): δ = −113.32 to −113.38 (m, 1F); MS (EI) m/z: 346 (M^+). HRMS (EI) m/z calcd. for $C_{21}H_{15}FN_2O_2$: 346.1118; Found: 346.1112.

4.3. Chemical transformation of fluorinated propargylamines

4.3.1. General procedure

Fluorinated propargylamines were mixed with montmorillonite clay doped with CuCl and ground into a ne, homogeneous mixture; then the mixture was put in a 25-mL round bottomed ask and exposed to microwave irradiation at proper power using a microwave oven for an appropriate time. After completion of the reaction (as monitored by TLC), the reaction mixture was diluted with ethyl acetate, and the catalyst and montmorillonite were ltered out. After removal of the solvent under vacuum, the crude material was puried by silica gel column (using petroleum ether:ethyl acetate = 10:1 as elute) to afford chalcones **5** [12] or quinoline derivatives **6**.

4.3.2. 3-(2-Fluorophenyl)-1-pnenyl-(2E)-2-propen-1-one **5a**

Pale brown solid, mp 87.1–88.2 °C. IR (KBr) ν: 1663, 1605, 1581, 1486, 1458, 1332, 1216, 983, 771 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 8.04–8.02 (m, 2H), 7.91 (d, J = 16 Hz, 1H), 7.66–7.63 (m, 2H), 7.59 (t, J = 7.5 Hz, 1H), 7.49 (t, J = 15 Hz, 2H), 7.39–7.35 (m, 1H), 7.19 (t, J = 7 Hz, 1H), 7.12 (t, J = 9 Hz, 1H). ^{19}F NMR ($CDCl_3$, 470 MHz): δ = −113.31 to −113.36 (m, 1F). MS (EI) m/z: 226 (M^+, 100).

4.3.3. 3-(3-Fluorophenyl)-1-pnenyl-(2E)-2-propen-1-one **5b**

Yellow solid, mp 87.4–88.2 °C. IR (KBr) ν: 1665, 1605, 1582, 1487, 1458, 1331, 1215, 983, 771 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 8.03–8.02 (m, 2H), 7.77 (d, J = 15.5 Hz, 1H), 7.61 (tt, J = 7.5, 1.5 Hz, 1H), 7.54–7.51 (m, 3H), 7.43–7.34 (m, 2H), 7.14–7.10 (m, 1H). ^{19}F NMR ($CDCl_3$, 470 MHz): δ = −112.39 (s, 1F). ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 190.1 (s), 164.0 (s), 162.0 (s), 143.3 (d, J = 2.5 Hz), 137.9 (s), 137.2 (d, J = 7.5 Hz), 133.0 (s), 130.5 (d, J = 7.5 Hz, 2 C), 128.6 (d, J = 20 Hz, 2 C), 124.6 (d, J = 4 Hz), 123.2 (s), 117.4 (d, J = 21 Hz), 114.5 (d, J = 22.5 Hz). MS (EI) m/z: 226 (M^+, 100).

4.3.4. 3-(4-Fluorophenyl)-1-pnenyl-(2E)-2-propen-1-one **5c**

Yellowish solid, mp 85.7–87.1 °C. IR (KBr) ν: 1662, 1605, 1581, 1485, 1459, 1330, 1216, 982, 770 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 8.03–8.01 (m, 2H), 7.79 (d, J = 16 Hz, 1H), 7.66–7.63 (m, 2H), 7.60 (t, J = 7.5 Hz, 1H), 7.53 (t, J = 15 Hz, 2H), 7.47 (d, J = 16 Hz, 1H), 7.14–7.10 (m, 2H). ^{19}F NMR ($CDCl_3$, 470 MHz): δ = −108.97 to −109.03(m, 1F). HRMS (EI) m/z calcd. for $C_{15}H_{11}FO$: 226.0794; Found 226.0791.

4.3.5. 3-(2,3-Difluorophenyl)-1-pnenyl-(2E)-2-propen-1-one **5d**

Yellow solid, mp 109.1–110.2 °C. IR (KBr) ν: 1664, 1609, 1582, 1485, 1459, 1330, 1276, 973, 767 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 8.04–8.02 (m, 2H), 7.87 (d, J = 15.5 Hz, 1H), 7.67 (tt, J = 7.5, 1.5 Hz, 1H), 7.61 (t, J = 7.5 Hz, 1H), 7.56–7.51 (m, 2H), 7.42–7.39 (m, 1H), 7.24–7.19 (m, 1H), 7.16–7.14 (m, 1H). ^{19}F NMR ($CDCl_3$, 470 MHz): δ = −136.76 to −136.84 (m, 1F), −142.73 to −142.80 (m, 1F). MS (EI) m/z: 244 (M^+, 100).

4.3.6. 3-(2,4-Difluorophenyl)-1-pnenyl-(2E)-2-propen-1-one **5e**

Yellow solid, mp 109.8–110.6 °C. IR (KBr) ν: 1662, 1607, 1589, 1485, 1459, 1330, 1274, 964, 776 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 8.02 (d, J = 7 Hz, 2H), 7.85 (d, J = 15.5 Hz, 1H), 7.66–7.58 (m, 3H), 7.53–7.50 (m, 2H), 6.97–6.89 (m, 2H). ^{19}F NMR ($CDCl_3$, 470 MHz): δ = −105.56 to −105.62 (m, 1F), −108.74 to −108.81 (m, 1F). ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 190.3 (s), 165.1 (d, J = 12.5 Hz), 163.1 (d, J = 12.5 Hz), 161.1 (d, J = 12.5 Hz), 137.9 (s), 136.5 (d, J = 7.5 Hz), 133.1 (s), 131.1 (s, 2C), 130.9 (t, J = 5 Hz, 2C), 124.2 (s), 119.7 (s), 112.3 (s), 105.0 (s); MS (EI) m/z: 244 (M^+, 100).

4.3.7. 3-(2,5-Difluorophenyl)-1-pnenyl-(2E)-2-propen-1-one **5f**

Yellow solid, mp 110.1–111.3 °C. IR (KBr) ν: 1662, 1605, 1487, 1458, 1333, 1269, 974, 726 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 8.04–7.98 (m, 2H), 7.85 (d, J = 15.5 Hz, 1H), 7.63–7.59 (m, 2H), 7.54–7.51 (m, 2H), 7.36–7.32 (m, 1H), 7.13–7.06 (m, 2H). ^{19}F NMR ($CDCl_3$, 470 MHz): δ = −118.17 to −118.25 (m, 1F), −119.45 to −119.57 (m, 1F). ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 190.0 (s), 159.8 (s), 158.8 (s), 157.8 (s), 137.8 (s), 136.1 (s), 133.2 (s), 128.8 (d, J = 17.5 Hz, 2 C), 125.5 (s, 2C), 125.4 (s), 118.3 (s), 117.5 (s), 115.2 (s). MS (EI) m/z: 244 (M^+, 100).

4.3.8. 3-(3,4-Difluorophenyl)-1-pnenyl-(2E)-2-propen-1-one **5g**

Yellow solid, mp 114.5–115.3 °C. IR (KBr) ν: 1661, 1606, 1514, 1455, 1332, 1276, 987, 775 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 8.02–8.01 (m, 2H), 7.71 (d, J = 15.5 Hz, 1H), 7.63–7.59 (m, 1H), 7.55–7.50 (m, 2H), 7.48–7.43 (m, 2H), 7.38–7.36 (m, 1H), 7.24–7.19 (m, 1H). ^{19}F NMR ($CDCl_3$, 470 MHz): δ = −135.68 to −137.25 (m, 1F), −137.25 to −137.34 (m, 1F). MS (EI) m/z: 244 (M^+, 100).

4.4. Synthesis of quinoline derivatives

4.4.1. General procedure

Fluorobenzaldehyde **1a–1g** (1 mmol), amine **2a–2c** (1 mmol), and phenylacetylene **3** (2 mmol) were mixed with montmorillonite doped with CuCl (0.3 mmol) and ground into a fine, homogeneous mixture; then the mixture was put in a 25-mL round bottomed ask and exposed to microwave irradiation at proper power using a microwave oven for an appropriate time. After completion of the reaction (as monitored by TLC), the reaction mixture was diluted with ethyl acetate, and the catalyst and montmorillonite clay were filtered out. After removal of the solvent under vacuum, the crude material was purified by silica gel column (using petroleum ether:ethyl acetate = 20:1 as elute) to afford pure product **6**.

4.4.2. 2-(2-Fluorophenyl)-6-nitro-4-phenyl-quinoline **6ac**

Offwhite solid, mp 258.3–259.1 °C. IR (KBr) ν: 3104, 1613, 1594, 1486, 1340, 1207, 1253, 759, 699 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 8.90 (d, J = 2.5 Hz, 1H), 8.51 (dd, J = 9, 2.5 Hz, 1H), 8.36 (d, J = 9 Hz, 1H), 8.20 (td, J = 8, 2 Hz, 1H), 8.02 (d, J = 2.5 Hz, 1H), 7.62–7.57 (m, 5H), 7.53–7.51 (m, 1H), 7.37 (t, J = 7.5 Hz, 1H), 7.22 (d, J = 8.5 Hz, 1H). ^{19}F NMR ($CDCl_3$, 470 MHz): δ = −116.02 to −116.06 (m, 1F). MS (EI) m/z: 344 (M^+). HRMS calcd. for $C_{21}H_{13}FN_2O_2$: 344.0961, Found 344.0962.

4.4.3. 2-(3-Fluorophenyl)-6-nitro-4-phenyl-quinoline **6bc**

Faint yellow solid, mp 209.7–210.1 °C. IR (KBr) ν: 3096, 3076, 1615, 1592, 1485, 1342, 1253, 883, 812 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 8.87 (d, J = 2.5 Hz, 1H), 8.51 (dd, J = 9, 2.5 Hz, 1H), 8.34 (d, J = 9 Hz, 1H), 8.01 (dd, J = 9, 2.5 Hz, 2H), 7.96 (s, 1H), 7.65–7.51 (m, 6H), 7.25–7.21 (m, 1H). ^{19}F NMR ($CDCl_3$, 470 MHz): δ = −112.04 to −112.09 (m, 1F). MS (EI) m/z: 344 (M^+). HRMS (EI) m/z calcd. for $C_{21}H_{13}FN_2O_2$: 344.0961; Found: 344.0958.

4.4.4. 2-(4-Fluorophenyl)-6-nitro-4-phenyl-quinoline **6cc**

Yellow solid, mp 226.4–227.1 °C. IR (KBr) ν: 3103, 3027, 1617, 1594, 1486, 1336, 1232, 836, 770 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 8.89 (d, J = 2.5 Hz, 1H), 8.50 (dd, J = 9, 2.5 Hz, 1H), 8.35 (d, J = 9 Hz, 1H), 8.27 (dd, J = 9, 5.5 Hz, 2H), 7.99 (d, J = 2.5 Hz, 1H), 7.67–7.56 (m, 6H), 7.13–7.10 (m, 1H). ^{19}F NMR ($CDCl_3$, 470 MHz): δ = −110.07 (s, 1F). MS (EI) m/z: 344 (M^+). HRMS (EI) m/z calcd. for $C_{21}H_{13}FN_2O_2$: 344.0961; Found: 344.0960.

4.4.5. 2-(2,4-Difluorophenyl)-6-nitro-4-phenyl-quinoline **6ec**

Offwhite solid, mp 232.3–233.1 °C. IR (KBr) ν: 3101, 1613, 1591, 1484, 1338, 1264, 846, 697 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 8.86 (d, J = 2.5 Hz, 1H), 8.50 (d, J = 9 Hz, 1H), 8.35 (d, J = 9 Hz, 1H), 8.27 (d, J = 9 Hz, 1H), 7.94 (s, 1H), 7.65–7.54 (m, 5H), 7.27–7.23 (m, 2H). ^{19}F NMR ($CDCl_3$, 470 MHz): δ = −105.53 to −105.60 (m, 1F); −108.72 to −108.78 (m, 1F). MS (EI) m/z: 362 (M^+). HRMS (EI) m/z calcd. for $C_{21}H_{12}F_2N_2O_2$: 362.0867; Found: 362.0865.

4.4.6. 2-(2,5-Difluorophenyl)-6-nitro-4-phenyl-quinoline **6fc**

Yellow solid, mp 232.5–233.2 °C. IR (KBr) ν: 3103, 3081, 1618, 1591, 1493, 1336, 1256, 816, 695 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 8.91 (d, J = 2.5 Hz, 1H), 8.53 (dd, J = 9.5, 2.5 Hz, 1H), 8.37 (d, J = 9.5 Hz, 1H), 8.05 (d, J = 6.5 Hz, 1H), 8.02–7.96 (m, 1H), 7.64–7.56 (m, 5H), 7.23–7.18 (m, 2H). ^{19}F NMR ($CDCl_3$, 470 MHz): δ = −117.72 (s, 1F); −121.60 (m, 1F). MS (EI) m/z: 362 (M^+). HRMS (EI) m/z calcd. for $C_{21}H_{12}F_2N_2O_2$: 362.0867; Found: 362.0868.

4.4.7. 2-(3-Fluorophenyl)-7-nitro-4-phenyl-quinoline **6bb**

Yellow solid, mp 209.9–210.7 °C. IR (KBr) ν: 3067, 1613, 1586, 1523, 1356, 1183, 828, 784, 703 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 8.49 (dd, J = 8.5, 1 Hz, 1H), 8.00–7.98 (m, 2H), 7.92 (s, 1H), 7.91

(d, J = 7.5 Hz, 1H), 7.81 (t, J = 8.5 Hz, 1H), 7.53–7.48(m, 4H), 7.42–7.41(m, 2H), 7.22 (t, J = 7.5 Hz, 1H). ^{19}F NMR ($CDCl_3$, 470 MHz): δ = −112.06 to −112.11(m, 1F). MS (EI) m/z: 344 (M^+). HRMS (EI) m/z calcd. for $C_{21}H_{13}FN_2O_2$: 344.0961; Found: 344.0965.

4.4.8. 2-(4-Fluorophenyl)-7-nitro-4-phenyl-quinoline ***6cb***

Offwhite solid, mp 226.1–227.1 °C. IR (KBr) ν: 3080, 1661, 1603, 1593, 1512, 1348, 1230, 839, 697 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 9.13 (d, J = 2.5 Hz, 1H), 8.27–8.22 (m, 2H), 8.06 (d, J = 9 Hz, 1H), 8.01 (d, J = 7 Hz, 1H), 7.95 (s, 1H), 7.61–7.59 (m, 3H), 7.56–7.55 (m, 1H), 7.25 (t, J = 3.5 Hz, 2H), 7.12 (t, J = 8.5 Hz, 1H). ^{19}F NMR ($CDCl_3$, 470 MHz): δ = −110.52 (s, 1F). MS (EI) m/z: 344 (M^+).

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