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Mechanochemical Aminochlorination of Electron-Deficient Olefins with Chloramine-T Promoted by (Diacetoxyiodo)benzene

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Abstract: A direct and convenient procedure for the solvent-free mechanochemical aminochlorination of electron-deficient olefins promoted by (diacetoxyiodo)benzene [$PhI(OAc)_2$] was described using commercially available and cheap chloramine-T as a nitrogen and chlorine source. The vicinal chloramine derivatives were obtained in high regio- and stereoselectivity with good yields. $PhI(OAc)_2$ was superior to metal salts for the aminochlorination of electron-deficient olefins.

Keywords: aminochlorination; chloramine-T; electron-deficient compounds; hypervalent compounds; mechanochemistry; solid-state reactions

Introduction

The aminohalogenation of olefins has been recognized as a very important transformation in organic chemistry because the resulting vicinal haloamines are very versatile intermediates for the synthesis of numerous pharmacologically active compounds.[1] Early efforts on the preparation of vicinal haloamine derivatives by the addition of *N*-halo and *N,N*-dihalo compounds to olefins under non-catalytic conditions confronted significant limitations such as narrow scope of substrates, poor yield and selectivity.[2] The highly regioselective and stereoselective aminohalogenation of olefins is still a challenging task for organic chemists and continues to be an active research area. Recently, Li's group[3] and others[4] have successfully established the aminohalogenation of various olefins under different catalytic systems. Particularly, Li's group has developed the elegant methodology on the transition metal-catalyzed aminohalogenation of cinnamates[3a–e] and α,β-unsaturated ketones[3f] by using *N,N*-dichloro-*p*-toluenesulfonamide[3a,c–f] and *N,N*-dichloro-*o*-nitrobenzenesulfonamide/sodium *o*-nitrobenzenesulfonamide combination[3b] as the nitrogen as well as chlorine sources. On the other hand, *N*-chloro-*N*-sodio-*p*-toluenesulfonamide, known as chloramine-T, is a cheap, commercially available, and highly reactive reagent.[5] Over the past a few years, chloramine-T has been extensively utilized as a nitrene-transfer agent to aziridinate olefins.[6] In sharp contrast, only a few examples for chloramine-T as an aminohalogenation agent were reported, and these protocols suffered from low yields and utilization of heavy metal catalysts.[7]

N-Chloro-*N*-sodio-*o*-nitrobenzenesulfonamide, a chloramine-T analogue, was used to aminochlorinate cinnamic esters, *trans*-stilbene, and styrene, again requiring a transition metal catalyst.[8] Very recently, Minakata, Komatsu, and co-workers reported the unique CO_2-induced vicinal aminochlorination of olefins, even though the role of the pressurized CO_2 remains to be clarified.[9] In spite of the fact that the resulting vicinal haloaminated carbonyl compounds are synthetically important intermediates, which can be converted to numerous useful organic molecules by replacing the halo atom with a series of nucleophiles, the aminohalogenation of enones with chloramine-T has not been realized until now.

Hypervalent iodine compounds have been used for various organic reactions such as oxidations, carbon-carbon, carbon-heteroatom, and heteroatom-heteroatom bond formations, oxidative fragmentations and rearrangements, etc.[10] RNH_2 and (diacetoxyiodo)-benzene [$PhI(OAc)_2$] have been employed directly as a nitrogen source in intramolecular C=C bond additions catalyzed by rhodium(II,II) dimers.[11] The metal catalyst-free intermolecular aziridination of a series of alkenes with *N*-substituted hydrazines mediated by $PhI(OAc)_2$ has also been developed.[12] However, the combination of $PhI(OAc)_2$ and chloramine-T as a nitrogen source to react with electron-deficient olefins has not been reported.

Solvent-free organic reactions have drawn the attention of the chemical community for many years

due to the public's increasing concern about environmentally benign processes, low costs, simplicity in process and handling, and even higher selectivity.[13] One of our contributions to solvent-free organic reactions is focused on mechanochemical reactions.[14] In continuation of our interest in solvent-free mechanochemical reactions, herein we report the successful application of the ball-milling technique to the highly regio- and stereoselective aminohalogenation of chalcones, cinnamate and cinnamide with chloramine-T promoted by $PhI(OAc)_2$.

Results and Discussion

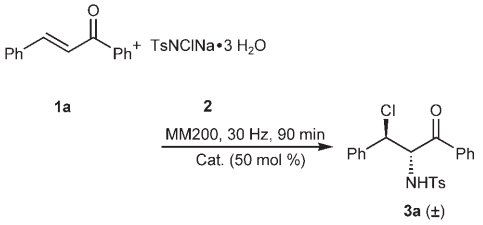
At the onset, we chose 1,3-diphenylpropenone (**1a**) as a model compound, and conducted its reaction with chloramine-T trihydrate ($TsNClNa{\cdot}3H_2O$, **2**) and varied amounts of $PhI(OAc)_2$ under our solventless ball-milling conditions.[14] As shown in entries 1–5 of Table 1, the $PhI(OAc)_2$-mediated reaction of **1a** with **2** did not produce any aziridine derivative, but rather afforded chloramino ketone **3a**. With 0.5 equivs. of $PhI(OAc)_2$, the reaction of **1a** with **2** proceeded smoothly and efficiently under mechanical milling conditions to give **3a** with good yield (77%) and diastereoselectivity (91/9) (entry 1, Table 1). Decreasing the amount of $PhI(OAc)_2$ to 0.25 equivs. resulted in decreased product yield (entry 2, Table 1), while increasing the amount of $PhI(OAc)_2$ up to 1.0 equiv. did not improve the product yield and diastereoselectivity (entries 3 and 4, Table 1). Two equivs. of **2** were necessary to obtain good product yield (entry 1 *vs.* entry 5, Table 1).

Readily available and cheap copper salts CuCl,[6a,g] $CuCl_2$[6a] and CuI[6g] have been applied to the catalytic aziridinations of styrene, substituted styrenes, norbornene,1,2-dihydronaphthalene, and cyclohexene by chloramine-T with either acetonitrile[6a] or water[6g] as the solvent. However, these copper salts have not been examined for the reactions of chalcones with chloramine-T. In order to compare the efficiency of $PhI(OAc)_2$ and metal salts, we examined the mechanochemical reaction of **1a** with **2** promoted by 0.5 equivs. of CuCl, $CuCl_2{\cdot}2H_2O$, and CuI (entries 6–8, Table 1) as well as other inorganic salts (entries 9–18, Table 1). All of the investigated metal salts except for CuI showed certain activity towards the formation of **3a**. Again, an aziridine derivative was not obtained in all cases. $InCl_3{\cdot}4H_2O$ exhibited the highest yield (75%) and good diastereoselectivity (89/11), but still did not exceed those of $PhI(OAc)_2$. Furthermore, when trying to extend the substrate scope with $InCl_3{\cdot}4H_2O$, it was disappointing to observe that the reaction process of unactivated chalcones was rather sluggish, and the yield was unsatisfactory.

With the satisfactory result for the $PhI(OAc)_2$-mediated reaction of **1a** with **2** in hand, we extended the substrate to substituted chalcones. Representative chalcones **1b–e** and **1f–i**, which were prepared from the reaction of acetophenone with various aromatic aldehydes bearing either an electron-donating group or an electron-withdrawing group on the phenyl ring, and from the reaction of 4′-methoxyacetophenone or 4′-chloroacetophenone with benzaldehyde or 4-chlorobenzaldehyde, respectively, were investigated. The yields and diastereoselectivity for the reactions of **1a–j** with **2** are listed in Table 2.

As seen from Table 2, all of the examined reactions of chalcones afforded vicinal chloramino ketones in moderate to good yields with good to excellent diastereoselectivity except for **3b**. It is interesting to note that an electron-withdrawing group on either the R^1- or the R^2-phenyl ring increased the diastereoselectivity (entries 3–6, 9, 10). Products **3c–f**, **3i**, and **3j** were practically obtained as a single isomer.

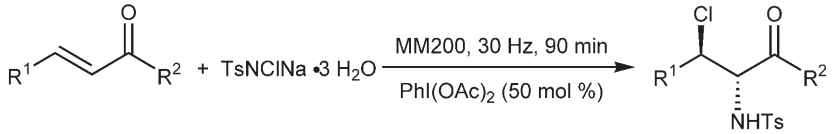
Table 1. Aminochlorination of 1,3-diphenylpropenone with various additives.[a]



Entry	Additive	Yield [%][b]	*dr* (*anti/syn*)[c]
1	$PhI(OAc)_2$	77	91/9
2	$PhI(OAc)_2$[d]	53	91/9
3	$PhI(OAc)_2$[e]	76	92/8
4	$PhI(OAc)_2$[f]	75	91/9
5	$PhI(OAc)_2$[g]	53	92/8
6	CuCl	29	89/11
7	$CuCl_2{\cdot}2H_2O$	55	91/9
8	CuI	0	/
9	$MnCl_2{\cdot}4H_2O$	7	90/10
10	$ZnCl_2$	11	87/13
11	$FeCl_3{\cdot}6H_2O$	51	87/13
12	$CoCl_2{\cdot}6H_2O$	24	92/8
13	$NiCl_2{\cdot}6H_2O$	20	93/7
14	$CrCl_3{\cdot}6H_2O$	62	90/10
15	$CeCl_3{\cdot}7H_2O$	69	89/11
16	$SnCl_2{\cdot}2H_2O$	57	90/10
17	$SnCl_4{\cdot}5H_2O$	42	87/13
18	$InCl_3{\cdot}4H_2O$	75	89/11

[a] Unless otherwise specified, all the reactions were performed with 0.2 mmol of **1a**, 0.4 mmol of **2**, 0.1 mmol of the employed additive.
[b] Isolated yields by flash column chromatography.
[c] Determined by ^1H NMR.
[d] 0.05 mmol of $PhI(OAc)_2$.
[e] 0.15 mmol of $PhI(OAc)_2$.
[f] 0.2 mmol of $PhI(OAc)_2$.
[g] 0.2 mmol of **1a**, 0.2 mmol of **2**, 0.1 mmol of $PhI(OAc)_2$.

Table 2. Solvent-free mechanochemical synthesis of vicinal chloroamino compounds promoted by $PhI(OAc)_2$.[a]



1 2 3 (±)

Entry	R^1	R^2	Product	Yield [%][b]	*dr (anti/syn)*[c]
1	Ph	Ph	**3a**	77	91/9
2	4-MeO-C_6H_4	Ph	**3b**	59	75/25
3	4-Cl-C_6H_4	Ph	**3c**	75	>99/1
4	2-Cl-C_6H_4	Ph	**3d**	63	>99/1
5	3,4-Cl_2-C_6H_4	Ph	**3e**	73	>99/1
6	4-NO_2-C_6H_4	Ph	**3f**[d]	63	>99/1
7	Ph	4-MeO-C_6H_4	**3g**	72	91/9
8	4-Cl-C_6H_4	4-MeO-C_6H_4	**3h**	78	90/10
9	Ph	4-Cl-C_6H_4	**3i**	70	>99/1
10	4-Cl-C_6H_4	4-Cl-C_6H_4	**3j**	75	>99/1
11	Ph	Me	**3k**	41	96/4
12	Et	Ph	**3l**	0	-
13	*i*-Bu	Me	**3m**	0	-
14	Ph	OMe	**3n**	65	>99/1
15	Ph	NEt_2	**3o**	52	>99/1

[a] Unless otherwise specified, all the reactions were performed with 0.2 mmol of **1a**, 0.4 mmol of **2**, 0.1 mmol of $PhI(OAc)_2$, the reaction time was 1.5 h.
[b] Isolated yield by flash column chromatography.
[c] Determined by the analysis of ^1H NMR.
[d] 0.8 mmol of **2** was used, and the reaction time was 3 h.

Furthermore, other electron-deficient olefins including aliphatic enones, cinnamate and cinnamide were investigated to show the scope and limitation of the present method. When the R^2 group of the enones was an alkyl substituent, the yield of chloramino ketone decreased rapidly, yet good diasteroselectivity was observed (entry 11). The reactions of enones with alkyl substituents attached to the C=C double bond failed to give any products (entries 12, 13). Much to our delight, cinnamate **1n** reacted smoothly under our conditions to give chloramino ester **3n** in 65% yield with excellent diasteroselectivity (entry 14). Further studies disclosed that cinnamide **1o**, which was considered as a more challenging substrate due to the reduced electrophilicity of the C=C double bond, was able to be aminochlorinated with moderate yield and excellent diasteroselectivity (entry 15).

Compounds **3a**,[3f] **3d**,[3f] **3f**,[3f] **3g**,[3f] **3i**,[3f] **3k**[3f] and **3n**[3a,c,d] have been previously reported and were confirmed by the comparison with their reported data. New products **3b**, **3c**, **3e**, **3h**, **3j** and **3o** were fully characterized by HR-MS, FT-IR, ^1H NMR, and ^{13}C NMR. The spectral data were consistent with their molecular structures. The *anti* configuration of **3c** was further unequivocally established by the X-ray structure of its single crystal, which was grown from petroleum ether/ethyl acetate (6:1) (Figure 1).

To demonstrate the advantages of the solvent-free mechanochemical reactions and explore the feasibility of this chloramination reaction in solution, we chose **1a** as the representative substrate to react with **2** promoted by different additives in several solvents. $PhI(OAc)_2$ and metal salts such as $InCl_3{\cdot}4H_2O$, $CuCl_2{\cdot}2H_2O$, CuCl and CuI were examined as the ad-

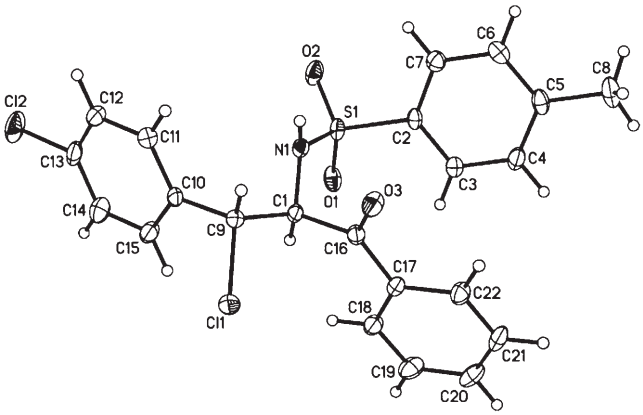
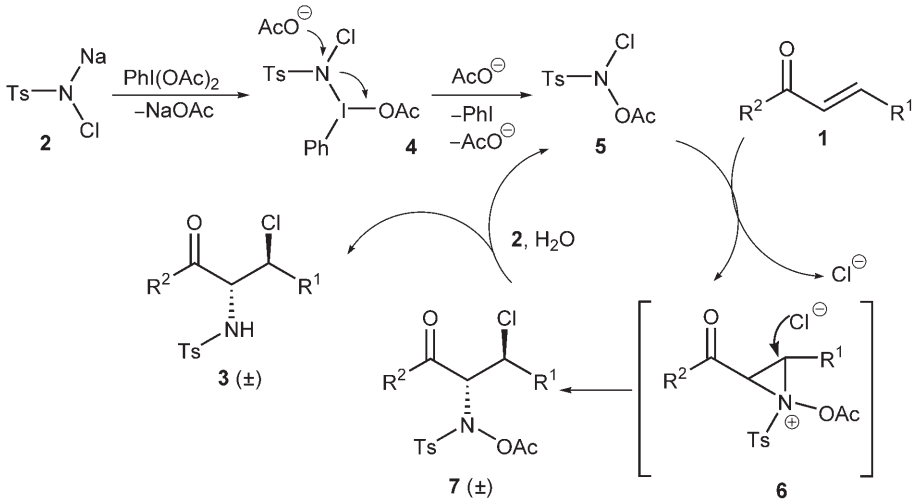


Figure 1. ORTEP diagram of **3c**.



Scheme 1. Proposed reaction mechanism for the $PhI(OAc)_2$-promoted aminochloration of olefins.

ditives. $PhI(OAc)_2$ failed to give any product in CH_3CN, which was used as a privileged solvent for chloramine-T,[6] either at room temperature or at reflux conditions. $PhI(OAc)_2$ afforded none or only trace amount of product **3a** in THF, DMF, MeOH, CCl_4, toluene and hexane. It is only in CH_2Cl_2 that product **3a** could be obtained in 53% yield with good diastereoselectivity (92/8) for the $PhI(OAc)_2$-mediated reaction of **1a** with **2** for 6 h. $InCl_3{\cdot}4H_2O$, CuCl and CuI could not promote the reaction in neither CH_3CN nor CH_2Cl_2. While $CuCl_2{\cdot}2H_2O$ did not give any product in CH_2Cl_2, it indeed generated product **3a** in CH_3CN after reaction for 24 h with 50% yield and the same diastereoselectivity. Even though it was possible to promote the reaction of **1a** with **2** in organic solvents by $PhI(OAc)_2$ and $CuCl_2{\cdot}2H_2O$, the solvent-free $PhI(OAc)_2$-promoted mechanochemical reaction was the most efficient one in term of product yield and reaction time.

Although the exact reaction mechanism is not clear right now, a possible pathway for the $PhI(OAc)_2$-promoted aminochlorination of electron-deficient olefins is shown in Scheme 1. Chloramine-T attacks $PhI(OAc)_2$ to generate intermediate **4**, which loses PhI to give *N*-aceto-*N*-chloro-*p*-toluenesulfonamide **5**.[10] Subsequent electrophilic reaction of intermediate **5** with olefin **1** produces aziridinium **6** and Cl^-,[3,8] due to the fact that chloride is a better leaving group than acetate. The β-position of the aziridinium **6** has more positive charge than the α-position due to the stabilization effect from the phenyl ring.[3] Thus, the ring opening of **6** by *in situ* formed nearby Cl^- *via* an S_N2 route preferably occurs at β-position to give intermediate **7**. Then, intermediate **7** reacts with another molecule of chloramine-T in the presence of a proton source (most probably water present in the system) to afford product **3** and regenerate intermediate **5**,[8] which continues to react with olefin **1** again. The proposed ring-opening process of aziridinium **6** by Cl^- *via* an S_N2 route can fully explain the observed regioselectivity and exclusive or dominant formation of the *anti*-diastereoisomer. The reason for the preferred nucleophilic ring opening by Cl^- over other species such as hydroxide coexisted in the reaction system is not known[3b] and needs further investigation.

Conclusions

In summary, an efficient, simple and solvent-free method for the aminochlorination of electron-deficient olefins including various α,β-unsaturated enones, a representative cinnamate and cinnamide promoted by $PhI(OAc)_2$ under ball-milling conditions has been developed. The use of inexpensive and stable chloramine-T as a nitrogen and chlorine source makes the reaction very convenient and easy to handle. $PhI(OAc)_2$ was superior to metal salts for the aminochlorination of electron-deficient olefins.

Experimental Section

General Remarks

Reagents and solvents were obtained from commercial suppliers and were used without further purification. All melting points were determined on an XT-4 binocular microscope (Beijing Tech Instrument Co., China) and are not corrected. Infrared spectra were recorded on a Vector-12 infrared spectrometer in KBr pellet and reported in cm^{-1}. ^1H NMR spectra were recorded on Bruker AV300 (300 MHz) spectrometer, chemical shifts (δ) are reported in

parts per million relative to tetramethylsilane. Splitting patterns are designated as s, singlet; d, doublet; t, triplet; m, multiplet. ^{13}C NMR spectra were recorded on Bruker AV300 (75 MHz) spectrometer with complete proton decoupling, chemical shifts are reported in parts per million relative to the solvent resonance as the internal standard ($CDCl_3$, $\delta = 77.16$ ppm). High-resolution mass spectra (HR-MS) were recorded on a Bruker VPEXII spectrometer with EI mode. Analytical TLC and column chromatography were performed on silica gel GF254, and silica gel H60, respectively.

General Procedure for the Aminochlorination of Electron-Deficient Olefins

A mixture of electron-deficient olefin **1** (0.2 mmol), chloramine-T trihydrate **2** (112.6 mg, 0.4 mmol), and a given amount of $PhI(OAc)_2$ along with a stainless ball of 7.0 mm diameter were introduced into a stainless steel jar (5 mL). The same mixture was also introduced into a second parallel jar. The two reaction vessels were milled simultaneously in a Retsch MM200 mixer mill (Retsch GmbH, Haan, Germany) at a frequency of 1800 revolutions per minute for 1.5 h. The resulting mixture from the two reaction vessels was extracted with ethyl acetate twice (10 mL × 2). The extraction was filtrated to remove the insoluble material and the filtrate was evaporated to dryness under vacuum. The residual was separated on a silica gel column with petroleum ether/ethyl acetate (8:1) as the eluent to get the desired product **3**.

Compounds **3a**,[3f] **3d**,[3f] **3f**,[3f] **3g**,[3f] **3i**,[3f] **3k**[3f] and **3n**[3a,c,d] have been previously reported and were characterized by comparison with their reported data. Physical and spectroscopic data of the newly synthesized compounds are given below.

3-Chloro-3-(4-methoxylphenyl)-1-phenyl-2-(tosylamino)-propan-1-one (3b): white solid, mp 132–134 °C. IR (KBr): $\nu = 3269$, 2924, 1668, 1595, 1514, 1447, 1335, 1263, 1161, 1090, 1029, 812, 671, 553, 531 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.76$ (d, $J = 7.2$ Hz, 2H), 7.60 (t, $J = 7.7$ Hz, 1H), 7.51 (d, $J = 8.5$ Hz, 2H), 7.43 (t, $J = 7.2$ Hz, 2H), 7.13 (d, $J = 8.5$ Hz, 2H), 7.03 (d, $J = 7.7$ Hz, 2H), 6.75 (d, $J = 8.5$ Hz, 2H), 5.51 (d, $J = 9.9$ Hz, 1H), 5.38 (dd, $J = 9.9$, 6.6 Hz, 1H), 5.07 (d, $J = 6.6$ Hz, 1H, exchangeable with D_2O), 3.79 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, all 1C unless indicated): $\delta = 196.5$, 160.2, 143.6, 136.9, 135.4, 134.2, 129.6, 129.5 (2C), 129.4 (2C), 128.9 (2C), 128.8 (2C), 127.2 (2C), 114.0 (2C), 61.7, 61.6, 55.4, 21.5; HR-MS (EI-TOF): $m/z =$ 407.1182, [M$^+$−HCl], calcd. for $C_{23}H_{21}NO_4S$: 407.1191.

3-Chloro-3-(4-chlorophenyl)-1-phenyl-2-(tosylamino)propan-1-one (3c): white solid, mp 147–149 °C. IR (KBr): $\nu =$ 3267, 2922, 1666, 1596, 1494, 1452, 1337, 1241, 1163, 1092, 809, 684, 665, 546, 527 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.76$ (d, $J = 8.0$ Hz, 2H), 7.59 (t, $J = 7.2$ Hz, 1H), 7.40–7.47 (m, 4H), 7.18–7.11 (m, 4H), 7.03 (d, $J = 8.0$ Hz, 2H), 5.52 (d, $J = 9.6$ Hz, 1H), 5.34 (dd, $J = 9.6$, 6.6 Hz, 1H), 5.01 (d, $J = 6.6$ Hz, 1H, exchangeable with D_2O), 2.29 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, all 1C unless indicated): $\delta =$ 196.5, 143.9, 136.8, 135.3, 135.2, 134.9, 134.4, 129.6 (2C), 129.5 (2C), 129.0 (2C), 128.9 (2C), 128.8 (2C), 127.1 (2C), 61.2, 61.1, 21.6; HR-MS (EI-TOF): $m/z = 411.0697$ [M$^+$−HCl], calcd. for $C_{22}H_{18}NO_3SCl$: 411.0696.

3-Chloro-3-(3,4-dichlorophenyl)-1-phenyl-2-(tosylamino)-propan-1-one (3e): white solid, mp 136–138 °C. IR (KBr): $\nu = 3178$, 2925, 1673, 1595, 1448, 1336, 1251, 1162, 1088, 971, 917, 791, 663, 572, 544 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.83$ (d, $J = 7.5$ Hz, 2H), 7.62 (t, $J = 7.5$ Hz, 1H), 7.44–7.48 (m, 4H), 7.28–7.25 (m, 2H), 7.05–7.09 (m, 3H), 5.63 (d, $J = 9.9$ Hz, 1H), 5.31 (dd, $J = 9.9$, 7.5 Hz, 1H), 4.95 (d, $J =$ 7.5 Hz, 1H, exchangeable with D_2O), 2.32 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, all 1C unless indicated): $\delta = 196.8$, 144.0, 136.8, 136.7, 135.4, 134.6, 133.4, 132.8, 130.5, 130.2, 129.6 (2C), 129.1 (2C), 128.9 (2C), 127.5, 126.9 (2C), 60.8, 60.2, 21.6; HR-MS (EI-TOF): $m/z = 445.0297$ [M$^+$−HCl], calcd. for $C_{22}H_{17}NO_3SCl_2$: 445.0306.

3-Chloro-3-(4-chlorophenyl)-1-(4-methoxylphenyl)-2-(tosylamino)propan-1-one (3h): white solid, mp 61–63 °C. IR (KBr): $\nu = 3258$, 2924, 1670, 1599, 1341, 1267, 1160, 1090, 832, 812, 664, 527 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta =$ 7.78 (d, $J = 8.7$ Hz, 2H), 7.46 (d, $J = 8.4$ Hz, 1H), 7.20–7.13 (m, 4H), 7.05 (d, $J = 8.4$ Hz, 2H), 6.91 (d, $J = 8.7$ Hz, 2H), 5.53 (d, $J = 9.9$ Hz, 1H), 5.30 (dd, $J = 9.9$, 7.0 Hz, 1H), 5.02 (d, $J = 7.0$ Hz, 1H, exchangeable with D_2O), 3.90 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, all 1C unless indicated): $\delta = 194.5$, 164.7, 143.7, 136.9, 135.1, 135.0, 131.5 (2C), 129.5 (4C), 128.7 (2C), 128.2, 127.0 (2C), 114.2 (2C), 61.1, 60.8, 55.8, 21.5; HR-MS (EI-TOF): $m/z = 441.0796$ [M$^+$−HCl], calcd. for $C_{23}H_{20}NO_4SCl$: 441.0802.

3-Chloro-1,3-bis(4-chlorophenyl)-2-(tosylamino)propan-1-one (3j): white solid, mp 146–148 °C. IR (KBr): $\nu = 3219$, 2923, 1685, 1588, 1492, 1337, 1161, 1090, 805, 674, 555 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.76$ (d, $J = 8.7$ Hz, 2H), 7.41–7.44 (m, 4H), 7.20–7.14 (m, 4H), 7.05 (d, $J = 8.1$ Hz, 2H), 5.57 (d, $J = 9.6$ Hz, 1H), 5.27 (dd, $J = 9.6$, 8.1 Hz, 1H), 4.97 (d, $J = 8.1$ Hz, 1H, exchangeable with D_2O), 2.27 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, all 1C unless indicated): $\delta = 196.0$, 144.0, 141.2, 136.7, 135.3, 135.0, 133.8, 130.4 (2C), 129.6 (2C), 129.5 (2C), 129.2 (2C), 128.8 (2C), 127.0 (2C), 60.8, 60.7, 21.6; HR-MS (EI-TOF): $m/z = 445.0302$ [M$^+$−HCl], calcd. for $C_{22}H_{17}NO_3SCl_2$: 445.0306.

3-Chloro-*N*,*N*-diethyl-3-phenyl-2-(tosylamino)propionamide (3o): white solid, mp 185–187 °C. IR (KBr): $\nu = 3179$, 2981, 2937, 1629, 1442, 1341, 1164, 1089, 928, 814, 721, 668, 567, 554, 526 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.39$ (d, $J = 8.1$ Hz, 2H), 7.33–7.24 (m, 5H), 7.10 (d, $J = 8.1$ Hz, 2H), 6.07 (d, $J = 9.3$ Hz, 1H), 4.98 (d, $J = 9.3$ Hz, 1H), 4.73 (t, $J =$ 9.3 Hz, 1H), 3.43–3.33 (m, 3H), 3.23–3.14 (m, 1H), 2.35 (s, 3H), 1.19 (t, $J = 7.2$ Hz, 3H), 1.02 (t, $J = 7.1$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$, all 1C unless indicated): $\delta = 168.5$, 143.3, 137.4, 137.2, 129.4 (2C), 128.9, 128.6 (2C), 128.4 (2C), 126.9 (2C), 62.4, 57.3, 42.5, 40.9, 21.5, 14.0, 12.4; HR-MS (EI-TOF): $m/z = 372.1507$ [M$^+$−HCl], calcd. for $C_{20}H_{24}N_2O_3S$: 372.1508.

Procedure for Aminochlorination of Chalcone 1a in Solution

To a solution of chalcone **1a** (208.0 mg, 1.0 mmol) in CH_2Cl_2 (5 mL) was added chloramine-T trihydrate **2** (563.5 mg, 2.0 mmol) and $PhI(OAc)_2$ (322.3 mg, 1.0 mmol). This mixture was allowed to stir at room temperature for 6 h. The same work-up afforded **3a**; yield: 220.7 mg (53 %).

Replacing $PhI(OAc)_2$ with $CuCl_2 \cdot 2H_2O$ (1.0 mmol, 153.0 mg) and CH_2Cl_2 with CH_3CN, and prolonged reaction time (24 h) also gave **3a**; yield: 207.3 mg (50%).

Determination of the X-Ray Crystal Structure of Compound 3c

Crystal was grown by slowly evaporating a solution of **3c** in petroleum ether/ethyl acetate (6:1). *Refinement details*: empirical formula: $C_{22}H_{19}Cl_2NO_3S$; formula weight: 448.34; $T=$ 153(2) K; wavelength: 0.71070 Å; crystal system: monoclinic; space group: $C2/c$; unit cell dimensions: $a=19.603(3)$ Å, $\alpha=90°$, $b=10.4638(14)$ Å, $\beta=92.116(3)°$, $c=20.380(2)$ Å, $\gamma=90°$; $V=4177.5(10)$ Å^3; $Z=8$; density (calculated): 1.426 mg m^{-3}; absorption coefficient: 0.435 mm^{-1}; F(000) = 1856; crystal size: $0.50\times0.48\times0.30$ mm3; θ range for data collection: 3.0 to 25.3; index ranges: $-23 \le h \le 23$, $-12 \le k \le 12$, $-20 \le l \le 24$; reflections collected: 19735; independent reflections: 3826 [R(int) = 0.0221]; completeness to $\theta=25.34$: 99.5%; absorption correction: multi-scan; max. and min. transmission: Full-matrix least-squares on $F2$; data/restraints/parameters: 3826/0/268; goodness-of-fit on $F2$: 1.104; final R indices [$I>2\sigma(I)$]: $R1=0.0339$, $wR2=$ 0.0819; R indices (all data): $R1=0.0361$, $wR2=0.0832$; largest diff. peak and hole: 0.307 and -0.355 e Å^{-3}.

Crystallographic data for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-614095. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax.: (internat.) + 44 1223/336–033; e-mail: deposit@ccdc.cam.ac.uk].

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