Does Nitroarylation of Phenylacetonitrile Proceed as a Phase-Transfer Catalyzed Process?†

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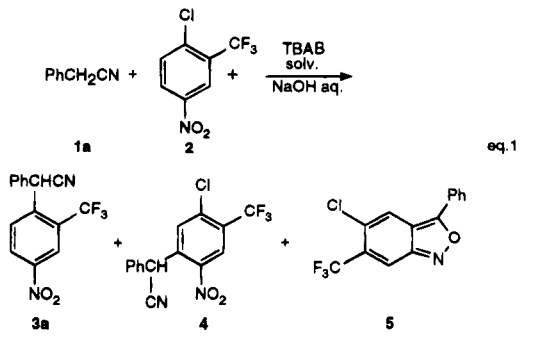
The phase-transfer catalyzed reaction of phenylacetonitrile with 4-chloro-3-(trifluoromethyl)-nitrobenzene produces 5-chloro-7-phenyl-4-(trifluoromethyl)benzisoxazole (**5**) not the nitroarylation product **3a** as was reported by Durantini et al. (Durantini, E. N.; Chiacchiera, S. M.; Silber, J. J. *J. Org. Chem.* **1993**, *58*, 7115). The catalytic nitroarylation does not occur because the product **3a** immediately forms a lipophilic carbanion which inhibits the catalytic process. The nitroarylation occurs under ion-pair extraction conditions when a stoichiometric amount of tetrabutylammonium bromide is used, whereas 2-phenylalkanenitriles are efficiently PTC nitroarylated. 4-Chloro-3-(trifluoromethyl)- and 2-chloro-5-(trifluoromethyl)nitrobenzenes enter vicarious nucleophilic substitution reactions with carbanions of chloromethyl *p*-tolyl sulfone. These results and formation of **5** show that carbanions add to these nitroarenes initially in positions occupied with hdyrogen.

Phase-transfer catalysis (PTC) is presently a well-established methodology in organic synthesis, its scope and limitations are well explored, and basic characteristic features and mechanistic principles are thoroughly studied and are reasonably well understood.[2,3] One of the most characteristic features of the PTC in application to reactions of carbanions is that reactions of carbanions of structure $Y-CH^{-}-Z$ with an electrophilic partner E^{+} giving YCHEZ should not produce a stronger CH acid than the starting YCH_2Z. In other words, the value of pK_a of the product cannot be lower than the pK_a of the substrate; otherwise the product is deprotonated immediately upon its formation and the produced lipophilic carbanion is associated with the catalyst cation in the organic phase, hence the catalytic process is arrested.[3] We have given an example of such a situation as early as in 1969 showing that, contrary to the two-phase alkylation of phenylacetonitrile, $PhCH_2CN$ (**1a**), which carried out in the presence of concentrated aqueous NaOH and the catalyst triethylbenzylammonium chloride, or other tetraalkyl ammonium salts, proceeds efficiently with a variety of alkyl halides, its nitroarylation with e.g. *p*-chloronitrobenzene does not proceed in the catalytic system.[4] The reason for this is the much higher acidity of the product (*p*-nitrophenyl)phenylacetonitrile than the starting phenylacetonitrile, thus the product is deprotonated as soon as it is formed and the corresponding anion forms with the catalyst cation a lipophilic ion pair which stays in the organic phase. On the other hand, α-phenylalkylacetonitriles and diphenylacetonitrile react readily with *p*- or *o*-nitrohaloarenes in the phase-transfer catalytic system because the nitroarylation products are not CH acids anymore. This rule was subsequently confirmed with other observations and appears unchallenged.

It was therefore a big surprise for us to find recently in this journal a paper in which the PTC nitroarylation of phenylacetonitrile (**1a**) with 4-chloro-3-(trifluoromethyl)nitrobenzene (**2**) was reported to proceed in high yield, and the detailed kinetic studies of this reaction fully confirmed the interfacial mechanism of the deprotonation of phenylacetonitrile in the PTC system.[5]

Since this observation violated the well-established rule and, if generalized, would promote a new, better understanding of the mechanistic features of the PTC, we decided to study this problem in detail. Our current interest in the reactions of carbanions with nitroarenes was an additional motivation for these studies.[6,7] First of all, we have attempted to repeat the preparative experiments described in the paper; however, in our hands the reaction of **1a** and **2** carried out without a solvent or in toluene in the presence of concd aqueous NaOH and tetrabutylammonium chloride or bromide (TBAC and TBAB) in spite of many repetitions invariably failed to give results reported in the paper. The expected product of S_NAr of the halogen (4-nitro-2-(trifluoromethyl)phenyl)phenylacetonitrile (**3a**)) was the minor product accompanied with some amounts of (3-chloro-6-nitro-4-(trifluoromethyl)phenyl)phenylacetonitrile (**4**), the product of oxidative nucleophilic substitution of hydrogen in **2**; the main product in these experiments was identified as 5-chloro-7-phenyl-4-(trifluoromethyl)benzisoxazole (**5**) (eq 1). Results of these experiments are given in Table 1.



† Dedicated to Professor Glen A. Russell on the occasion of his 70th birthday.

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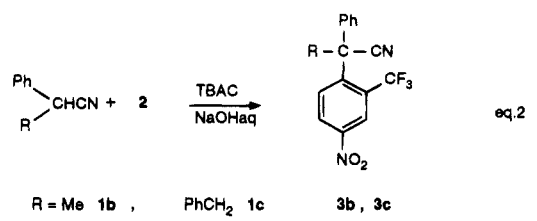
Table 1. Reactions of 1a with 2 (eq 1) under Various Conditions[a]

	solvent	TBAB, mol %	yield of products, % 3a	4	5
1	none	6	8	10	28
2	none	none	7	5	25
3	PhMe	6	9	5	44
4	PhMe	none	<1	<1	<1
5	MeCN	6	50	<1	<1
6	MeCN	none	43	2	<1
7	none	100	>90	<1	<1
8	PhMe	100	77	<1	<1

[a] For conditions, see Experimental Section.

Product **5** is formed *via* addition of the carbanion of **1a** at position 6 of **2**, followed by the transformation of the σ^H adduct along the way described by Davis in 1960;[8] product **4** is formed *via* the same σ^H adduct which is oxidized, apparently with the atmospheric oxygen. One should stress that the reaction carried out under similar conditions, in acetonitrile or without a solvent, gives almost the same results regardless of the presence of the catalyst. Slightly higher yields of **4** and **3a** when the catalyst was present are apparently due to rapid nitroarylation of **1a** *via* ion-pair extraction till conversion equal to the amount of the catalyst is attained. These results indicate that the catalyst does not exert meaningful action in this process when it is carried out without toluene solvent. We have observed, however, a peculiar effect of the catalyst in the reaction carried out in toluene (entry 3). The major catalytic process was the formation of isoxazole **5**; without the catalyst there was practically no reaction at all. It should be stressed that the total conversion in the catalytic process in toluene was substantially higher than without the solvent, whereas it is well known that PTC reactions are usually deccelerated when carried out in nonpolar solvents.[2,3] We suppose that formation of **3a** and **4** in experiments without solvents inhibits the catalytic process because the lipophilic carbanions of the products are associated with the catalyst. It appears that in toluene the initially formed σ^H adducts in position 6 are rapidly converted to **5** with liberation of CN^- anions which do not affect the catalytic process. In the course of the reaction, **3a** and **4** are also produced so the catalytic process is finally arrested. On the other hand, when TBAC was used in a stoichiometric amount, the nitroarylation proceeded smoothly giving expected **3a** in high yield even when carried out in toluene. Thus, once again the well-established rule presented at the beginning of this paper and formulated in 1969 was proven to be correct. As we have expected, 2-phenylpropionitrile (**1b**) and 2,3-diphenylpropionitrile (**1c**) in the presence of concd aqueous NaOH and catalytic amounts of TBAB (4 mol %) reacted with **2** smoothly, giving the product of S_NAr of the halogen **3b** and **3c** (eq 2).



In these instances the catalytic process proceeds efficiently because the products are not CH acids anymore. Moreover, analysis of the results obtained in our laboratory according to the procedure described in the paper[5] indicates that the addition of the carbanion of **1a** occurs initially at position 6, occupied by hydrogen, not at position 4, occupied by the halogen. This observation is in accord with the numerous observations and a general rule formulated in our preceding papers concerning the relation of rates of addition of nucleophiles to halonitroarenes, namely that the nucleophilic addition to halonitroarenes always proceeds faster in positions occupied by hydrogen than in those occupied by a halogen.[6,7,9] From the literature data[8] and our early observations,[10] it appears that transformation of the σ^H adduct in position 6 to form **5** proceeds *via* protonation–elimination of water and needs a protic medium. The standard conditions for synthesis of such isoxazoles from arylacetonitriles and *p*-substituted nitroarenes consists of using NaOH or KOH solutions in aqueous methanol.[8] Indeed, when a solution of **1a** and **2** in methanol was treated with aqueous KOH, the only isolated product was benzisoxazole **5** in a yield of 77%. Thus one can speculate that the formation of **5** in the two-phase system without toluene solvent takes place at the interface, not in the bulk of the organic phase. It is therefore surprising that **5** is also the major product of the reaction carried out in toluene, and its formation is efficiently catalyzed by TBAC. Since a similar reaction carried out according to the ion-pair extraction methodology using an equimolar amount of tetrabutylammonium hydrogen sulfate gave exclusively **3a**, one can speculate that **1a**, which is used in a great excess in the catalytic processes, effects the protonation of the σ^H adduct during its conversion to **5**. Formation of **4** *via* oxidation of the σ^H adduct was unprecedented for reactions of arylacetonitriles with nitroarenes, although it is well known for other carbanions,[9,11] being in some cases the dominant process.[11b] The formation of **4** should be promoted by the presence of oxygen, factors disfavoring equilibration of the addition process and perhaps also by an excess of base, because in a preceding paper from our laboratory we have shown that the oxidation of σ^H adducts occurs apparently *via* a dianion produced by their deprotonation.[11b] Following this reasoning, the conditions in which **1a** and **2** gave **4** as the major product were found (see Experimental Section).

In order to learn more about behavior of chloro(trifluoromethyl)nitrobenzenes in the reactions with carbanions, particularly concerning feasibility of the PTC nitroarylation and initial addition of carbanions at positions occupied with hydrogen, we have also studied the similar reactions of phenylacetonitrile and its derivatives **1a–c** with 2-chloro-5-(trifluoromethyl)nitrobenzene (**6**), an isomer of **2** having Cl *ortho* to the nitro group, as well as the vicarious nucleophilic substitution (VNS) of hydrogen in both of these nitroarenes **2** and **6**.

In the reaction of phenylacetonitrile and its derivatives with **6**, the results were similar to those obtained in the analogous reactions of **2**. Thus the PTC nitroarylation of **1a** with **6** does not occur for the reasons discussed at the beginning of this paper, whereas when TBAC was

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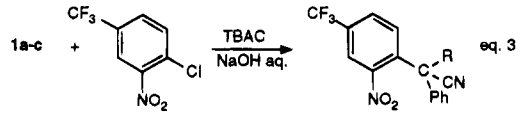
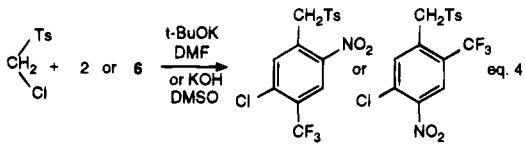
used in an equimolar amount, **7a**, the expected product of nitroarylation of **1a** with **6**, was obtained in good yield. On the other hand, 2-phenyl- and 2,3-diphenylpropionitriles **1b** and **1c** are efficiently PTC nitroarylated with **6** because the products **7b** and **7c** do not have CH acid character so the catalyst can operate efficiently (eq 3).



In previous papers we have presented a new reaction of nucelophilic substitution of hydrogen in nitroarenes with α-halocarbanions,[6] alkyl hydroperoxide anions,[12] and sulfenamides.[13] The process named vicarious nucleophilic substitution of hydrogen (VNS) is of general character; moreover as a rule VNS, of hydrogen occurs faster than typical S_NAr of halogen located in similarly activated positions of nitroarenes. Even in the case of 2,4-dinitrofluorobenzene, the Sanger reagent, in which substitution of fluorine occurs very rapidly, the VNS of hydrogen with α-halocarbanions is still the dominant process.[14] We expected therefore that in chloro(trifluoromethyl)nitrobenzenes **2** and **6** VNS of hydrogen with α-halocarbanions should proceed readily. Indeed when these nitroarenes were treated with chloromethyl *p*-tolyl sulfone in the presence of strong bases, the expected VNS products **8** and **9** were obtained in good yields (eq 4). Among two typical conditions for the VNS reaction (t-BuOK/DMF and KOH/DMSO), for the reaction of **2** and **6** with the chlorosulfone the latter gave better results. Thus similarly to many other halonitroarenes, nucleophilic replacement of hydrogen in **2** and **6** occurs faster than that for the halogen.



Our results once again confirm the general rule of the PTC reactions of carbanions, according to which the catalytic process cannot operate for such reactions in which the CH acids stronger than starting materials are produced. The results published in ref 5 unfortunately appear erroneous.

Analyzing reasons for the reported erroneous results, we can suppose that the authors have not separated benzisoxaloze **5** and S_NAr product **3a** because, although they claim a 97% yield (which we could not reproduce) of the crystalline product **3a** and gave its spectral characteristics, no melting point is reported. Moreover, the reported spectral characteristics appear to be a superposition of those for **3a** and **5**. The ^1H NMR data correspond well with those of our product **3a**, but the reported UV $\lambda_{max} = 360$ nm (in CH_2Cl_2) is that of isoxazole **5**, λ_{max} 360 nm, log $\epsilon = 4.02$ (in CH_2Cl_2), whereas the UV–vis spectrum of the anionic form of **3a** reported λ_{max} = 560 nm (CH_2Cl_2) corresponding properly with our data for λ_{max} 546 nm (MeOH). The data of Figure 1 of ref 5 in which the rate of the S_NAr process is followed by UV based on the absorption band at 360 mm shows in fact formation of the benzisoxazole **5**.

This confusion is apparently caused by similar behavior of **3a** and **5** in chromatographic analysis and separation. GLC analysis using a capillary column (Experimental Section) shows negligible difference in R_f of **3a** and **5**; on a regular column there is no separation.

Thus although we can agree with the final conclusion of the paper[5] concerning interfacial deprotonation of **1a** in the two-phase system which we postulated as early as in 1975,[3] the evidences presented in the paper appear to be invalid.

Experimental Section

^1H and ^{13}C NMR spectra were recorded on a Varian Gemini (200 MHz) spectrometer, mass spectra on a AMD-604 Interctra spectrometer, IR spectra on an Acculab 1 Beckman spectrometer, and UV–vis spectra on an Array ASD-87 spectrophotometer. GLC analysis was carried out on a Shimadzu GC-14A instrument using a fused silica capillary column (0.25 mm × 25 m, SE-52-DF-0.25 permabond). All melting points are not corrected. All chemicals were reagent grade; solvents were dried and distilled before use. 4-Chloro-3-(trifluoromethyl)-nitrobenzene (**2**)[15] and 2-chloro-5-(trifluoromethyl)nitrobenzene (**6**)[16] were prepared *via* nitration of 2- and 4-(trifluoromethyl)-chlorobenzenes correspondingly.

2: yield 90%; bp 98–101 °C (9 mm); mp 21.5–22.5 °C (lit.[15] bp 92–93 °C (10 mm)); ^1H NMR ($CDCl_3$) δ 7.77 (d, J = 8.8 Hz, 1H), 8.39 (dd, J = 2.7, 8.8 Hz, 1H), 8.58 (d, J = 2.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 121.6 (q, J = 272 Hz), 123.1 (q, J = 5.6 Hz), 127.5, 129.7 (q, J = 33 Hz), 132.8, 139.3, 146.1.

6: yield 73%; bp 94–96 °C (10 mm) (lit.[16] bp 92–93 °C (10 mm)); ^1H NMR ($CDCl_3$) δ 7.73 (d, J = 8.5 Hz, 1H), 7.80 (dd, J = 1.8, 8.4 Hz, 1H), 8.16 (d, J = 1.9 Hz, 1H).

2-Phenylpropionitrile (**1b**) and 2,3-diphenylpropionitrile (**1c**) were prepared *via* PTC alkylation of phenylacetonitrile.[17]

General Procedure for the Reaction of 1a and 2 (Table 1). To a vigorously stirred mixture of **1a** (260 mg, 2.2 mmol), **2** (225 mg, 1 mmol), and when needed tetrabutylammonium bromide (20 mg, 0.06 mmol) and solvent (see Table 1) was added 50% aqueous NaOH (2 mL) in one portion. The mixture immediately turns deep blue, and after a few minutes, an exothermic reaction takes place. The temperature of the reaction mixture was kept at 40 °C and should be controlled initially by cooling. The reaction was carried out for 3 h; the mixture was diluted with water, acidified with 10% HCl, and extracted with CH_2Cl_2 (three times).

The extract was dried (Na_2SO_4) and chromatographed on silica gel using hexane/CH_2Cl_2 eluent as in ref 5, but a better system is hexane/ether = 50/1 with the concentration gradient. After **5** was eluted, a mixture of all other products was collected, and yields of **3a** and **4** were estimated on the basis of ^1H NMR spectra and GLC. The both methods gave similar results. In TLC the R_fs of the components of the mixture (hexane/ether 6:1) are as follows: R_f(**2**) = 0.60, R_f(**5**) = 0.62, R_f(**3a**) = 0.28, R_f(**4**) = 0.32.

5-Chloro-7-phenyl-4-(trifluoromethyl)benzisoxazole (5). To a vigorously stirred mixture of **2** (225 mg, 1 mmol) and **1a** (129 mg, 1.1 mmol) in aqueous MeOH (50% v/v, 2 mL) was added a solution of KOH (840 mg, 15 mmol) in aqueous MeOH (50% v/v, 2 mL) in one portion. The reaction was carried out at room temperature for 6 h and quenched with water (200 mL); the product was extracted with CH_2Cl_2 (3 × 30 mL) and dried with Na_2SO_4, the solvent was evaporated, and the residue was purified by passing its hexane solution through a short layer of silica gel. Concentration of this solution to 3

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mL and cooling to 0 °C for 2 h gave pure **5**: 230 mg, 77% mp 130.0–131.0 °C (hexane); ^{1}H NMR ($CDCl_3$) δ 7.55–7.65 (m, 3H), 7.95–8.05 (m, 2H), 8.02 (m, 1H), 8.12 (dq, J = 0.8, 1.1 Hz, 1H); ^{13}C NMR δ 114.5, 117.6 (q, J = 6.6 Hz), 122.0 (q, J = 274 Hz), 123.0, 125.7, 126.6, 127.2, 129.5, 131.1 (q, J = 30 Hz), 131.2, 155.0, 165.6; IR (KBr) 3112, 3059, 1551, 1499, 1461, 1336, 1270, 1161, 1140, 1081, 1001, 994, 868, 806, 773, 740, 727, 685, 648, 490 cm^{-1}; UV–vis λ_{max} (log ε) (CH_2Cl_2) 360 nm (4.02); MS *m/z* (rel intensity) 299 (^{37}Cl M$^+$, 41), 297 (^{35}Cl M$^+$, 100), 262 (77), 234 (53), 77 (43), 51 (14); HRMS calcd for $C_{14}H_7ClF_3NO$ 297.0168, found 297.0167. Anal. Calcd for $C_{14}H_7ClF_3NO$: C, 56.57; H, 2.36; N, 4.71; Cl, 11.95. Found: C, 56.71; H, 1.98; N, 4.84; Cl, 11.90.

4-Nitro-2-(trifluoromethyl)phenylacetonitrile (3a). A mixture of **1a** (300 mg, 2.5 mmol), tetrabutylammonium hydrogen sulfate (850 mg, 2.5 mmol), toluene (5 mL), and 50% aqueous NaOH (1 mL) was deoxygenated via a vacuum–argon cycle repeated twice. To this mixture was added a deoxygenated solution of **2** (450 mg, 2.5 mmol) in toluene (3 mL), and the whole was stirred for 5 min at 40 °C. The mixture was diluted with water, acidified with 10% hydrochloric acid, and extracted with methylene chloride. The organic solution was dried, the solvent evaporated, and the residue chromatographed (silica gel, hexane eluent) to give **3a**, 615 mg, 77%, mp 78 °C from hexane: ^{1}H NMR ($CDCl_3$) δ 5.69 (s, 1H), 7.3–7.5 (m, 5H), 7.75 (d, J = 8.6 Hz, 1H), 8.41 (dd, J = 2.4, 8.6 Hz, 1H), 8.61 (d, J = 2.4 Hz, 1H); ^{1}H NMR (DMSO-d_6) δ 6.15 (s,-1H), 7.3–7.5 (m,5H), 8.00 (d, J = 8.6 Hz, 1H), 8.52 (d, J = 2.5 Hz, 1H), 8.60 (dd, J = 2.4, 8.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 38.00 (q, J = 2.4 Hz), 117.5 (C≡N), 121.9 (q, J = 5.9 Hz), 122.5 (q, J = 275 Hz), 127.4, 128.9, 129.4, 129.6 (q, J = 32.3 Hz), 132.8, 133.4, 141.1, 147.3 (C–NO_2); IR (KBr) 2250 (CN), 1538, 1357 (NO_2) cm^{-1}; UV–vis λ_{max} 257 nm (neutral form, CH_2Cl_2), 255 nm (neutral form, MeOH), 546 nm (anionic form, MeOH); HRMS calcd for $C_{15}H_9F_3N_2O_2$ 306.0616, found 306.0663. Anal. Calcd for $C_{15}H_9F_3N_2O_2$: C, 58.82; H, 2.94; N, 9.15. Found: C, 58.78; H, 2.71; N, 9.10.

(2-Nitro-4-(trifluoromethyl)phenyl)phenylacetonitrile (7a). The nitrile **7a** was prepared by the same method as **3a**. Chromatography on silica gel (eluent hexane/CH_2Cl_2, concentration gradient) gave pure (TLC, GC) **7a** as a colorless oil: yield 190 mg, 62%; ^{1}H NMR ($CDCl_3$) δ 6.20 (s, 1H), 7.25–7.40 (m, 5H), 7.90 (d, J = 8.3 Hz, 1H), 7.96 (dd, J = 1.7, 8.3 Hz, 1H), 8.32 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 38.2, 117.8 (C≡N), 122.3 (q, J = 273 Hz), 123.1 (q, J = 3.8 Hz), 127.8, 129.0 (q, J = 29.0 Hz), 129.1, 129.5, 130.5 (q, J = 3.4 Hz), 132.0, 131.9, 133.1, 134.3 (C–NO_2); IR (film) 2250 (CN), 1544, 1327 (NO_2) cm^{-1}; UV–vis λ_{max} 244 nm (MeOH, neutral form), 611 nm (MeOH, anionic form); MS *m/z* (rel intensity) 306 (M$^+$, 4), 289 (100), 272 (79), 263 (66), 235 (51), 202 (15), 190 (53), 166 (18), 149(19), 105 (22), 77 (33); HRMS calcd for $C_{15}H_9F_3N_2O_2$ 306.0616, found 306.0615. Anal. Calcd for $C_{15}H_9F_3N_2O_2$: C, 58.82; H, 2.94; N, 9.15. Found: C, 58.95; H, 2.70; N, 9.04.

(3-Chloro-6-nitro-4-(trifluoromethyl)phenyl)phenylacetonitrile (4). To the vigorously stirred solution of 50% aqueous NaOH (1 mL) at 15 °C with intensive bubling of O_2 was added a mixture of **1a** (117 mg, 1 mmol), **2** (225 mg, 1 mmol), and TBAC (14 mg, 0.05 mmol) dropwise during 1 h. The reaction mixture was acidified with 10% HCl, the products were extracted with CH_2Cl_2 (3 × 20 mL) and dried (Na_2SO_4), and the solvent was evaporated. The residue was chromatographed on silica gel (hexane/CH_2Cl_2 gradient). From the mixture of unresolved products (see general procedure), pure (TLC) **4** was obtained as a crystalline solid after being kept for 2 days at room temperature: yield 100 mg, 30%, mp 102–103 °C (hexane); ^{1}H NMR ($CDCl_3$) δ 6.22 (s, 1H), 7.28–7.46 (m, 5H), 7.88 (s, 1H), 8.42 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 38.1, 117.4 (CN), 121.3 (q, J = 274 Hz), 125.5 (q, J = 5.5 Hz), 127.9, 129.4, 129.8, 130.2 (q, J = 33.0 Hz), 132.6, 134.0, 135.7, 138.8, 145.3 (C–NO_2); IR (KBr) 2249 (C≡N), 1536, 1351 (NO_2) cm^{-1}; UV–vis λ_{max} neutral form 264 nm (CH_2Cl_2), 256 nm (MeOH), anionic form 621 nm (CH_2Cl_2), 606 nm (MeOH); MS *m/z* (rel intensity) 342 (^{37}Cl M$^+$, 1.1) 340 (^{35}Cl M$^+$, 3.2), 325 (^{37}Cl (M – F)$^+$, 33), 323 (^{35}Cl (M – F)$^+$, 100), 308 (^{37}Cl, 29), 306 (^{35}Cl, 78), 297 (32), 288 (18), 269 (21), 234 (31); MS LSIMS 363 ((M + Na)$^+$). Anal. Calcd for $C_{15}H_8ClF_3N_2O_2$: C, 52.86; H, 2.32; N, 8.22; Cl, 10.43. Found: C, 52.62; H, 2.52; N, 8.49; Cl, 10.14.

General Procedure for Nitroarylation of 1b and 1c with 2 and 6. A solution of equimolar amounts of the nitriles and nitroarenes (1 mmol of each) and TBAC (14 mg, 0.05 mmol) in toluene (5 mL) and 50% aqueous NaOH (1.5 mL) was vigorously stirred at 30 °C for 4 h (**1b**) or overnight (**1c**). Then the mixture was diluted with water (100 mL) and acidified with 10% HCl (10 mL), the product was extracted with CH_2Cl_2 (3 × 30 mL), washed with water (20 mL), and dried with Na_2SO_4, and the solvents were evaporated. The solid products were recrystallized whereas **7b** was purified by column chromatography on silica gel.

2-(4-Nitro-2-(trifluoromethy)phenyl)-2-phenylpropionitrile (3b): yield 204 mg, 64%, mp 131–131.5 °C (hexane/CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 2.24 (s, 3H), 7.1–7.4 (m, 5H), 8.07 (d, J = 8.8 Hz, 1H), 8.50 (dd, J = 2.5, 8.8 Hz, 1H), 8.62 (d, J = 2.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 31.1, 45.6, 120.9 (C≡N), 122.3 (q, J = 275 Hz), 124.5 (q, J = 6.3 Hz), 125.6, 126.5, 128.2, 128.9, 130.8 (q, J = 33.7 Hz), 130.8, 140.3, 144.1, 147.5 (C–NO_2); IR (KBr) 2244 (C≡N), 1527, 1360 (NO_2) cm^{-1}; MS *m/z* (rel intensity) 320 (M$^+$, 92), 305 (100), 275 (14), 259 (41), 190 (56), 130 (40), 103 (18), 77 (11); HRMS calcd for $C_{16}H_{11}F_3N_2O_2$ 320.0773, found 320.0772. Anal. Calcd for $C_{16}H_{11}F_3N_2O_2$: C, 60.00; H, 3.44; N, 8.75. Found: C, 59.88; H, 3.12; N, 8.80.

2-(2-Nitro-4-(trifluoromethyl)phenyl)-2-phenylpropionitrile (7b). Flash chromatography on SiO_2 (eluent hexane) gave **7b** (260 mg, 82%) as a colorless oil (>96% GLC) which crystallized after prolonged standing at room temperature: mp 64.5–65.5 °C (hexane); ^{1}H NMR ($CDCl_3$) δ 2.26 (s, 3H), 7.2–7.4 (m, 5H), 7.95 (dd, J = 1.3, 9.5 Hz, 1H), 7.97 (d, 1H), 8.05 (d, J = 8.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 29.0, 45.1, 120.7 (CN), 122.4 (q, J = 273 Hz), 123.0 (q, J = 3.7 Hz), 126.1, 128.1 (q, J = 6.0 Hz), 128.6, 129.0, 130.5, 132.4 (q, J = 36.6 Hz), 137.3, 138.1, 149.7 (C–NO_2); IR (KBr) 2242 (CN), 1541, 1329 (NO_2) cm^{-1}; MS *m/z* (rel intensity) 320 (M$^+$, 75), 305 (20), 302 (22), 275 (32), 260 (35), 259 (44), 227 (83), 199 (62), 190 (100), 178 (22), 172 (31), 130 (24), 103 (21), 94 (47), 77 (25); HRMS calcd for $C_{16}H_{11}F_3N_2O_2$ 320.0773, found 320.0788. Anal. Calcd for $C_{16}H_{11}F_3N_2O_2$: C, 60.00; H, 3.44; N, 8.75. Found: C, 60.13; H, 3.17; N, 8.75.

2-(4-Nitro-2-(trifluoromethyl)phenyl)-2,3-diphenylpropionitrile (3c): yield 325 mg, 41%, mp 163–166 °C (hexane/CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 3.73 (d, J = 12.8 Hz, 1H), 3.91 (d, J = 12.6 Hz, 1H), 6.79–6.85 (m, 2H), 7.0–7.4 (m, 8H), 8.01 (d, J = 9.0 Hz, 1H), 8.36 (dd, J = 2.5, 8.9 Hz, 1H), 8.61 (d, J = 2.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 45.9, 52.2, 120.1 (CN), 122.2 (q, J = 276 Hz), 124.7 (q, J = 6.6 Hz), 126.0, 127.3, 127.8, 128.0, 128.6, 130.6, 130.8 (q, J = 43 Hz), 131.7, 133.0, 133.8, 137.7, 144.0, 147.3 (C–NO_2); IR (KBr) 2246 (CN), 1536, 1357 (NO_2) cm^{-1}; MS *m/z* (rel intensity) 396 (M$^+$, 4.7), 275 (5.3), 206 (2.4), 190 (3.0), 91 (100), 65 (8.3); HRMS calcd for $C_{22}H_{15}F_3N_2O_2$ 396.1086, found 396.1085. Anal. Calcd for $C_{22}H_{15}F_3N_2O_2$: C, 66.67; H, 3.79; N, 7.07. Found: C, 67.15; H, 3.27; N, 6.88.

2-(2-Nitro-4-(trifluoromethyl)phenyl)-2,3-diphenylpropionitrile (7c): mp 179–180 °C (hexane); ^{1}H NMR ($CDCl_3$) δ 3.76 (d, J = 12.7 Hz, 1H), 4.21 (d, J = 12.8 Hz, 1H), 6.94–7.05 (m, 2H), 7.1–7.4 (m, 8H), 7.62 (d, J = 9.0 Hz, 1H), 7.67 (dd, J = 1.8, 8.5 Hz, 1H), 7.83 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 43.7, 51.9, 120.4 (CN), 122.4 (q, J = 273 Hz), 122.5 (q, J = 3.7 Hz), 127.5, 127.9 (q, J = 5.6 Hz), 127.8, 128.9, 128.9, 129.0, 130.5, 132.1 (q, J = 35.0 Hz), 132.1, 133.5, 135.7, 136.0, 150.0 (C–NO_2); IR (KBr) 2240 (CN), 1549, 1327 (NO_2) cm^{-1}; MS *m/z* (rel intensity) 396 (M$^+$, 5.6), 279 (5.6), 190 (2.8), 91 (100), 65 (6.0); HRMS calcd for $C_{22}H_{15}F_3N_2O_2$ 396.1086, found 396.1085. Anal. Calcd for $C_{22}H_{15}F_3N_2O_2$: C, 66.67; H, 3.79; N, 7.07. Found: C, 66.52; H, 3.57; N, 6.98.

5-Chloro-2-nitro-4-(trifluoromethyl)benzyl *p*-Tolyl Sulfone (8). A solution of **2** (451 mg, 2 mmol) and chloromethyl *p*-tolyl sulfone (409 mg, 2 mmol) in DMF (5 mL) was added dropwise during 10 min to a solution of t-BuOK (560 mg, 5 mmol) in DMF (10 mL) at −20 °C. The reaction was carried out at −20 °C for 2 h. Then the mixture was acidified with 10% HCl (3 mL) and diluted with water (200 mL), and the product was extracted with CH_2Cl_2 (5 × 20 mL). The extract

was washed with water and dried with Na_2SO_4, and the solvent was evaporated. The residue was recrystallized from hexane/CH_2Cl_2 to give **8**: 460 mg, 58%, mp 167–168 °C; ^{1}H NMR ($CDCl_3$) δ 2.47 (s, 3H), 4.92 (s, 2H), 7.34 (d, J = 8.1 Hz, 2H), 7.62 (d, J = 8.3 Hz, 2H), 7.63 (s, 1H), 8.33 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 21.6, 57.9, 120.2 (C≡N), 121.2 (q, J = 274 Hz), 124.9 (q, J = 5.4 Hz), 128.2, 129.9 (q, J = 33.0 Hz), 130.0, 134.6, 136.9, 137.4, 145.9, 146.9; IR (KBr) 1533 (NO_2), 1345 (SO_2), 1313 (NO_2), 1145 (SO_2) cm^{-1}; HRMS calcd for $C_{15}H_{11}ClF_3NO_4S$ 393.0049, found 393.0051. Anal. Calcd for $C_{15}H_{11}ClF_3NO_4S$: C, 45.80; H, 2.80; N, 3.56. Found: C, 45.86; H, 2.89; N, 3.61.

5-Chloro-4-nitro-2-(trifluoromethyl)benzyl *p*-Tolyl Sulfone (9). To a stirred suspension of powdered KOH (1.12 g, 20 mmol) in DMSO (5 mL) was added a solution of **6** (451 mg, 2 mmol) and chloromethyl *p*-tolyl sulfone (409 mg, 2 mmol) in DMSO (2 mL) during 2 min at 20 °C. The reaction was carried out at 20 °C for 2 h; the mixture was poured into water (100 mL) and acidified with 10% HCl (3 mL). The product was extracted with CH_2Cl_2 (5 × 20 mL), the extract was washed with water (3 × 50 mL) and dried with Na_2SO_4, the solvent was evaporated, and the residue was recrystallized from hexane to yield **9**: 555 mg, 70%, mp 122–123 °C; ^{1}H NMR ($CDCl_3$) δ 2.46 (s, 3H), 4.52 (s, 2H), 7.35 (d, J = 8.0 Hz, 2H), 7.65 (d, J = 8.3 Hz, 2H), 7.98 (s, 1H), 8.18 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 21.6, 57.8, 121.9 (q, J = 275 Hz), 124.0 (q, J = 5.7 Hz), 128.3, 129.5 (q, J = 30.8 Hz), 130.0, 131.0, 132.4, 135.0, 136.6, 145.8, 147.0 (C–NO_2); IR (KBr) 1544 (NO_2), 1356 (SO_2), 1322 (NO_2), 1149 (SO_2) cm^{-1}; MS *m/z* (rel intensity) 395 (^{37}Cl M^+, 1.6), 393 (^{35}Cl M^+, 4.7), 290 (0.6), 223 (1.2), 208 (3.5), 192 (3.0), 172 (3.8), 155 (96), 91 (100), 65 (15); HRMS calcd for $C_{15}H_{11}ClF_3NO_4S$ 393.0049, found 393.0051. Anal. Calcd for $C_{15}H_{11}ClF_3NO_4S$: C, 45.80; H, 2.80; N, 3.56. Found: C, 45.74; H, 2.49; N, 3.38.

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