Superacidic Activation of α,β-Unsaturated Amides and Their Electrophilic Reactions[‡]

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The electrophilic reactivity of α,β-unsaturated amides towards weak nucleophiles such as arenes and cyclohexane, initiated either with triflic acid (CF_3SO_3H) or with excess $AlCl_3$, has been studied. The amides generally condense readily with aromatics in the presence of $AlCl_3$ to give 3-arylpropionamides and related compounds in excellent yields, while some amides also undergo selective ionic hydrogenation with cyclohexane to give saturated amides. The proposed mechanism of these reactions involves dicationic intermediates (superelectrophiles). The direct observation of a dicationic species (by low-temperature NMR) is reported.

Introduction

Despite their broad utility in organic chemistry, little work has been done to investigate the reactivity of amides towards weak nucleophiles such as nonactivated arenes and alkanes. Their reactions in Friedel−Crafts-type chemistry are unusual and are mostly known for Bischler−Napieralski and related methods of preparation of heterocyclic compounds.[2,3] The use of amides has serious limitations because of competing hydrolysis and other acid-catalysed reactions. In contrast, Friedel−Crafts reactions involving other carbonyl compounds are well known and are widely used in organic synthesis; α,β-unsaturated aldehydes, ketones and carboxylic acids (common structure **1**), for example, offer a route to a variety of corresponding β-arylated derivatives **2** (Scheme 1).[4] In liquid superacids, compounds **1** generally give indanones and indenes as secondary products.[5−7] Ketones **1** (Y = Alk, Ar) also undergo selective ionic hydrogenation with cyclohexane in superacidic media.[8−10] The key reactive intermediates in this range of reactions (provided R = Alk or Ar) were recognised to be superelectrophilic[11−13] dicationic species **3**.[7−10,14] The concentrations of these species, the result of a second protonation of the less reactive monocationic form **4**, are generally too low for direct observation by NMR as long-living dications. The intermediacy of a dicationic species is, however, strongly supported by kinetic studies,[5,15] theoretical calculations[7,10] and, in some cases, low-temperature NMR observations.[7,14]

The analogous reactivity of α,β-unsaturated amides has not thus far been investigated. However, superacidic activation of the amides could involve their *O*-protonation[16,17] or *O*-complexation[18] with Lewis acid, with subsequent additional protonation of C=C (or C≡C) bonds. Thus, it was recently shown that cinnamanilide **5** cleanly undergoes intramolecular cyclization in triflic acid to give quinolinone **6** in good yield.[19] It was postulated that superelectrophilic activation involved *O*,*C*-diprotonation of **5** to produce dications **7** (X = H; Scheme 2). Similar reaction also occurred under classical Friedel−Crafts conditions at elevated temperature to give **6**, albeit in lower yields due to its subsequent reversible conversion into carbostyril **8**.[19−21] The latter reaction is predominant, for example, upon treatment of **5** with excess $AlCl_3$ in chlorobenzene.[22] Remarkably, similar treatment of **5** in benzene mostly gives product **9**, due to competing intermolecular reaction (Scheme 2).[22]

Given the reactivities of unsaturated carbonyl compounds **1** and amide **5**, it seemed likely that a variety of α,β-unsaturated amides might also generally exhibit analogous reactivity. In this paper we wish to present our study on superacid-induced reactivity of α,β-unsaturated amides towards aromatic compounds and cyclohexane.

Results and Discussion

Benzene was used as the first aromatic substrate, in reactions with amides **10a**−**h** in the presence of $AlCl_3$. As expected, β-addition products **11a**−**h** were mostly produced (Table 1). The reaction takes place under mild conditions,

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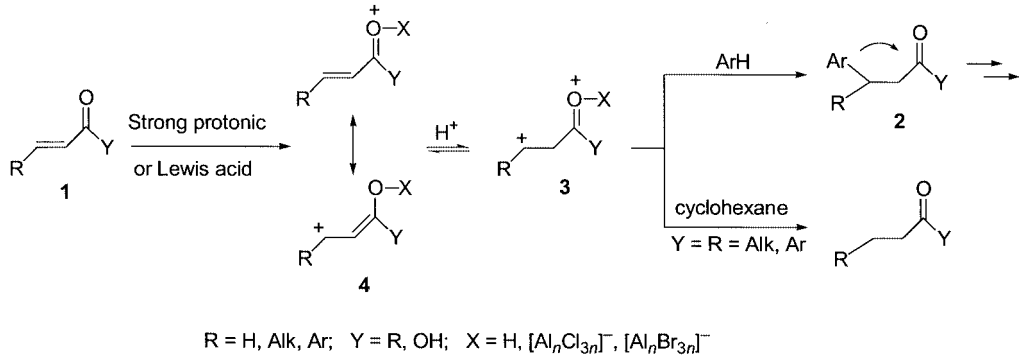
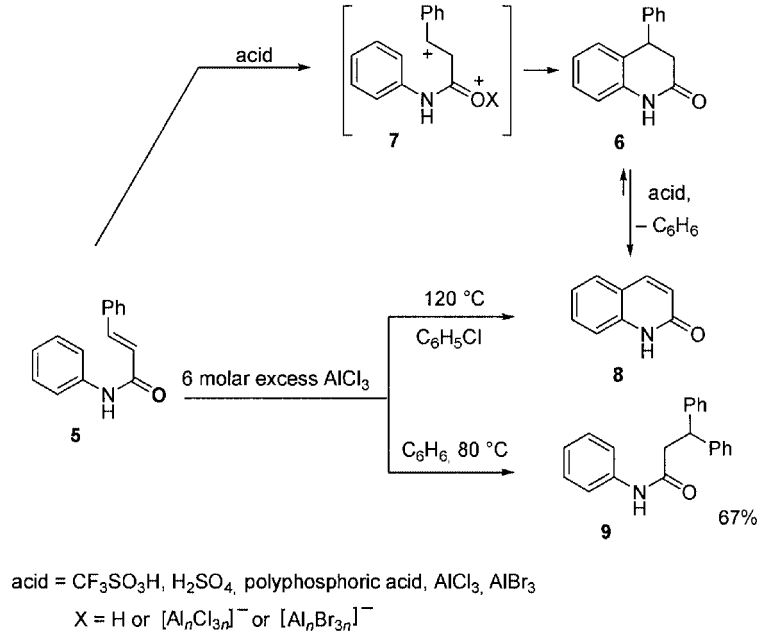


Scheme 1. Reactions of compounds **1** with aromatics and cyclohexane



Scheme 2. Electrophilic reactions of cinnamanilide **5**

at room temperature, and appears to be fast (reaction time 0.5 to 5 h) in the presence of a 2.5-fold molar excess of $AlCl_3$. This procedure is very clean and gives the products in good or quantitative yields. In the case of methacrylamide (**10b**) both β- and α-phenylated derivatives **11b** and **14** were obtained, with the former dominating, in reaction behaviour similar to that of the analogous methacrylic acid.[2] The reactivities of acetylenic amides **10h** and **10i** appeared to be similar to those of their ethylenic analogues **10d** and **5**. Remarkably, the cyclization of **10i** into 4-phenylcarbostyril (**15**) was previously known to occur in large excesses of polyphosphoric acid, requiring 120 °C in order to proceed.[23]

It was also demonstrated, with the examples of amides **10a**, **10e** and **10i**, that the same reactions were initiated, but not as efficiently, by triflic acid (Table 1). This result is in agreement with earlier observations: the efficiency of electrophilic activation through the action of excesses of aluminium halides is similar to that achieved by strong superacids such as $CF_3SO_3H-SbF_5$ (Ho −16 to −18.5[9]) and even $HF-SbF_5$ (Ho < −20 [9]).[19,24–26] This may be related to the ability of excess quantities of aluminium halides to produce low concentrations of highly acidic protonic superacids, such as $HAlHal_4$ and $HAl(OH)Hal_3$ (Hal = Cl, Br), through reaction with water (usually present in "dry" commercially available materials).[9,27] For purposes of comparison, the $HBr/AlBr_3$ system (Ho −17.5[9]) has been claimed to be a 10^3 times stronger acid than triflic acid (Ho = −14.1[9]).

When amides **10a–e**, **10g** and **10h** were involved in reaction with *o*-dichlorobenzene, a poor nucleophile normally inert towards electrophilic alkylation,[28] notable differences in their reactivities were demonstrated. Precursors **10c–e**, **10g** and **10h**, unlike **10a–b**, reacted readily with this arene to give mostly the corresponding addition products **12** (Table 1). Similar differences in reactivity were also found for reaction with cyclohexane: compound **10g** smoothly underwent selective ionic hydrogenation to give the saturated derivative **13g**. Amide **10d** also reacted with cyclohexane under mild conditions, but to give a complex reaction mixture, probably due to secondary reactions similar to those previously described for analogous ionic hydrogen-

ation of ketones **1** (R = Ph).[10] Compound **10c** did not react at room temperature, but at elevated temperature it gave **13c** in good yield (93%). In contrast, amides **10a** and **10b** reacted slowly with cyclohexane at elevated temperature to give **13a** and **13b** in low yields (Table 1).

There are two possible mechanistic pathways for the electrophilic reactions of amides **10a**−**g**. At least in case of precursors **10c**−**g**, the proposed reaction mechanism suggests the formation of superelectrophilic dicationic intermediates such as α-*C*-protonated complexes **16** (X = $Al_nCl_{3n}^-$) or analogous *O*,*C*-diprotonated dications **16** (X = H) in low concentrations (Scheme 3).

Similarly, dicationic species **7** may be regarded as key alkylating intermediates in the reaction **5** → **9** (Scheme 2). In our opinion, to view these reactions as "traditional" Friedel−Crafts alkylations (ionic hydrogenations) involving the intermediacy only of monocationic species **17** cannot explain all the experimental results, such as: (i) the lower reactivity in triflic acid, which is acidic enough for exhaustive *O*-protonation of the amides,[16] (ii) the higher reactivities of **10e** and **10f** than of **10a**−**b** toward benzene, whereas the latter should produce significantly stronger monocationic electrophiles **17**, (iii) and, moreover, the remarkably high reactivities of amides **10d**−**g** towards such weak nucleophiles as *o*-dichlorobenzene and cyclohexane. For this reason we suggest that the reactive intermediate is the dicationic species **16**, probably in equilibrium with the corresponding monocations **17**. In the cases of amides **10a** and **10b**, however, the key intermediates are most probably monocationic species **17**. These species seem to be electrophilic enough to react with benzene under mild conditions, but not sufficiently reactive towards cyclohexane and *o*-dichlorobenzene.

In view of the close basicity of C=C and C≡C bonds,[29] we also suggest the reactivity of acetylenic amides **10h** and **10i** be considered as involving the intermediacy of dicat-

Table 1. Electrophilic reactions of amides **10a**−**i**

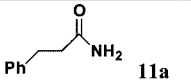
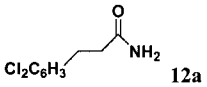
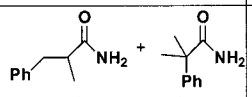
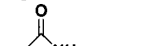
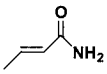
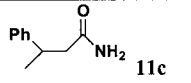
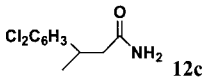
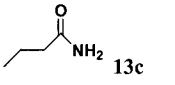
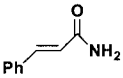
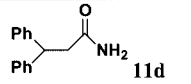
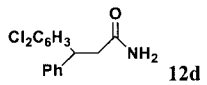
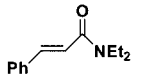
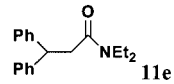
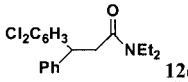
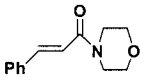
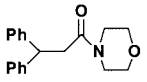
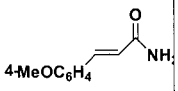
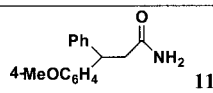
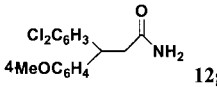
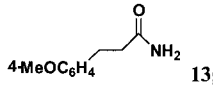
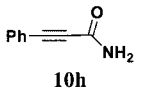
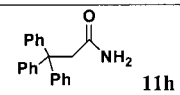
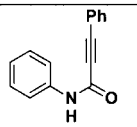
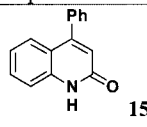
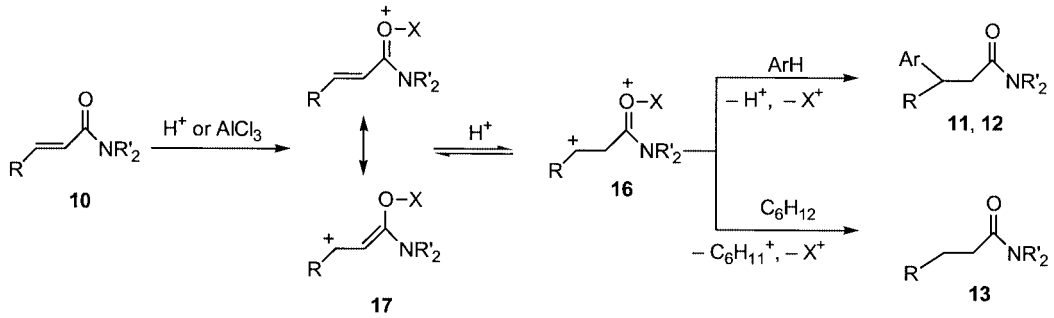
Substrate	Reaction conditions				Product	Yield[a] (%)
	Nucleophile	Acid (molar excess), solvent	Time [h]	*T* [°C]		
 **10a**	C_6H_6	$AlCl_3$ (2.5)	2	25	 **11a**	99
	C_6H_6	CF_3SO_3H (10)	20	25		17[b]
	o-$Cl_2C_6H_4$	$AlCl_3$ (3)	24	25	 **12a**	0
	o-$Cl_2C_6H_4$	$AlCl_3$ (3)	1	130		24[c]
	cyclohexane	$AlCl_3$ (3)	15	130	 **13a**	16
 **10b**	C_6H_6	$AlCl_3$ (2.5)	3	25	 **14** **11b**	97[d]
	C_6H_6	CF_3SO_3H (15)	20	25		0
	o-$Cl_2C_6H_4$	$AlCl_3$ (3)	24	25	no reaction	0
	o-$Cl_2C_6H_4$	$AlCl_3$ (3)	1	130	complex mixture	–
	cyclohexane	$AlCl_3$ (3)	5	130	 **13b**	27
 **10c**	C_6H_6	$AlCl_3$ (2.5)	3	25	 **11c**	93
	o-$Cl_2C_6H_4$	$AlCl_3$ (3)	18	25	 **12c**	55[c]
	o-$Cl_2C_6H_4$	$AlCl_3$ (3)	0.5	130		84[c]
	cyclohexane	$AlCl_3$ (3), CH_2Cl_2	70	25	 **13c**	0
	cyclohexane	$AlCl_3$ (4)	1	130		93
 **10d**	C_6H_6	$AlCl_3$ (2.5)	4	25	 **11d**	97
	o-$Cl_2C_6H_4$	$AlCl_3$ (4)	3	25	 **12d**	86[c]
	cyclohexane	$AlCl_3$ (3), CH_2Cl_2	1	25	complex mixture	–

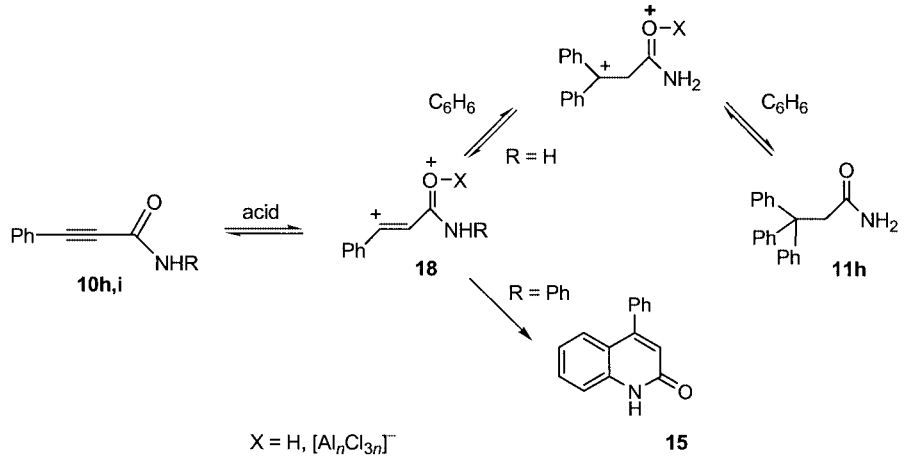
Table 1 *(continued)*

Substrate	Reaction conditions				Product	Yield[a] (%)
	Nucleophile	Acid (molar excess), solvent	Time [h]	*T* [°C]		
 **10e**	C_6H_6	$AlCl_3$ (2.5)	0.5	25	 **11e**	100
	C_6H_6	CF_3SO_3H (7)	15	25		99
	o-$Cl_2C_6H_4$	$AlCl_3$ (2.5)	6	25	 **12e**	95[c]
 **10f**	C_6H_6	$AlCl_3$ (2.5)	0.5	25	 **11f**	100
 **10g**	C_6H_6	$AlCl_3$ (5)	5	25	 **11g**	98
	o-$Cl_2C_6H_4$	$AlCl_3$ (5)	6	25	 **12g**	90[c]
	cyclohexane	$AlCl_3$ (5), CH_2Cl_2	7	25	 **13g**	78
	cyclohexane	CF_3SO_3H (15)	3	25	complex mixture	–
 **10h**	C_6H_6	$AlCl_3$ (4)	1.5	25	 **11h**	55
	o-$Cl_2C_6H_4$	$AlCl_3$ (4)	1	25	complex mixture[e]	–
 **10i**	–	$AlCl_3$ (5), CH_2Cl_2	10	25	 **15**	61
	–	CF_3SO_3H (37)	100	25		97

[a] The yields are of isolated, pure products. [b] Recovery of **10a** is 80%. [c] The overall yield of isomeric 3-(2,3- and 3,4-dichlorophenyl)propionamides. [d] The overall yield of mixture **11b** and **14** in 2:1 ratio. [e] Predominant formation of 3,3-diaryl-2-propenamides was detected by NMR monitoring.



Scheme 3. Proposed mechanism for the electrophilic reactions of amides **10c–g**



Scheme 4. Proposed mechanism for the electrophilic reactions of amides **10h** and **10i**

ionic species **18** (Scheme 4). A similar mechanism, invoking *O*,*C*-diprotonated species, was suggested and supported by theoretical calculations for the "parent" reaction between phenylacetylenecarboxylic acid and benzene in the presence of triflic acid.[7]

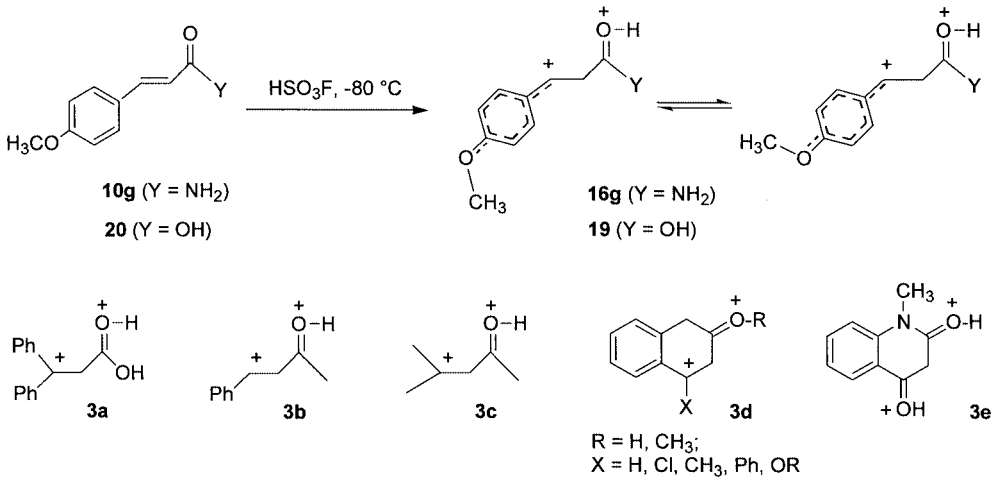
Our attempts to observe cationic or dicationic intermediates as long-lived species by NMR under superacid conditions gave the following results:

1. In $HSO_3F-SbF_5(-SO_2)$ and $CF_3SO_3H-SbF_5$, compounds **10d**−**g** and **5** essentially gave side products, most probably due to oxidation by SbF_5.

2. In the weaker superacids, HSO_3F (Ho = −15.1[9]) or CF_3SO_3H, only *O*-monoprotonated cations were observed when **10d**−**f** and **5** were dissolved.

3. The ^1H and ^{13}C NMR spectra obtained when **10g** was dissolved in HSO_3F or CF_3SO_3H at −80 °C (−30 °C, respectively) showed total conversion of the compound into *O*,*C*-diprotonated dication **16g** (Scheme 5). This, due to hindered rotation about the $C-C_6H_4-OCH_3$ bonds, shows two "frozen" conformers (*cis*/*trans* isomers) of the dication in 1:2 ratio (HSO_3F, −80 °C). The spectra show the CH_2 group signal around δ = 4.6 ppm in the proton NMR and δ = 36 ppm in the carbon NMR. The proton spectrum also shows the signal of the hydrogen bound to the carbonyl oxygen at δ = 10.6 ppm and the signal of the amino hydrogens at δ = 8.7 ppm (HSO_3F, −80 °C), similarly to chemical shifts of *O*-protonated amides.[16] The chemical shifts of signals assigned to the benzylic site of the dication are in agreement with those reported for analogous benzylic dicationic systems.[30] Furthermore, we also succeeded in observing a similar *O*,*C*-diprotonated dication **19** by protonation of 4-methoxycinnamic acid (**20**) in fluorosulfuric acid. Dications **16g** and **19** are believed to be close analogues of dications **3a**−**e** previously generated upon protonation of β-phenylcinnamic acid,[7] α,β-unsaturated ketones,[14] 2-naphthols[31,32] and 4-hydroxy-1-methyl-2(1*H*)quinolinone,[19] respectively, in the stronger superacids $HSO_3F(HF)-SbF_5-SO_2ClF$ or $CF_3SO_3H-SbF_5$ (Scheme 5).

4. Our attempts to generate dicationic species **16** by treatment with aluminium halides were unsuccessful. Dissolving amide **10g** in an $AlBr_3/CH_2Br_2$ system gave, as expected,



Scheme 5. Generation of long-living dications **16g** and **19** and related structures **3a**−**e**

the corresponding complex **17** (X = $Al_nBr_{3n}^-$), but subsequent saturation of the obtained solution with gaseous HBr resulted in side reactions.

From the synthetic point of view, the studied reactions may represent a convenient alternative to known preparations of 3-arylpropionamides, important intermediates in organic synthesis.[33−36] It is also worth noting that the utility of $AlCl_3$ as a plausible alternative to strong protic (super)acids to initiate reactions involving superelectrophilic species has probably been underestimated. Whereas the presence of small amounts of base (water) drastically decreases the acidity of superacid,[37] traces of humidity are rather beneficial to the reactivity of aluminium halides, which may be used without special dryness of starting materials or solvent and do not require inert gas atmospheres. Recently, we have also found that many reactions proceeding through dicationic, superelectrophilic intermediates can be successfully mediated by H-form zeolites and other available solid acids.[38] Among other reactions, the transformations **5** → **6**, **10i** → **15** and **10e** → **11e**, **12e** have been performed.[38]

During the preparation of this paper we have learned of new data in press concerning the possibility of superelectrophilic activation of amides with triflic acid, which provided an increase in the reactivities both of a protonated amide group and of closely situated protonated functional groups, resulting in acylation or alkylation of aromatics.[39] This is in agreement with our results.

Conclusion

A direct, one-step synthesis of β-arylpropionamides and related compounds through superacid-induced reactions between α,β-unsaturated amides and aromatic species has been developed. α,β-Unsaturated amides also undergo selective ionic hydrogenation with cyclohexane to give their saturated derivatives. We suggest that dicationic electrophiles, such as those directly observable by low-temperature NMR when α,β-unsaturated amides are dissolved in liquid superacids, offer a convenient explanation consistent with the reaction mechanism. In general, the ability of α,β-unsaturated amides to undergo activation in the presence of strongly acidic agents through the formation of dicationic intermediates makes it possible for the latter to act as a novel synthons and extends the applicability of Friedel−Crafts-type reactions in the field of amides.

Experimental Section

General Remarks: The ^1H and ^{13}C NMR spectra were recorded with a Bruker ADVANCE 300 spectrometer at 300.17 and 75.48 MHz, respectively. The chemical shifts were measured relative to the solvent signals ($CDCl_3$, δ = 7.26 ppm and δ_C = 77.0 ppm). The chemical shifts of dications **16g** and **19** in fluorosulfuric acid were measured relative to internal dichloromethane (δ = 5.32 ppm and δ_C = 54.0 ppm) with a Bruker AM 400 spectrometer at 400 and 100 MHz, respectively. Triflic and fluorosulfuric acids, aluminium chloride, benzene and compounds **10a**, **10b**, **10d** and **20** were purchased and used as received. Amides **10c** and **10e**−**i** were prepared from the corresponding commercially available carboxylic acids by treatment with excess $SOCl_2$, followed by quenching with aqueous ammonia or an amine. Antimony pentafluoride was distilled twice under argon. Elevated temperature reactions were carried out in 15 mL pressure tubes.

Dications **16g** and **19** were generated by carefully dissolving samples of **10g** and **20** (10 mg), respectively, in NMR tubes filled with 0.5 mL of fluorosulfuric (triflic) acid at −78 °C (−30 °C).

Dication 16g, Major Isomer: (HSO_3F, −80 °C) ^1H NMR: δ = 4.52 (s, 3 H), 4.57 (s, 2 H), 7.36 (d, *J* = 7 Hz, 1 H), 7.53 (d, *J* = 7 Hz, 1 H), 8.31 (s, 1 H), 8.32 (d, *J* = 7 Hz, 1 H), 8.4 (d, *J* = 7 Hz, 1 H), 8.66 (br. s, 2 H), 10.6 (br. s, 1 H) ppm. ^{13}C NMR: δ = 35.7, 62.2, 118.7, 127, 136.3, 143.2, 158.1, 171.4, 177.2, 188.7 ppm. **Minor Isomer:** ^1H NMR: δ = 4.52 (s, 3 H), 4.57 (s, 2 H), 7.32 (d, *J* = 7 Hz, 1 H), 7.59 (d, *J* = 7 Hz, 1 H), 8.17 (d, *J* = 7 Hz, 1 H), 8.31 (s, 1 H), 8.57 (d, *J* = 7 Hz, 1 H), 8.66 (br. s, 2 H), 10.6 (br. s, 1 H) ppm. ^{13}C NMR: δ = 35.7, 62.2, 120, 125.5, 136.3, 147.8, 153.2, 171.4, 177.2, 188.6 ppm.

Dication 19, Major Isomer: (HSO_3F, −80 °C) ^1H NMR: δ = 4.54 (s, 3 H), 4.83 (s, 2 H), 7.37 (d, *J* = 7 Hz, 1 H), 7.55 (d, *J* = 7 Hz, 1 H), 8.3 (s, 1 H), 8.29 (d, *J* = 7 Hz, 1 H), 8.4 (d, *J* = 7 Hz, 1 H) ppm. ^{13}C NMR: δ = 36.3, 62.3, 119, 127.1, 136.2, 143.3, 158.2, 168.2, 189, 189.3 ppm. **Minor Isomer:** ^1H NMR: δ = 4.54 (s, 3 H), 4.83 (s, 2 H), 7.33 (d, *J* = 7 Hz, 1 H), 7.61 (d, *J* = 7 Hz, 1 H), 8.2 (d, *J* = 7 Hz, 1 H), 8.3 (s, 1 H), 8.55 (d, *J* = 7 Hz, 1 H) ppm. ^{13}C NMR: δ = 36.3, 62.4, 120.2, 125.7, 136.1, 147.9, 153.2, 168, 188.9, 189.3 ppm.

Quenching of these acidic solutions with ice provided the starting materials once more, whereas their preliminary warming to −30−0 °C caused irreversible changes.

Reactions with Benzene

3-Phenylpropionamide (11a): Compound **10a** (0.2 g, 2.8 mmol) was added to a stirred mixture of $AlCl_3$ (0.95 g, 7.1 mmol) and benzene (3 mL). The resulting mixture was stirred at 25 °C for 2 h, and was then poured over several grams of ice and extracted with CH_2Cl_2. The organic phase was separated, dried with anhydrous Na_2SO_4 and concentrated in vacuo to give white crystalline **11a** (0.419 g, 99%): M.p. 103−104 °C, ref.[40a] m.p. 104−105 °C. ^1H NMR: δ = 2.52 (t, *J* = 7.8 Hz, 2 H), 2.96 (t, *J* = 7.8 Hz, 2 H), 5.49 (br. s, 1 H), 5.86 (br. s, 1 H), 7.1−7.3 (m, 5 H) ppm.[40b] ^{13}C NMR: δ = 31.4, 37.5, 126.3, 128.3, 128.6, 140.7, 174.8 ppm.[40b]

2-Methyl-3-phenylpropionamide (11b) and 2-Methyl-2-phenylpropionamide (14): A mixture of $AlCl_3$ (0.95 g, 7.1 mmol) and **10b** (0.2 g) in benzene (3 mL) was stirred at 25 °C for 3 h followed by workup as described above to give a solid mixture of **11b** and **14** (0.41 g, 97%) in 2:1 ratio. $C_{10}H_{13}NO$ (163.2): calcd. C 73.6, H 8, N 8.6; found C 73.4, H 7.9, N 8.2. **Compound 11b:** ^1H NMR: δ = 1.17 (d, *J* = 6.8 Hz, 3 H), 2.53 (m, 1 H), 2.66 (dd, *J* = 13.0 Hz7, 7.2 Hz, 1 H), 2.99 (dd, *J* = 13.0 Hz7, 7.3 Hz, 1 H), 5.3 (br. s, 1 H), 5.6 (br. s, 1 H), 7.1−7.4 (m, 5 H) ppm. ^{13}C NMR: δ = 17.6, 40.2, 42.8, 126.3, 128.4, 129, 139.7, 178.7 ppm. **Compound 14:** ^1H NMR: δ = 1.58 (s, 6 H), 5.2 (br. s, 1 H), 5.7 (br. s, 1 H), 7.1−7.4 (m, 5 H) ppm. ^{13}C NMR: δ = 26.9, 46.8, 127, 128.4, 128.7, 145, 180.4 ppm.

3-Phenylbutyramide (11c): A mixture of $AlCl_3$ (0.37 g, 2.8 mmol) and **10c** (0.1 g, 1.2 mmol) in benzene (3 mL) was stirred at 25 °C for 3 h and after usual workup gave **11c** (0.178 g, 93%) as a white crystalline solid: M.p. 104−105 °C, ref.[41a] m.p. 104−105 °C. ^1H

NMR: δ = 1.31 (d, *J* = 7 Hz, 3 H), 2.41 (dd, *J* = 14.3, 7.8 Hz, 1 H), 2.5 (dd, *J* = 14.3, 7.8 Hz, 1 H), 3.26 (m, 1 H), 5.45 (br. s, 1 H), 5.87 (br. s, 1 H), 7.15−7.3 (m, 5 H) ppm.[41b] ^{13}C NMR: δ = 17.8, 36.8, 44.8, 126.5, 126.8, 128.6, 145.8, 174.5 ppm.

3,3-Diphenylpropionamide (11d): A mixture of $AlCl_3$ (0.5 g, 3.7 mmol) and **10d** (0.2 g, 1.4 mmol) in benzene (3 mL) was stirred at 25 °C for 4 h and after usual workup gave **11d** (0.298 g, 97%) as a white crystalline solid: M.p. 127−128 °C, ref.[42a] m.p. 125−126 °C. ^{1}H NMR: δ = 2.94 (d, *J* = 7.8 Hz, 2 H), 4.55 (t, *J* = 7.8 Hz, 1 H), 5.29 (br. s, 1 H), 5.41 (br. s, 1 H), 7.15−7.3 (m, 10 H) ppm.[42b] ^{13}C NMR: δ = 42.4, 47.2, 126.6, 127.7, 128.6, 143.6, 173.4 ppm.

***N*,*N*-Diethyl-3,3-diphenylpropionamide (11e). Method a:** A mixture of $AlCl_3$ (0.6 g, 4.5 mmol) and **10e** (0.4 g, 2 mmol) in benzene (4 mL) was stirred at 25 °C for 0.5 h and after workup gave **11e** (0.554 g, 100%) as a white crystalline solid: M.p. 77−78 °C, ref.[43] m.p. 76 °C. ^{1}H NMR: δ = 0.99 (t, *J* = 7.2 Hz, 3 H), 1.06 (t, *J* = 7.2 Hz, 3 H), 3.01 (d, *J* = 7.5 Hz, 2 H), 3.16 (q, *J* = 7.2 Hz, 2 H), 3.29 (q, *J* = 7.2 Hz, 2 H), 4.75 (t, *J* = 7.5 Hz, 1 H), 7.1−7.3 (m, 10 H) ppm. ^{13}C NMR: δ = 12.7, 14.2, 38.9, 40.2, 41.7, 47.1, 126.1, 127.8, 128.2, 144.1, 169.9 ppm. **Method b:** Compound **10e** (0.2 g, 1 mmol) was introduced into a mixture of triflic acid (1 g, 6.7 mmol) and benzene (1 mL) and the mixture was stirred at 25 °C for 15 h. After the reaction mixture had been poured over several grams of ice, the resulting mixture was extracted with diethyl ether. The organic phase was washed with water and aqueous ammonia, dried (Na_2SO_4) and concentrated to give **11e** (0.274 g, 99%).

4-(3,3-Diphenylpropionyl)morpholine (11f): A mixture of $AlCl_3$ (0.29 g, 2.15 mmol) and **10f** (0.15 g, 0.69 mmol) in benzene (3 mL) was stirred at 25 °C for 0.5 h and after usual workup gave **11f** (0.2039 g, 100%) as a white crystalline solid: M.p. 144−146 °C. ^{1}H NMR: δ = 3.04 (d, *J* = 7.6 Hz, 2 H), 3.29 (s, 4 H), 3.52 (s, 4 H), 4.67 (t, *J* = 7.6 Hz, 1 H), 7.15−7.3 (m, 10 H) ppm. ^{13}C NMR: δ = 38.5, 42, 46.2, 47.5, 66.4, 66.8, 126.5, 127.9, 128.6, 144, 169.9 ppm. $C_{19}H_{21}NO_2$ (295.4): calcd. C 77.3, H 7.2, N 4.7; found C 77.2, H 7.3, N 4.5.

3-(4-Methoxyphenyl)-3-phenylpropionamide (11g): A mixture of $AlCl_3$ (0.4 g, 3 mmol) and **10g** (0.1 g, 0.57 mmol) in benzene (3 mL) was vigorously stirred at 25 °C for 5 h and after workup gave **11g** (0.141 g, 98%) as a white solid: M.p. 141−143 °C, ref.[44] m.p. 140 °C. ^{1}H NMR: δ = 2.91 (d, *J* = 7.8 Hz, 2 H), 3.76 (s, 3 H), 4.51 (t, *J* = 7.8 Hz, 1 H), 5.25 (br. s, 1 H), 5.36 (br. s, 1 H), 6.81 (d, *J* = 8.1 Hz, 2 H), 7.1−7.3 (m, 7 H) ppm. ^{13}C NMR: δ = 42.7, 46.4, 55.2, 114.1, 126.5, 127.6, 128.6, 128.7, 135.6, 143.9, 158.2, 173.4 ppm.

3,3,3-Triphenylpropionamide (11h): A mixture of $AlCl_3$ (0.34 g, 2.5 mmol) and **10h** (0.09 g, 0.62 mmol) in benzene (2 mL) was stirred at 25 °C for 1.5 h. After usual workup the obtained residue was recrystallized from ethanol to provide **11h** (0.103 g, 55%) as a white crystalline solid: M.p. 193−194 °C, ref.[45a] m.p. 192 °C. ^{1}H NMR: δ = 3.61 (s, 2 H), 4.8 (br. s, 1 H), 5.4 (br. s, 1 H), 7.2−7.3 (m, 15 H) ppm .[45b] ^{13}C NMR: δ = 48.5, 55.9, 126.6, 128.2, 129.2, 146.1, 173.4 ppm.[45b]

Reactions with *o*-Dichlorobenzene were carried out similarly to the procedures described above (compound **10a** reacted at 130 °C). Subsequent silica gel chromatographic purification with CH_2Cl_2 gave products **12** (mixtures of isomers **12-1** and **12-2)** as colourless solids or viscous liquids.

3-(3,4-Dichlorophenyl)propionamide (12a-1) and 3-(2,3-Dichlorophenyl)propionamide (12a-2): Ratio 2:1. $C_9H_9Cl_2NO$ (218.1): calcd. C 49.6, H 4.2, N 6.4; found C 49.4, H 4.3, N 6.3. **Compound 12a-1:** ^{1}H NMR: δ = 2.51 (t, *J* = 7.4 Hz, 2 H), 2.93 (t, *J* = 7.4 Hz, 2 H), 5.5 (br. s, 1 H), 5.8 (br. s, 1 H), 7.05 (dd, *J* = 8.2, 2.1 Hz, 2 Hz, 1 H), 7.31 (d, *J* = 2.1 Hz, 2 Hz, 1 H), 7.35 (d, *J* = 8.2 Hz, 1 H) ppm. **Compound 12a-2:** ^{1}H NMR: δ = 2.55 (t, *J* = 7.4 Hz, 2 H), 3.13 (t, *J* = 7.4 Hz, 2 H), 5.6 (br. s, 1 H), 5.7 (br. s, 1 H), 7.07 (t, *J* = 7.6 Hz, 1 H), 7.13 (dd, *J* = 7.6 Hz, 2 Hz, 1 H), 7.26 (d, *J* = 7.6 Hz, 1 H) ppm.

3-(3,4-Dichlorophenyl)butyramide (12c-1) and 3-(2,3-Dichlorophenyl)butyramide (12c-2): Ratio 2.5:1. $C_{10}H_{11}Cl_2NO$ (232.1): calcd. C 51.8, H 4.8, N 6; found C 51.7, H 4.9, N 6.1. **Compound 12c-1:** ^{1}H NMR: δ = 1.31 (d, *J* = 6.9 Hz, 3 H), 2.3−2.6 (m, 2 H), 3.25 (m, 1 H), 5.7 (br. s, 1 H), 5.9 (br. s, 1 H), 7.15−7.3 (m, 3 H) ppm. **Compound 12c-2:** ^{1}H NMR: δ = 1.28 (d, *J* = 6.9 Hz, 3 H), 2.3−2.6 (m, 2 H), 3.8 (m, 1 H), 5.7 (br. s, 1 H), 6.1 (br. s, 1 H), 7.15−7.3 (m, 3 H) ppm.

3-(3,4-Dichlorophenyl)-3-phenylpropionamide (12d-1) and 3-(2,3-Dichlorophenyl)-3-phenylpropionamide (12d-2): Ratio 5:1. $C_{15}H_{13}Cl_2NO$ (294.2): calcd. C 61.2, H 4.5, N 4.8; found C 61, H 4.6, N 4.5. **Compound 12d-1:** ^{1}H NMR: δ = 2.88 (dd, *J* = 8.1 Hz, 1 Hz, 2 H), 4.51 (t, *J* = 8.1 Hz, 1 H), 5.7 (br. s, 1 H), 5.9 (br. s, 1 H), 7−7.3 (m, 8 H) ppm. ^{13}C NMR: δ = 41.8, 46.2, 126.7, 127, 127.6, 128.7, 128.9, 129.7, 130.5, 132.5, 142.5, 144, 173.2 ppm. **Compound 12d-2:** ^{1}H NMR: δ = 2.91 (dd, *J* = 8.1 Hz, 1 Hz, 2 H), 5.05 (t, *J* = 8.1 Hz, 1 H), 5.8 (br. s, 1 H), 6 (br. s, 1 H), 7−7.3 (m, 8 H) ppm.

3-(3,4-Dichlorophenyl)-*N*,*N*-diethyl-3-phenylpropionamide (12e-1) and 3-(2,3-Dichlorophenyl)-*N*,*N*-diethyl-3-phenylpropionamide (12e-2): Ratio 7:1. $C_{19}H_{21}Cl_2NO$ (350.3): calcd. C 65.1, H 6, N 4; found C 64.9, H 6.2, N 3.7. **Compound 12e-1:** ^{1}H NMR: δ NMR: δ = 0.99 (t, *J* = 7.2 Hz, 3 H), 1.08 (t, *J* = 7.2 Hz, 3 H), 2.98 (dd, *J* = 7.5 Hz, 1 Hz, 2 H), 3.21 (q, *J* = 7.2 Hz, 2 H), 3.31 (q, *J* = 7.2 Hz, 2 H), 4.7 (t, *J* = 7.5 Hz, 1 H), 7−7.3 (m, 8 H) ppm. ^{13}C NMR: δ = 12.9, 14.4, 38.8, 40.4, 46.3, 126.8, 127.5, 127.8, 128.5, 128.7, 129.8, 130.3, 132.3, 143.2, 144.7, 169.4 ppm. **Compound 12e-2:** ^{1}H NMR: δ = 0.99 (t, *J* = 7.2 Hz, 3 H), 1.08 (t, *J* = 7.2 Hz, 3 H), 3.01 (d, *J* = 7.5 Hz, 2 H), 3.21 (q, *J* = 7.2 Hz, 2 H), 3.31 (q, *J* = 7.2 Hz, 2 H), 5.21 (t, *J* = 7.5 Hz, 1 H), 7−7.3 (m, 8 H) ppm.

3-(3,4-Dichlorophenyl)-3-(4-methoxyphenyl)propionamide (12g-1) and 3-(2,3-Dichlorophenyl)-3-(4-methoxyphenyl)propionamide (12g-2): Ratio 5:1. $C_{16}H_{15}Cl_2NO_2$ (324.2): calcd. C 59.3, H 4.7, N 4.3; found C 58.7, H 4.9, N 3.9. **Compound 12g-1:** ^{1}H NMR: δ = 2.83 (dd, *J* = 7.7, 1.5 Hz, 2 H), 3.76 (s, 3 H), 4.47 (t, *J* = 7.7 Hz, 1 H), 5.5 (br. s, 1 H), 5.7 (br. s, 1 H), 6.8−7.3 (m, 7 H) ppm. ^{13}C NMR: δ = 42.1, 45.4, 55.3, 114.2, 127.2, 128.6, 128.9, 129.5, 130.5, 132.5, 134.4, 144.4, 158.5, 173 ppm. **Compound 12g-2:** ^{1}H NMR: δ = 2.92 (dd, *J* = 7.7, 1.5 Hz, 2 H), 3.75 (s, 3 H), 4.97 (t, *J* = 7.7 Hz, 1 H), 5.5 (br. s, 1 H), 5.8 (br. s, 1 H), 6.8−7.3 (m, 7 H) ppm.

Reactions with Cyclohexane

Propionamide (13a): A mixture of $AlCl_3$ (1.4 g, 10.5 mmol) and **10a** (0.3 g, 3.5 mmol) in cyclohexane (4 mL) was stirred at 130 °C for 15 h. After cooling, the mixture was poured over several grams of ice and extracted with diethyl ether. The aqueous phase was separated and then concentrated to a volume of 4 mL, followed by extraction with $CHCl_3$ (5 × 10 mL). The organic phase was dried (Na_2SO_4) and concentrated to give a mixture of **10a** and **13a** (0.12 g, ratio 1:1). The mixture was separated by silica gel chromatography with CH_2Cl_2/acetone to provide **13a** (0.05 g, 16%): M.p. 80−81 °C (benzene/hexane), ref.[46a] m.p. 80.5−81.5 °C. ^{1}H NMR: δ = 1.09 (t, *J* = 7.1 Hz, 3 H), 2.2 (q, *J* = 7.1 Hz, 2 H), 5.9 (br. s,

1 H), 6.3 (br. s, 1 H) ppm.[46b] ^{13}C NMR: δ = 9.5, 28.9, 177.3 ppm.[46b]

2-Methylpropionamide (13b): A mixture of $AlCl_3$ (1.4 g, 10.5 mmol) and **10b** (0.3 g, 3.5 mmol) in cyclohexane (4 mL) was stirred at 130 °C for 5 h. After cooling, the mixture was poured over several grams of ice and extracted with CH_2Cl_2. The organic phase was separated, dried (Na_2SO_4) and concentrated to give the residue, which was washed with hexane to provide a mixture of **10b** and **13b** (ratio 2:1). The mixture was separated by silica gel chromatography with CH_2Cl_2/$CHCl_3$ to give **13b** (0.083 g, 27%): M.p. 128−130 °C, ref.[46a] m.p. 129.5−130 °C. ^{1}H NMR: δ = 1.15 (d, *J* = 7 Hz, 6 H), 2.39 (m, *J* = 7 Hz, 1 H), 5.9 (br. s, 2 H) ppm.[46c] ^{13}C NMR: δ = 18.6, 34.9, 179.9 ppm.[46c]

Butyramide (13c): A mixture of $AlCl_3$ (0.7 g, 5.2 mmol) and **10c** (0.11 g, 1.3 mmol) in cyclohexane (3 mL) was stirred at 130 °C for 1 h to provide, after usual workup and chromatographic purification, compound **13c** (0.105 g, 93%): M.p. 115−116 °C (benzene), ref.[46a] m.p. 115−116 °C. ^{1}H NMR: δ = 0.96 (t, *J* = 7.4 Hz, 3 H), 1.65 (m, 2 H), 2.19 (t, *J* = 7.3 Hz, 2 H) 5.5 (br. s, 1 H), 5.7 (br. s, 1 H) ppm.[46d] ^{13}C NMR: δ = 13.7, 18.9, 37.8, 175.7 ppm.

3-(4-Methoxyphenyl)propionamide (13g): Compound **10g** (0.1 g, 0.57 mmol) was added to a stirred mixture of $AlCl_3$ (0.37 g, 2.8 mmol) and CH_2Cl_2 (3 mL), followed by cyclohexane (1 mL). The resulting mixture was stirred at 25 °C for 7 h to give, after usual workup and chromatographic purification, compound **13g** (0.079 g, 78%): M.p. 126−127 °C ($CHCl_3$), ref.[47a] m.p. 125−126 °C. ^{1}H NMR: δ = 2.45 (t, *J* = 7.4 Hz, 2 H), 2.86 (t, *J* = 7.4 Hz, 2 H), 3.73 (s, 3 H), 5.7 (br. s, 2 H), 6.77 (d, *J* = 11.7 Hz, 2 H), 7.07 (d, *J* = 11.7 Hz, 2 H) ppm.[47b] ^{13}C NMR: δ = 30.5, 37.7, 55.2, 113.9, 129.2, 132.8, 158, 174.7 ppm.

4-Phenylcarbostyril (15). Method a: A mixture of $AlCl_3$ (0.07 g, 0.52 mmol) and **10i** (0.025 g, 0.11 mmol) in CH_2Cl_2 (4 mL) was stirred at 25 °C for 10 h. After usual workup, the obtained residue was purified by silica gel chromatography with $CHCl_3$ to give **15** (0.0153 g, 61%) as a white crystalline solid: M.p. 260 °C, ref.[23] m.p. 259−261 °C. ^{1}H NMR: δ = 6.75 (s, 1 H), 7.19 (t, *J* = 8.1 Hz, 1 H), 7.4−7.6 (m, 8 H) ppm.[48] ^{13}C NMR: δ = 117.1, 119.8, 120, 123, 126.8, 128.7, 128.9, 129, 131, 136.9, 138.7, 154.1, 163.9 ppm.[48]

Method b: A mixture of triflic acid (3 g, 20 mmol) and **10i** (0.12 g, 0.54 mmol) was stirred at 25 °C for 100 h. After the reaction mixture had been poured over several grams of ice, the resulting precipitate was filtered off and washed with water to provide **15** (0.1164 g, 97%).

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