JOC Article

Superacid-Catalyzed Reactions of Cinnamic Acids and the Role of Superelectrophiles[1]

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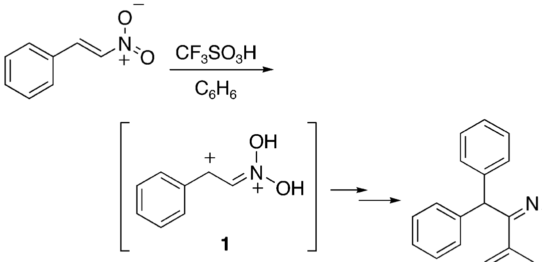
Received October 27, 2003

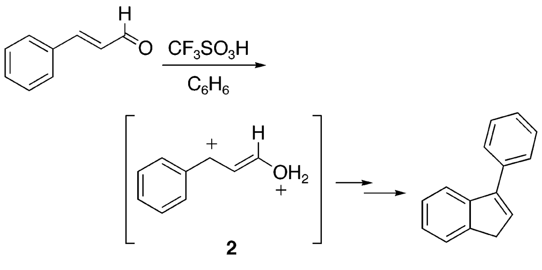
The chemistry of cinnamic acids and related compounds has been studied. In superacid-catalyzed reactions with arenes, two competing reaction mechanisms are proposed. Both mechanisms involve the formation of dicationic intermediates (superelectrophiles), and the reactions can lead to either chalcone-type products or indanone products. The direct observation of a dicationic species (by low-temperature ^{13}C NMR) is reported. We provide clear evidence that protonated carboxylic acid groups (or the corresponding acyl cation) can enhance the reactivity of an adjacent electrophilic center. Triflic acid is also found to be an effective acid catalyst for the direct synthesis of some electron-deficient chalcones and heterocyclic chalcones from cinnnamic acids.

Introduction

The importance of superelectrophilic intermediates has been recognized since Olah's pioneering studies in the 1970s.[2] Recent work has shown that superelectrophiles and related dicationic electrophiles can be exceedingly reactive and generally useful in synthetic chemistry.[3] For example, studies by Shudo and Ohwada demonstrated that nitroolefins and α,*β*-unsaturated aldehydes (eqs 1 and 2) can form highly reactive electrophiles in the Brønsted superacid, CF_3SO_3H (triflic acid, TfOH).[4,5]



(1)

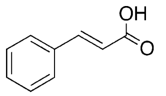


(2)

Diprotonated, superelectrophilic species **1** and **2** were proposed as intermediates in the conversions. Our own studies of the superacid-catalyzed reactions of α-ketoacids suggested the formation of dicationic intermediates from the protonation of carboxylic acids and adjacent ketone groups.[6] In the present study, we examine the electrophilic chemistry of cinnamic acids and related compounds. In addition to several new synthetic reactions, we also report the direct observation of a dicationic, superelectrophilic species by low-temperature ^{13}C NMR and propose a general mechanistic scheme in which diprotonated species are generated from cinnamic acids in superacidic media. Moreover, the results from this study provide further evidence that protonated carboxylic acid groups can strongly activate adjacent electrophilic sites.

Results

Cinnamic acid (**3a**) is a substance that was first reported in the 1800s, and its reactions with benzene and strong acids or superacids have been described.[7] It has



Cinnamic Acid (**3a**)

been noted in these earlier reports that cinnamic acid (**3a**) gives 3,3-diphenylpropionic acid from strong acid (H_2SO_4 or $AlCl_3$) reactions with benzene but gives 3-phenylindan-1-one (**4a**) from superacidic reactions (CF_3SO_3H

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[1] Presented in part at the National Meeting of the American Chemical Society: Rendy, R.; Zhang, Y.; McElrea, A.; Gomez, A.; Dang, H.; Klumpp, D. A. Superacid-Catalyzed Reactions of Cinnamic Acids and the Role of Superelectrophiles. In *Abstracts of Papers*, 225th National Meeting of the American Chemical Society, New Orleans, LA, March 2003; American Chemical Society: Washington, DC, 2003; Abstract ORGN 503.

[2] Olah, G. A.; Germain, A.; Lin, H. C.; Forsyth, D. *J. Am. Chem. Soc.* **1975**, *97*, 2928.

10.1021/jo030327t CCC: $27.50

or >3 equiv of $AlCl_3$). The 3-arylindan-1-ones are valuable pharmaceutical intermediates, and the synthesis of these products from cinnamic acids has been reported, both in the patent literature[7f] and in published manuscripts.[7e,g] In the case of the proprietary work, the synthesis of indanones requires two steps: a reaction of the cinnamic acid with H_2SO_4 and C_6H_6 to give a 3,3-diarylpropionic acid and then a reaction with chlorosulfonic acid to yield the cyclized product (an indanone).

To explore the synthetic scope of the reactions of cinnamic acids in superacid, a series of cinnamic acids were reacted with CF_3SO_3H (triflic acid, TfOH) and C_6H_6 (Table 1). In general, two major types of reactions were found to occur. Cinnamic acids with alkyl groups or weakly electron-withdrawing groups give the indanone products (**4a**,**h**,**i**,**g**,**e**) in good yields. With increased substitution by electron-withdrawing groups, a mixture of indanones and chalcones (**4j**/**5j**; **4k**/**5k**; **4l**/**5l**) are obtained.[8] When the aryl ring of cinnamic acid is substituted by strong electron-withdrawing groups, the chalcone products (**5b**,**c**,**d**,**m**,**n**) are obtained by acylation. In the cases of the heterocyclic derivatives **3p**−**q**, the heterocyclic ring is fully protonated in the TfOH and acts like a strong electron-withdrawing group. Interestingly, the nitro-substituted derivative (ortho regioisomer, **3o**) does not give product from the reaction, but instead the starting material is recovered. While the methyl-substituted cinnamic acid (**3r**) gives the indanone product (**4r**) in almost quantitative yield, the indene derivatives **16** and **17** give acylation products (entries 18 and 19). A series of 2-substituted cinnamic acids (**3s**−**u**) were also reacted with TfOH and benzene. Both **3s** and **3t** gave the cyclization products (indanones) **4s** and **4t**, respectively. However, the fluoro-substituted derivative (**3u**) did not react. This unexpected outcome is probably the result of a strong inductive effect involving the fluorine atom. In the case of **3v**, acylation is apparently the major reaction path, but the lactone **22** is formed in a secondary reaction. When the fluorenylidene derivative (**18**) is reacted with TfOH and C_6H_6, arylation and cyclization give the novel ketone (**23**). The results shown above demonstrate that cinnamic acids can be converted in superacid to either indanones or chalcones, depending on the cinnamic acid substituents.

The effects of substitutuents were further studied in reactions of cinnamic acid derivatives (**3a**−**h**, Table 2). When the cinnamic acid derivatives **3a**−**h** react with C_6H_6 in an excess of triflic acid, three types of products are observed and the product distributions are similar to those found in the above synthetic studies (Table 1). For the para-substituted cinnamic acids (**3a**,**e**−**h**), the 3-arylindanones (**4a**,**e**−**h**) are the major products. Chalcones (**5b**−**d**) are the only products in some cases (**3b**−**d**), and the propanones (**6a**,**e**−**h**) are also formed in varying amounts. When the substituents are compared, a consistent trend emerges: strongly electron-withdrawing groups favor arylation at the acyl carbon to give chalcones (**5b**−**d**), while other groups tend to favor the indanone cyclization products. A good correlation is seen between the relative product yields and the σ_p^+ values for the different substituents,[9] suggesting that indanone (**4a**−**h**) product formation involves the generation of positive charge adjacent to the aryl ring. Similar results are obtained with ortho-substituted cinnamic acids.

In studying the effect of acid strength on the electrophilic chemistry of cinnamic acids, a series of reactions were done with cinnamic acid **3a** and 3,3-diphenylpropionic acid (Table 3). With varying quantities of TfOH, it is seen that 1.1 equiv of TfOH acid gives a small amount (20%) of addition product (**7a**), but no indanone (**4a**) or propanone (**6a**) products. With an increasing amount of TfOH (3.0 equiv), cyclization product (**4a**) is observed, but the propanone (**6a**) product is still not formed. With increasing amounts of TfOH, the bulk acidity of the solution rises to near H_o −14 (pure TfOH), and the propanone (**6a**) begins to be formed as a significant product. The chalcone product (**5a**) is not observed as a product in any of the conversions, which is consistent with the earlier report that 1,3-diphenyl-2-propen-1-one (**5a**) gives the addition product **6a** from the reaction with TfOH and C_6H_6.[4] In a similar respect, the acidity of the medium can be varied using the CF_3SO_3H/CF_3CO_2H (TfOH/TFA) system designed by Shudo and Ohwada.[10] The addition product (**7a**) is formed at low acidity (H_o −2.7), while the indanone **4a** begins to be formed at higher acidities. The propanone product (**6a**) is only formed when the solution is superacidic ($H_o < -12$).

These results suggest that the indanone product (**4a**) arises from the cyclization of **7a**, and **7a** is an initial product from the reaction of cinnamic acid **3a** with TfOH and C_6H_6. When compound **7a** is reacted with TfOH (or weaker acids, $-14.1 < H_o < -10$) and C_6H_6, the indanone **4a** is the sole product (Table 3). Other considerations include: **7a** does not generate product **6a**; product **6a** is formed by an addition reaction involving chalcone (**5a**); product **4a** is stable under these reaction conditions. Thus, it is reasonable to conclude that cinnamic acid (**3a**) reacts with TfOH and C_6H_6 by two competing reaction paths. At high levels of acidity and at 25°C, cinnamic acid acylates benzene to yield chalcone products **5a**, while cinnamic acid also can undergo an addition reaction to yield **7a**. Olah and co-workers provided evidence that carboxylic acids may be diprotonated in superacid and the resulting dicationic species can generate the acyl

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(3) (a) Olah, G. A. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 2, 767. (b) Olah, G. A.; Laali, K. A.; Wang, Q.; Prakash, G. K. S. *Onium Ions*; Wiley: New York, 1998; Chapter 10.

(4) Ohwada, T.; Okabe, K.; Ohta, T.; Shudo, K. *Tetrahedron* **1990**, *46*, 7539. (b) See also, Shildneck, P. R. *Organic Syntheses*; Wiley: New York, 1943; Collect. Vol. II, p 236.

(5) Ohwada, T.; Ohta, T.; Shudo, K. *J. Am. Chem. Soc.* **1986**, *108*, 3092.

(6) Klumpp, D. A.; Garza, M.; Lau, S.; Shick, B.; Kantardjieff, K. *J. Org. Chem.* **1999**, *64*, 7635.

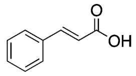
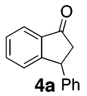
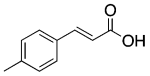
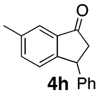
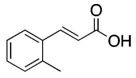
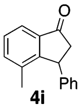
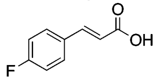
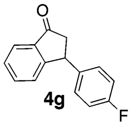
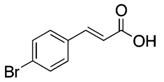
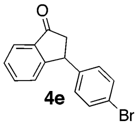
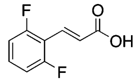
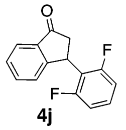
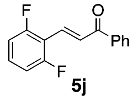
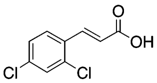
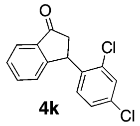
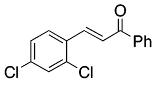
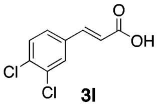
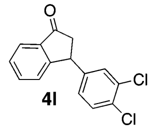
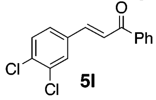
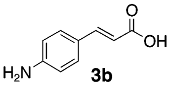
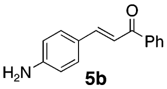
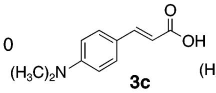
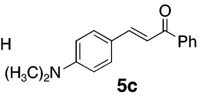
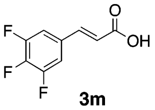
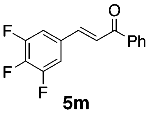
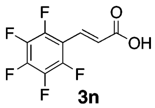
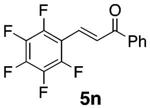
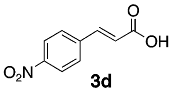
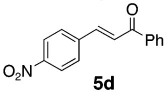
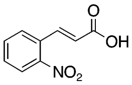
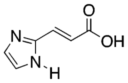
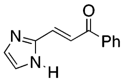
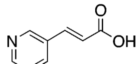
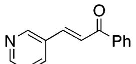
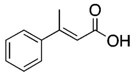
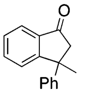
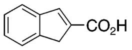
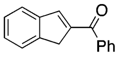
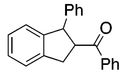
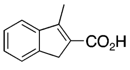
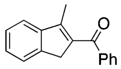
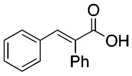
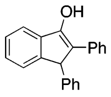
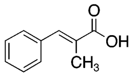
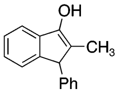
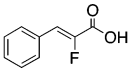
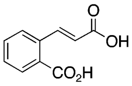
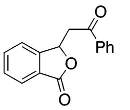
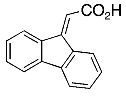
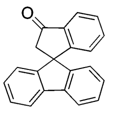
(7) (a) Koncos, R.; Friedman, B. S. In *Friedel−Crafts and Related Reactions*; Olah, G. A., Ed.; Wiley: New York, 1964; Vol 2, pp 318−320 and references cited therewithin. (b) Liebermann, C.; Hartmann, A. *Chem. Ber.* **1892**, *25*, 2124. (c) Simons, J. H.; Archer, S. *J. Am. Chem. Soc.* **1939**, *61*, 1521. (d) Dippy, J. F.; Young, J. T. *J. Chem. Soc.* **1952**, 1817. (e) Prakash, G. K. S.; Yan, P.; Torok, B.; Olah, G. A. *Catal. Lett.* **2003**, *87(3−4)*, 109. (f) Moussa, A. M.; Haider, R.; Taft, H.; Jurayj, J.; Wang, W.; Suh, H. International Patent No. PCT/US99/00225, 1999, International Publ. No. WO 99/35119. (g) Koelsch, C. F.; Hochmann, H.; Le Claire, C. D. *J. Am. Chem. Soc.* **1943**, *65*, 1521. (h) See also: Begitt, K.; Heesing, A. *Chem. Ber.* **1979**, *112*, 689.

(8) Trace quantities of the propanone products (**6j**−**l**) could also be detected by GCMS, however these minor products could not be isolated.

(9) (a) Okamato, Y.; Inukai, T.; Brown, H. C. *J. Am. Chem. Soc.* **1958**, *80*, 4969. (b) March, J. *Advanced Organic Chemistry*, 4th Ed; Wiley: New York, 1992; pp 279−280.

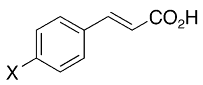
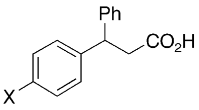
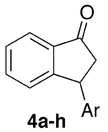
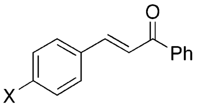
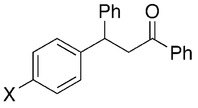
(10) Saito, S.; Saito, S.-i.; Ohwada, T.; Shudo, K. *Chem. Pharm. Bull.* **1991**, *39*, 2718.

TABLE 1. Products and Yields from the Reactions of Cinnamic Acids and Related compounds with CF_3SO_3H (100 equiv) and C_6H_6 at 25 °C[a–c]

ENTRY	STARTING MATERIAL	PRODUCT(S)	YIELD
1	 **3a**	 **4a**	68%
2	 **3h**	 **4h**	98%
3	 **3i**	 **4i**	95%
4	 **3g**	 **4g**	90%
5	 **3e**	 **4e**	61%
6	 **3j**	 **4j**	29%
		 **5j**	60%
7	 **3k**	 **4k**	80%
		 **5k**	19%
8	 **3l**	 **4l**	28%
		 **5l**	71%
9	 **3b**	 **5b**	69%
10	 **3c**	 **5c**	98%
11	 **3m**	 **5m**	97%
12	 **3n**	 **5n**	92%
13	 **3d**	 **5d**	85%
14	 **3o**	-------------	0%
15	 **3p**	 **5p**	61%
16	 **3q**	 **5q**	85%
17	 **3r**	 **4r**	96%
18	 **16**	 **19**	37%
		 **20**	55%
19	 **17**	 **21**	74%
20	 **3s**	 **4s**	97%
21	 **3t**	 **4t**	92%
22	 **3u**	-------------	0%
23	 **3v**	 **22**	85%
24	 **18**	 **23**	96%

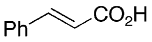
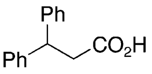
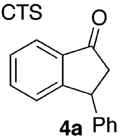
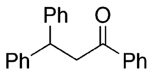
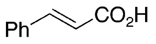
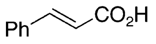
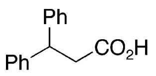
[a] Isolated yields of pure products. [b] Product **5p** isolated as the triflate salt; product **4t** exists as a mixture of keto−enol forms. [c] Products **4a**,**e** were obtained from reaction at −15 °C.

TABLE 2. Products and Relative Yields[a] from the Reactions of Para-Substituted Cinnamic Acids with C_6H_6 and CF_3SO_3H (100 equiv; 12 h at 25 °C)

 **3a-h**	σ_p^+	 **7a-h**	 **4a-h**	 **5a-h**	 **6a-h**
3b X = NO_2	0.79	0%	0% **4b**	100% **5b**	0% **6b**
3c X = $\overset{+}{N}H_3$	0.4[b]	0%	0% **4c**	100% **5c**	0% **6c**
3d X = $\overset{+}{N}H(CH_3)_2$	0.4[b]	0%	0% **4d**	100% **5d**	0% **6d**
3e X = Br	0.15	0%	78% **4e**	2% **5e**	20% **6e**
3f X = Cl	0.11	0%	85% **4f**	0% **5f**	15% **6f**
3g X = F	0.00	0%	92% **4g**	0% **5g**	8% **6g**
3a X = H	−0.07	0%	95% **4a**	0% **5a**	5% **6a**
3h X = CH_3	−0.31	0%	100% **4h**[c]	0% **5h**	0% **6h**

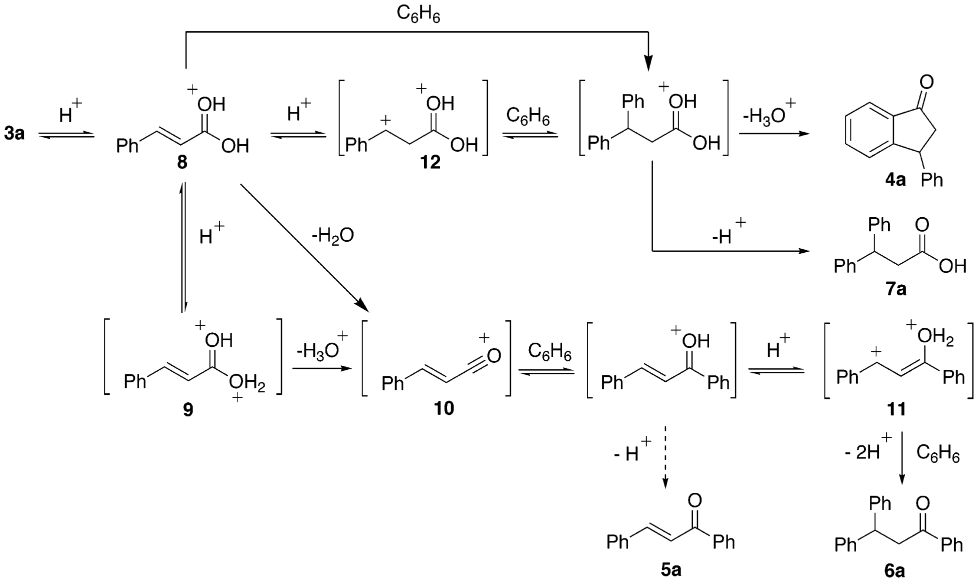
[a] Relative yields were determined by GC−FID analysis; the products are assumed to have FID response factors near unit. [b] These values are estimated from the value of 0.41 for the trimethylammonium group; starting materials (**3c**,**d**) are the amino-substituted cinnamic acids. [c] Cyclization produces exclusively 5-methyl-3-phenyl-1-indanone (**4h**).

TABLE 3. Products and Relative Yields[a] from the Reactions of Cinnamic or 3,3-Diphenylpropionic Acid with C_6H_6 and Acid

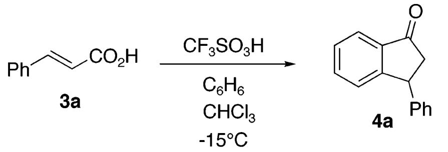
STARTING MATERIAL	EQUIVALENTS OF ACID	H_O	PRODUCTS  **3a**	 **7a**	 **4a**	 **6a**
 **3a**	1.1 TfOH	...	70%	20%	0%	0%
	3.0 TfOH	...	27%	47%	23%	0%
	10 TfOH	...	0%	0%	88%	9%
	100 TfOH	-14.1	0%	0%	57%	26%
 **3a**	100 TFA	-2.7	68%	8%	0%	0%
	100 TfOH:TFA (5:95)	-10.6	2%	0%	85%	0%
	100 TfOH:TFA (45:55)	-11.5	0%	0%	96%	0%
	100 TfOH:TFA (90:10)	-12.5	0%	0%	83%	16%
	100 TfOH	-14.1	0%	0%	57%	26%
 **7a**	100 TFA	-2.7	0%	100%	0%	0%
	100 TfOH:TFA (5:95)	-10.6	0%	0%	100%	0%
	100 TfOH:TFA (45:55)	-11.5	0%	0%	100%	0%
	100 TfOH:TFA (90:10)	-12.5	0%	0%	100%	0%
	100 TfOH	-14.1	0%	0%	100%	0%

[a] Determined by GC−MS and GC−FID; TFA, CF_3CO_2H; TfOH, CF_3SO_3H.

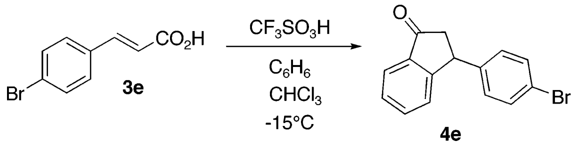
SCHEME 1



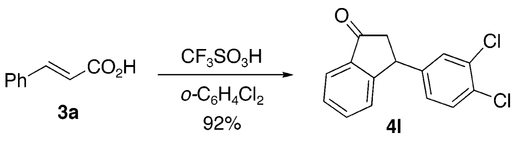
cation at temperatures above −10 °C.[11] When cinnamic acids **3a** or **3e** are reacted with TfOH, C_6H_6, and $CHCl_3$ (as an anti-freeze) at −15 °C, indanones **4a** and **4e** are the only products formed (eqs 3 and 4). In contrast, both **3a** and **3e** give significant quantities of the propanone (**6a**, **e**) products at 25 °C. This suggests that the chalcone (**5**) products are formed by the reactions of the appropriate acyl cations. When cinnamic acid is reacted with *o*-dichloro benzene and excess of TfOH (25 °C), the indanone product (**4l**) is formed as the major product in 92% yield (eq 5). Since *o*-dichlorobenzene is a significantly deactivated arene, this indicates that cinnamic acid forms a highly reactive electrophile in superacidic solution. Products **4e** and **4l** also clearly show the preference for cyclization toward the more electron-rich aryl ring.



(3)



(4)



(5)

Several earlier reports have described the acid-catalyzed conversions of chalcone (**5a**) to give the indanone product (**4a**).[12] These reactions employed forcing conditions (130−180 °C) in large excess of acid ($AlCl_3$−NaCl or polyphosphoric acid). The reactions are thought to occur by an electrocyclization mechanism involving the protonated (or Lewis acid complexed) chalcone. The cyclization is also similar to the superacid-catalyzed reaction of 1-phenyl-2-propen-1-ones to give 2-phenyl-1-indanone,[13] which was studied recently by Shudo and Ohwada. However, in the case of cinnamic acid **3a**, the indanone product **4a** does not arise from cyclization of the intermediate chalcone product (**5a**). Chalcones **5a** and **5j** were reacted with a large excess (100 equiv) of TfOH (60 h at 25 °C) and no indanone products were formed. As noted previously, chalcone **5a** is known to react preferentially with benzene in superacidic medium and yield **6a**.[4]

Based on these considerations, we propose a mechanism that invokes the formation of diprotonated, superelectrophilic intermediates (Scheme 1; alternative monocationic routes are also shown). The first protonation occurs at the carboxyl group to give the carboxonium ion (**8**). Arnett estimated the pK_b of cinnamic acid to be about −6,[14] so it is reasonable to assume that cinnamic acid is fully protonated in superacid. This suggests an equilibrium is established with the diprotonated species (**9**) which cleaves to the acyl cation (**10**). The acyl cation then acylates benzene and rapidly reacts with a second benzene (via **11**)[4] to yield product **6a**. Given the formation of product **7a** at relatively low acid strength ($H_o = -2.7$), it appears that some phenylation of cinnamic acid can occur by reaction of the monoprotonated species (**8**). However, arylation of cinnamic acid with *o*-dichlorobenzene suggests a more reactive species is involved (in superacidic reactions). It is proposed that arylation at the olefinic site occurs through a diprotonated intermediate. Two likely diprotonated species could lead to the indanone product (**4a**): the *O,O*-diprotonated species (**9**) or the *C,O*-diprotonated species (**12**). Protonation of the carboxyl group is followed by protonation at the olefinic

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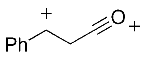
[11] Prakash, G. K. S.; Rasul, G.; Liang, G.; Olah, G. A. *J. Phys. Chem.* **1996**, *100*, 15805.

[12] Allen, J. M.; Johnson, K. M.; Jones, J. F.; Shotter, R. G. *Tetrahedron* **1977**, *33*, 2083.

[13] Suzuki, T.; Ohwada, T.; Shudo, K. *J. Am. Chem. Soc.* **1997**, *119*, 6774.

[14] Arnett, E. M. *Prog. Phys. Org. Chem.* **1963**, *1*, 233.

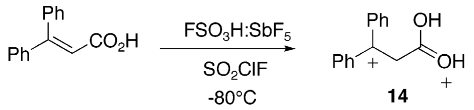
position to give dication **12** and reaction with benzene gives the phenylated product which then cyclizes to **4a**. Alternatively, dication **9** could react with benzene at the 3-position by delocalization of the positive charge leading to **4a** (not shown). Ab initio calculations were done on dications **9** and **12** at the B3LYP/6-311g (d,p)//B3LYP/6-311g (d,p) level of theory[15] and two stationary points were found (see the Supporting Information). Structures **9** and **12** were characterized as true minima with **12** (the *C,O*-diprotonated species) residing at the global energy minimum and 28 kcal·mol^{-1} more stable than **9** (the *O,O*-diprotonated species). These calculated gas-phase structures and energies suggest that the preferred reaction pathway for cinnamic acid involves initial protonation at the carboxylic acid group followed by protonation at the C-2 to give dication **12**. A recent report also proposes the formation of dication **13** in this reaction.[7e] While formation of the acyl-carbenium dication (**13**) is plausible, intermediate **13** is not likely in the reactions done at low temperatures (<−10 °C), due to the slow formation of the acyl cation. Interestingly, cinnamic acid (**3a**) favors the *C,O*-diprotonated (**12**) structure, while the analogous systems of cinnamaldehyde (eq 2) and β-nitrostyrene (eq 1), appear to prefer the *O,O*-diprotonated structures (**1** and **2**).



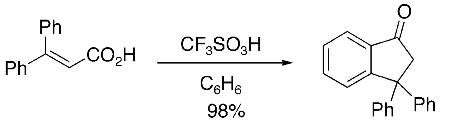
13

When the results from Table 2 are considered, the proposed mechanism (Scheme 1) offers an explanation for the relationship between the $\sigma_p{}^+$ values and relative product yields. The compounds with large positive $\sigma_p{}^+$ values (**3b**−**d**) have strong electron-withdrawing substituents, and these starting materials give the chalcone products (**5b**−**d**) exclusively. The nitro and ammonium substituents of compounds **3b**−**d** would be expected to destabilize intermediates generating benzylic, carbocationic centers (similar to **12**, Scheme 1), and this tends to favor intermediates such as **9** and **10**, which lead to acylation reactions and the chalcones (**5b**−**d**). Moreover, the nitro and ammonium groups should destabilize intermediates such as **11**, so phenylation of the chalcones (**5b**−**d**) to give the propanones (**6b**−**d**) does not occur. With compound **3h**, the methyl substituent is slightly electron donating (large negative $\sigma_p{}^+$ value) and the benzylic intermediate (analogous to **12**) is significantly stabilized. The stabilization of the benzylic intermediate leads to rapid phenylation and cyclization to **4h**, while the formation of the acyl cation (similar to **10**) is a considerably slower process so neither the chalcone (**5h**) or propanone (**6h**) is produced (Table 2). The compounds with intermediate $\sigma_p{}^+$ values ($0.15 > \sigma_p{}^+ > -0.07$; **3a**,**e**−**g**) give products from both mechanistic pathways. Only in the case of **3e** (Br substituent) is there any chalcone product (**5e**) detected, and the other cinnamic acids give the respective propanones (**6a**,**f**,**g**) as products. The compounds having intermediate $\sigma_p{}^+$ values should be able to form intermediates such as **11**, and thus react with benzene to give the propanone products (**6a**,**f**,**g**).

Using low temperature ^{13}C NMR spectroscopy, an effort was made to directly observe the diprotonated species arising from cinnamic acid (**3a**) in superacid, however no cleanly formed species could be observed from $FSO_3H/SbF_5/SO_2ClF$ (1:1:1) solution. When β-phenylcinnamic acid is mixed with $FSO_3H/SbF_5/SO_2ClF$ (1:1:1) at −80 °C, a reddish-orange solution is produced and a well resolved ^{13}C NMR spectrum is seen (Figure 1). Seven resonance signals appear in the spectrum: 40.4, 132.0, 139.9, 143.4, 150.1, 186.8, and 201.2 ppm. The signals are consistent with the *C,O*-diprotonated species (**14**, eq 6). The resonance signal at 201.2 ppm is assigned to the diphenylmethyl carbocation center, which suggests extensive delocalization of charge into the phenyl rings. The signal at 186.8 ppm is assigned to the carboxylic carbon of **14**, which is comparable to the carboxonium signals from protonated acetic acid ($CH_3CO_2H_2{}^+$, 191 ppm) and benzoic acid ($C_6H_5CO_2H_2{}^+$, 181 ppm).[16] At −80 °C, the signal at 143.4 ppm is significantly broadened, but upon warming to −60 to −40 °C, the signal sharpens. This suggests that there is restricted rotation about the phenyl groups at low temperature. At the warmer temperatures, new ^{13}C signals (about 10−15 new signals) also begin to appear, indicating that dication **14** decomposes at temperatures warmer than −80 °C. According to calculations done at the B3LYP/6-311G (d,p)//B3LYP/6-311G (d,p) level of theory, the *C,O*-diprotonated species (**14**) is considerably more stable (by 30 kcal·mol^{-1}) than the corresponding *O,O*-diprotonated species (**15**, see Supporting Information). Reaction of β-phenylcinnamic acid with TfOH and C_6H_6 gives a nearly quantitative yield of the indanone product (eq 7). The indanone product likely arises from phenylation of the dication **14** at the benzylic position and subsequent cyclization.[6]



(6)



(7)

In addition to cinnamic acids, we examined the superacid-catalyzed reactions of related carboxylic acids with benzene. Cyclopropanes are known to exhibit chemistry

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[15] (a) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, R. E.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; M. Head-Gordon, M.; Pople, J. A. *Gaussian 98*, revision A.5; Gaussian, Inc.: Pittsburgh, PA, 1998. (b) For details of the computational studies, see the Supporting Information.

[16] (a) Olah, G. A.; White, A. M. *J. Am. Chem. Soc.* **1967**, *89*, 7072. (b) Other peak assignments: 40.4 ppm, methylene carbon; 132.0 ppm, meta-position; 139.9 ppm, ortho-position; 143.4 ppm, ipso-position; 150.1 ppm, para-position. These assignments are made by comparison to other related diphenylmethyl cations, see: Olah, G. A.; Prakash, G. K. S.; Liang, G.; Westerman, P. W.; Kunde, K.; Chandrasekhar, J.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1980**, *102*, 4485.

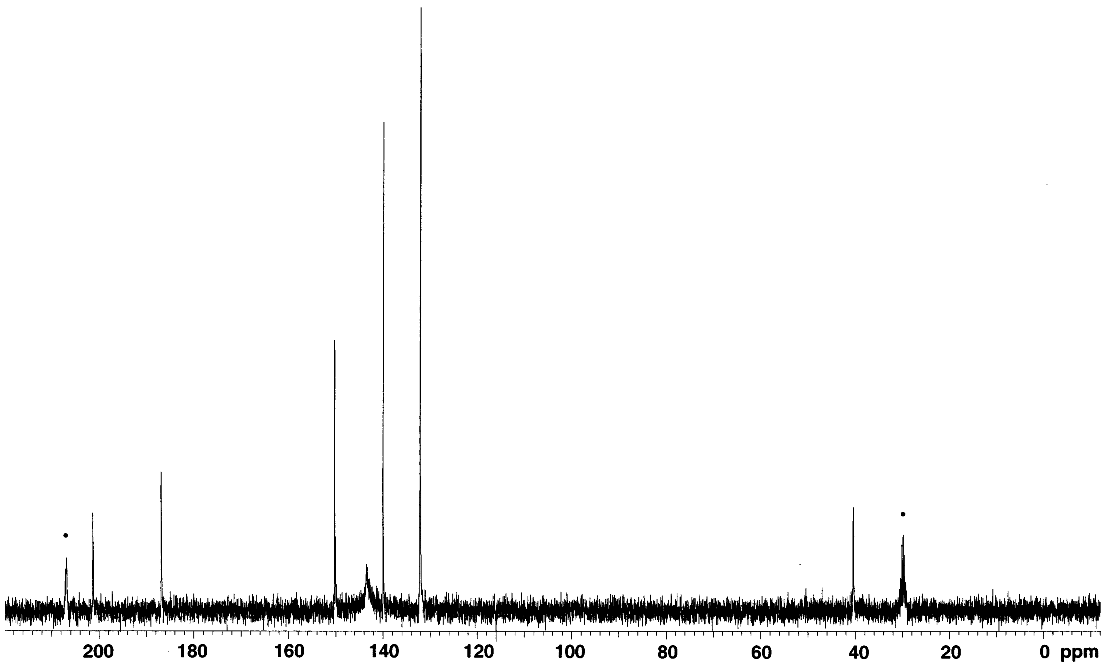
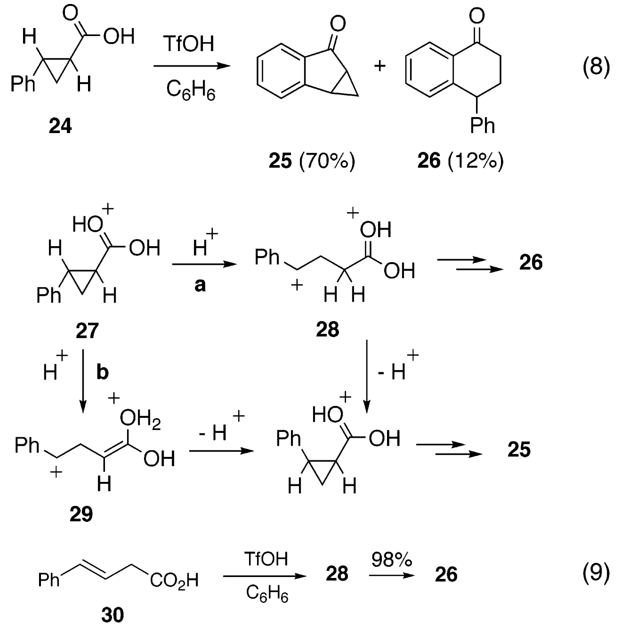


FIGURE 1. ^{13}C NMR spectrum of superelectrophilic dication **14** in FSOH/SbF$_5$/SO$_2$ClF at −80 °C (●, acetone-d_6 peak).

SCHEME 2



similar to olefins.[17] When *trans*-2-phenyl-1-cyclopropanecarboxylic acid (**24**) is mixed with triflic acid and benzene, two products are observed (Scheme 2, eq 8). The major product (**25**) has been prepared previously by the reaction of *trans*-2-phenylcyclopropanecarbonyl chloride with AlCl$_3$,[18] but to our knowledge, this is the first report of a direct transformation of carboxylic acid **24** to the product **25** via Brønsted acid catalysis. Additionally, a small amount of 4-phenyl-1-tetralone (**26**) is formed in the conversion. It was verified in a subsequent experiment that **25** is not converted to **26** when mixed with TfOH and C$_6$H$_6$.

Protonated carboxylic acids typically have pK_a values around −6 to −7, which roughly corresponds to the H_o value at half-protonation. Pure triflic acid is estimated to be H_o −14.1, so carboxylic acid **24** is fully protonated in this superacid, and equilibration with the diprotonated intermediates is plausible (Scheme 2). Protonation of the acid group gives ion **27** and this species could conceivably be protonated at the cyclopropyl ring (route a) to give **28**, or a second protonation at the acid group could give the ring opening reaction (route b) and yield the dication **29**.[20] Both ions (**28** and **29**) could undergo ring closure and acylation reactions leading to product **25**, while phenylation of **28** would then yield **26** by intramolecular acylation. When dication **28** is directly generated from the reaction of compound **31** in TfOH and benzene, product **26** is formed quantitatively (eq 9). Computational studies also indicate that dication **28** is considerably more stable than dication **29** (by more than 30 kcal·mol^{-1}), suggesting that direct ring protonation may be favored (route a, Scheme 2). Although the reaction of **24** in TfOH is consistent with the formation of dications, the monocationic species including acyl cations cannot be ruled out as possible intermediates.[18, 19]

When phenylpropionic acid (**31**) is reacted with TfOH and C$_6$H$_6$, 3,3-diphenylindanone (**32**) is formed quantitatively (Scheme 3). This conversion also involves diprotonated species such as **33** and **14**. Theoretical studies suggest that protonation occurs at the carboxyl group and then at the C-2 position. Dication **33** is estimated to be more than 30 kcal·mol^{-1} more stable than the dication (**34**; see the Supporting Information) arising from double protonation of the carboxylic acid group. Intermediate **14**

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[17] Boche, G., Walborsky, H. M. In *Cyclopropane Derived Reactive Intermediates*; Patai, S., Rappoport, Z., Eds.; Wiley: New York: 1990.

[18] Elling, G. R.; Hahn, R. C.; Schwab, G. *J. Am. Chem. Soc.* **1973**, *95*, 5659.

[19] A similar monocationic ring opening has been proposed recently, see: Mohanta, P. K.; Peruncheralathan, S.; Ila, H.; Junjappa, H. *J. Org. Chem.* **2001**, *66*, 1503.

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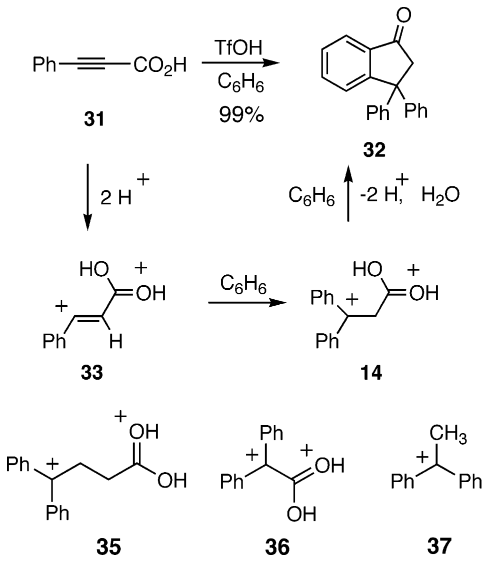
SCHEME 3



is similar to dicationic species (i.e., **35**) which are thought to be involved in the reactions of α-ketoacids with superacid and benzene,[6] and **36** which is generated from ionization of benzylic acid in superacid and undergoes electrocyclization.[20] Dications **14** and **35**−**36** all exhibit significantly enhanced reactivity when compared to the analogous monocation (**37**). In the cases of **14** and **35**, the dications are sufficiently electrophilic to react with benzene, while under the same conditions (TfOH/C_6H_6) cation **37** is stable.[21] Clearly, the protonated carboxylic acid group enhances the reactivity of the adjacent carbocation center in these dicationic species. This activation is similar to that shown for ammonium groups,[22] protonated *N*-heteroaromatic groups,[23] and phosphonium groups,[24] and it is consistent with Olah's general concept of superelectrophilic activation.[3a]

Although the protonated carboxylic acid group can enhance the reactivity of an adjacent carbocationic site, it appears that this activation drops off with increasing distance between the two cationic charge centers. When compound **30** is reacted with a large excess of TfOH (500 equiv) and *o*-dichlorobenzene, little arylation-cyclization product is formed. Even at elevated temperature, compound **30** is recovered almost quantitatively. This is in contrast to the chemistry of cinnamic acid (**3a**), which gives a good conversion to product **4l** from TfOH and *o*-dichlorobenzene (eq 5). We and others have noted that the reactivities of dicationic systems can be influenced by the proximity of the charge centers.[25] In the case of compound **30**, reaction with superacid gives the 1,5-dication (**28**, Scheme 2), while cinnamic acid forms the 1,4-dication (**12**, Scheme 1). The increased separation of cationic charge centers renders the 1,5-dication (**28**) unreactive toward the deactivated arene, *o*-dichlorobenzene.

Summary

We have found that cinnamic acids and related compounds form highly reactive electrophilic species in the Brønsted superacid CF_3SO_3H. The cinnamic acids give chalcone products when the aryl group is deactivated by substituents or give indanone products when the aryl group is not deactivated by substituents. Chalcone product formation can also be suppressed by low temperatures (−15 °C). Experimental evidence suggests two competing reaction mechanisms.[26] We propose that cinnamic acids and related compounds form diprotonated species in CF_3SO_3H and the protonated carboxylic acid group can activate adjacent electrophilic groups (like carbocations). In some cases, diprotonated cinnamic acids can be directly observed. Triflic acid is shown in the present results to be an effective catalyst in the preparation of either substituted indanones or chalcones from cinnamic acids.[27]

Acknowledgment. We are grateful to the NIH for support of this work (SO6GM53933-0251). We are indebted to Professors George A. Olah and G. K. Surya Prakash for the use of their NMR instruments at the University of Southern California. We also thank the reviewers for their helpful comments.

Supporting Information Available: ^1H and ^{13}C NMR spectra for new compounds (**4h**, **4j**, **5m**, **19**, **20**, and **23**), general experimental procedures, and computation data for dications **9**, **12**, **14**, **15**, **28**, **30**, **34**, and **35**. This material is available free of charge via the Internet at http://pubs.acs.org.

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