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Preparation of Trifluoromethylated Dihydrocoumarins, Indanones, and Arylpropanoic Acids by Tandem Superacidic Activation of 2-(Trifluoromethyl)acrylic Acid with Arenes

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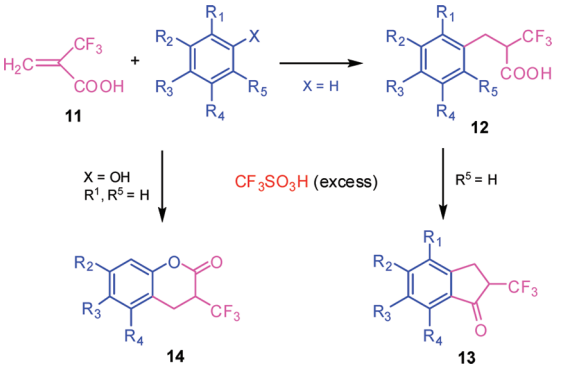
Received December 11, 2009



Indanones and coumarins are important intermediates for the convenient synthesis of many pharmaceutical and biologically active compounds. Fluoroorganics play a vital role in the design of very effective therapeutics due to significant enhancement in their lipophilicity, bioavailability, and fast uptake by the presence of fluorine in these molecules. Herein, we report an efficient one-pot synthesis of trifluoromethylated arylpropanoic acids, indanones, and dihydrocoumarins using Friedel−Crafts alkylation or tandem Friedel−Crafts alkylation−cycloacylation of arenes/phenols with 2-(trifluoromethyl)acrylic acid under superacidic conditions using trifluoromethanesulfonic acid. The results have been rationalized by the structure energy calculations of the involved reaction intermediates using ab initio theoretical methods.

Introduction

1-Indanone **1** and dihydrocoumarin (DHC) **6** ring systems constitute the core structures of many biologically important compounds. 1-Indanones are present in cytotoxic natural compound pterosines **2**,[1] the potent and selective COX-2 inhibitor flosulide **3**,[2] and the acetylcholinesterase inhibitor donepezil hydrochloride **4**, used for the treatment of Alzheimer's disease[3] (Figure 1). 1-Indanones have also been used as intermediates in the synthesis of sulindac **5a**, a nonsteroidal anti-inflammatory drug (NSAID),[4a−c] and other novel biologically important compounds.[4d,e−g] 1-Indanones are also important synthetic precursors for the synthesis of the substituted indenyl ligand, which is used in a broad range of metallocene catalysts **5b** for olefin polymerization.[5] A number of synthetic approaches have been reported for the synthesis of the 1-indanone ring system.

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DOI: 10.1021/jo9026275 Published on Web 03/10/2010

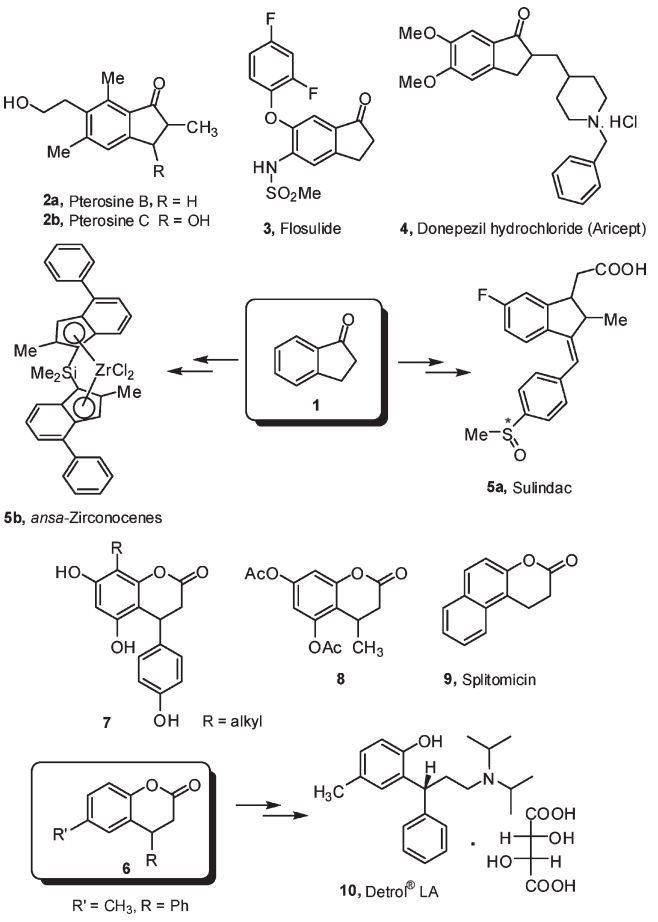

FIGURE 1. Biologically active 1-indanones and coumarins and their use as synthetic precursors.

Major methods for the synthesis of 1-indanones are based on Friedel−Crafts reaction,[6] Pd-catalyzed annulation methodology,[7] tandem Knoevenagel condensation−cycloalkylation process,[8] photochemical process,[9] and ring-closing metathesis.[10] However, little attention has been paid for the synthesis of trifluoromethylated 1-indanones. Trifluoromethylated 1-indanones have been previously prepared through electrophilic trifluoromethylation of silyl enol ether[11a] or enolate anion of 1-indanones.[11b]

3,4-Dihydro-4-arylcoumarins (neoflavonoids) are present in natural compounds such as calomelanols.[12] Polyphenolic compound **7** shows biological activity similar to estrogen.[13] Diacetoxy dihydrocoumarin **8** is a protein transacetylase compound.[14] Splitomicin **9** and its analogues are known to be Sir2 inhibitors.[15] Natural dihydrocoumarins (DHC) are of great interest in the flavor industry as well.[16] Furthermore, DHCs have been used extensively as precursors for the synthesis of important bioactive compounds such as Detrol LA (tolterodine tartrate) **10**, which is a muscarine receptor antagonist used for the treatment of urinary bladder disorder (Figure 1).[17]

The synthesis of the 3,4-dihydrocoumarin ring system has been accomplished in many ways, such as hydroarylation of cinnamic acids with phenols in presence of strong acids,[18] the catalytic hydrogenation of coumarins,[19] reaction of 5-alkylidene Meldrum's acids with phenol,[20] Baeyer−Villiger oxidation of 1-indanones,[21] and palladium-catalyzed cyclocarbonylation of 2-vinylphenols,[22a] etc.[22b−d] Fluorine substitution, in particular, the presence of trifluoromethyl group in organic compounds, often changes their physicochemical and biological properties significantly.[23] Knowing the importance of dihydrocoumarin and indanone ring systems, one-pot synthesis of trifluoromethylated dihydrocoumarins

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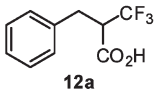
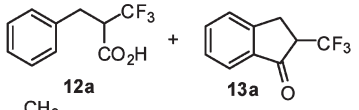
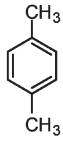
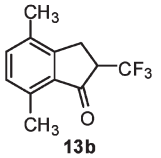
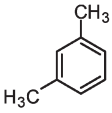
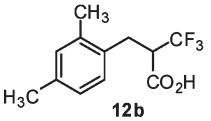
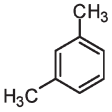
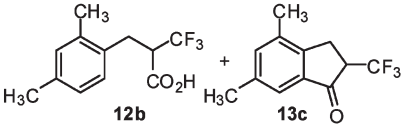
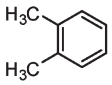
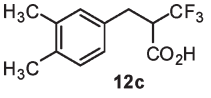
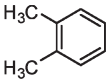
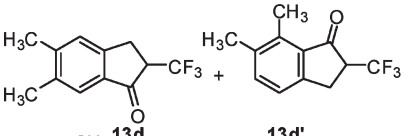
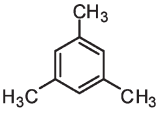
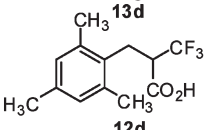
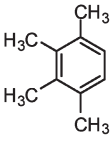
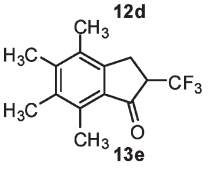
TABLE 1. Triflic Acid Catalyzed Preparation of 2-Trifluoromethylindanones and 2-Trifluoromethyl-3-arylpropanoic Acids

Entry	Ar	Temp (°C)	Time (h)	Products	Yield (%)
1*		45	7	 **12a**	68
2		70	24	 **12a** + **13a**	6, 80
3		RT	4	 **13b**	90
4		RT	4	 **12b**	76
5		70	24	 **12b** + **13c**	28, 70
6		RT	2	 **12c**	85
7		70	24	 **13d** + **13d'**	50, 33
8		RT	5	 **12d**	70
9		RT	3	 **13e**	95

*Conversion was 88%.

and indanones using trifluoromethyl-containing building blocks would be highly desirable.

Herein, we report an efficient direct synthesis of 3-arylpropanoic acids, 2-trifluoromethyl-1-indanones, and 3-trifluoromethyl-3,4-dihydrocoumarins through superacidic trifluoromethanesulfonic acid (triflic acid) catalyzed condensation of 2-(trifluoromethyl)acrylic acid (**11**) with aromatics. 3-Phenylpropanoic acids are important intermediates in the synthesis of bioactive compounds such as anti-AIDS, nonsteroidal, anti-inflammatory, and antipsychotic drugs.[24] Since the α-position to the carboxylate moiety has a significant influence on the biological activity of the compounds, the synthesis of α-trifluoromethylated carboxylic acids are important[25] and can be achieved easily by the developed methodology. The synthetic results have been augmented with theoritical calculations of the structure and energy of respective protonated and diprotonated 2-(trifluoromethyl)acrylic and 2-methylacrylic acids.

Results and Discussion

The nature of the products isolated during the superacid induced reaction of 2-(trifluoromethyl)acrylic acid (**11**) with arenes is highly dependent on the reaction conditions. For

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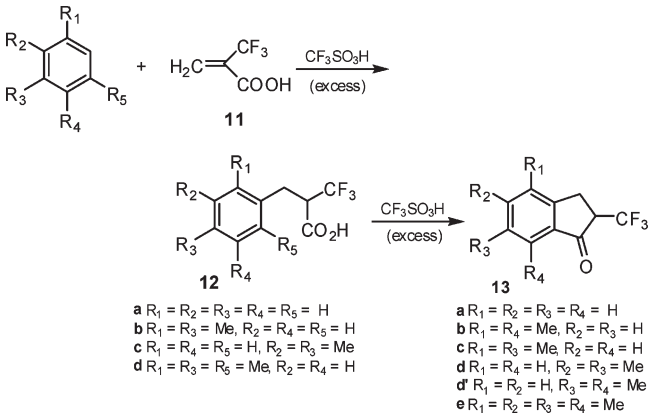
SCHEME 1. Triflic Acid Catalyzed Synthesis of 2-Trifluoromethyl-3-aryl-1-Propanoic Acids (12) and 2-Trifluoromethyl-1-indanones (13)

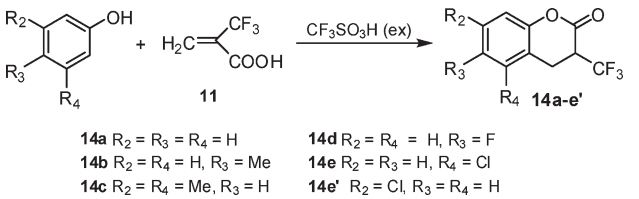


example, reaction of **11** with benzene at 45 °C resulted in 2-trifluoromethyl-3-phenyl propanoic acid (**12a**) as the only isolated product after 7 h (Table 1, entry 1). When the temperature was increased to 70 °C, the cyclized product 2-trifluoromethyl-1-indanone (**13a**) was obtained in 80% yield along with a small amount (6%) of 2-trifluoromethyl-3-phenylpropanoic acid (**12a**) (Table 1, entry 2). This indicates that acid **12** formed by intermolecular Friedel−Crafts alkylation can undergo Friedel−Crafts intramolecular cycloacylation at higher temperature to form the indanone **13**. Therefore, this reaction can be properly tuned and optimized for the selective preparation of trifluoromethylated indanones or propanoic acids (Scheme 1, Table 1) under suitable reaction conditions. However, none of these products were obtained when the reaction was repeated using weaker acid such as methanesulfonic acid showing the higher acidity requirement for the reaction.

Reaction of toluene with 2-(trifluoromethyl)acrylic acid in excess triflic acid led to a mixture of products, which could not be separated pure. *p*-Xylene at room temperature afforded indanone **13b** in 90% yield (Table 1, entry 3). No arylpropanoic acid was isolated. However, it is interesting to note that the reaction of *m*-xylene under similar conditions gave rise to the corresponding arylpropanoic acid **12b** only. When the temperature was increased to 70 °C, the major product was indanone **13c** (Table 1, entry 5). At room temperature, reaction of *o*-xylene also led to arylpropanoic acid **12c** as the only product as observed in the case of *m*-xylene. When the temperature was increased to 70 °C, the trifluoromethylated indanones (**13d** and **13d′**) were obtained in 50% and 33% yields, respectively. Highly reactive mesitylene, at room temperature, provided only arylpropanoic acid **12d** due to the absence of free *ortho* position for further cyclization (Table 1, entry 8). However, reaction of 1,2,3,4-tetramethylbenzene afforded the corresponding indanone **13e** at room temperature in high yield (Table 1, entry 9).

Reactions of phenol and its derivatives with 2-(trifluoromethyl)acrylic acid (**11**) in the presence of excess triflic acid gave rise to 3,4-dihydro-3-trifluoromethyl-2*H*-1-benzopyran-2-ones (3,4-dihydrocoumarins) **14** in a single step in high yield and purity (Scheme 2). Condensation of phenol with 2-(trifluoromethyl)acrylic acid (**11**) at room temperature gave the expected trifluoromethylated 3,4-dihydrocoumarin **14a**

SCHEME 2. Triflic Acid Catalyzed Reaction of 2-(Trifluoromethyl)acrylic Acid with Phenols



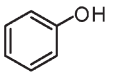
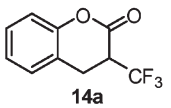
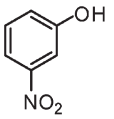
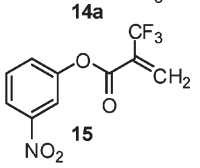
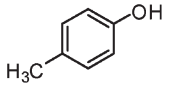
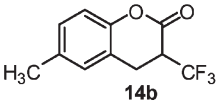
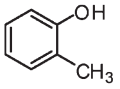
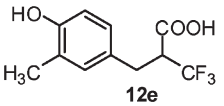
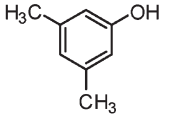
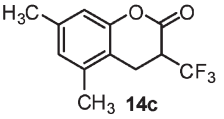
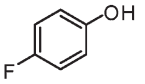
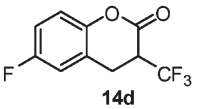
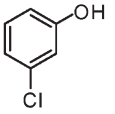
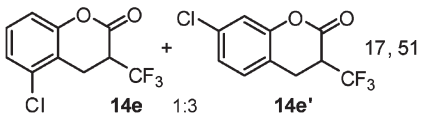
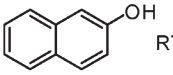
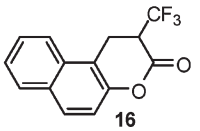
in 80% yield after 7 h. Activated phenol such as *p*-cresol with **11** gave coumarin **14b** in a shorter reaction time (4 h) at room temperature (Table 2, entry 3). However, deactivated phenols such as 3-nitrophenol gave only the uncyclized vinyl aryl ester **15** as the final product even at 55 °C after 48 h (Table 2, entry 2).

Compared to *p*-cresol (which possesses "uncongested" *ortho* position that can participate in cyclization), condensation of 3,5-dimethylphenol with **11** was found to be slower due to the steric effect imparted by the methyl group at the *ortho* position to the cyclization center (Table 2, entry 5). Reaction of 3-chlorophenol gave a mixture of *ortho*- and *para*-cyclized products (**14e**, **14e′**) with high *para* selectivity as expected (Table 2, entry 7). Condensation of 2-naphthol with **11** proceeded smoothly at room temperature with complete conversion after 5 h yielding a splitomicin analogue bearing a CF_3 group (**16**) in excellent yield (Table 2, entry 8). To the best of our knowledge, synthesis of a splitomicin analogue bearing a CF_3 has not been reported. Unlike 2-naphthol, the reaction with 1-naphthol at room temperature was much slower, and an unidentified mixture of products was obtained when the reaction was attempted at 70 °C over 24 h.

For a better comparison, Friedel−Crafts reactions of different arenes with 2-methylacrylic acid (**17**, the methyl analogue of **11**) in the presence of excess triflic acid have been studied. Along with the corresponding indanones (**18**), 2-methyl-1,3-diaryl-1-propanone (**19**) and vinyl aryl ketone (**20**) were also obtained (Scheme 3). No arylpropanoic acids were isolated. The results are summarized in (Table 3).

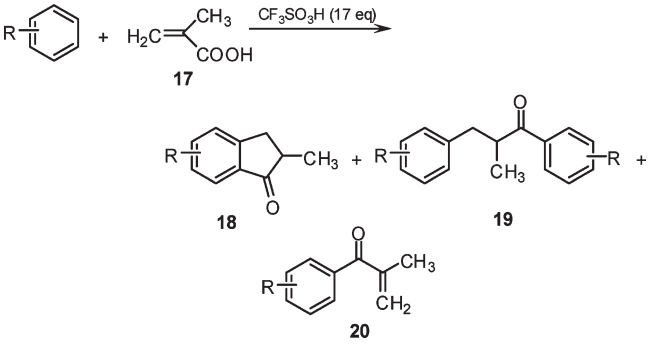
The reaction of benzene with 2-methylacrylic acid (**17**) at 75 °C afforded 2-methyl-1-indanone **18a** in 93% yield (Table 3, entry 1). Lowering the reaction temperature to 45 °C gave rise to same product in 12−42% yield, whereas 2-(trifluoromethyl)acrylic acid (**11**) gave 2-trifluoromethyl-3-arylpropanoic acid **13a** as the only product under similar reaction conditions (Table 1). Activated arenes such as *o*-xylene and *p*-xylene undergo successive intermolecular Friedel−Crafts alkylation and acylation affording the corresponding 2-methyl-1,3-diaryl-1-propanone (**19**, 25−35%) along with indanones (**18**, 12−45%) in moderate yields. With *p*-xylene, 2-(trifluoromethyl)acrylic acid (**11**) afforded indanone **13b** as the only product under similar reaction conditions (Table 1, entry 3), and with *o*-xylene the corresponding arylpropanoic acid **12c** was the only product (Table 1, entry 6). With mesitylene, the reaction was not clean. Reaction of phenol with 2-methylacrylic acid (**17**) at room temperature did not lead to coumarin derivatives. Rather, the acylated product **20** was formed exclusively along with a trace of unknown compounds (Table 3, entry 4). In contrast, condensation of 2-(trifluoromethyl)-acrylic acid (**11**) with phenols, as discussed, afforded 3,4-dihydrocoumarin **14** as the only products in most cases (Table 2).

TABLE 2. Triflic Acid Catalyzed Preparation of 3,4-Dihydro-3-trifluoromethyl-2*H*-1-benzopyrane-2-ones

Entry	Phenol	Temp (°C)	Time (h)	Products	Yield (%)
1		RT	7	 **14a**	84
2		55	48	 **15**	15
3		RT	4	 **14b**	91
4*		RT	4	 **12e**	50
5*		RT	12	 **14c**	60
6		50	24	 **14d**	65
7		35	24	 **14e** 1:3 **14e'**	17, 51
8		RT	5	 **16**	95

*Conversion was 80%.

SCHEME 3. Triflic Acid Catalyzed Reaction of 2-Methylacrylic Acid with Arenes

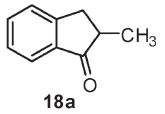
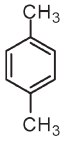
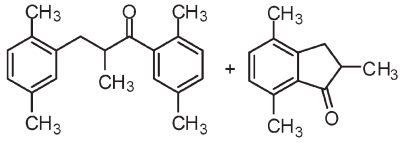
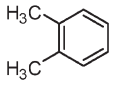
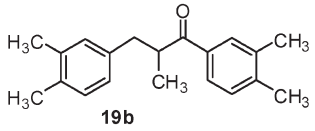
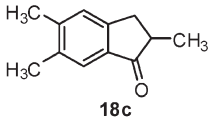
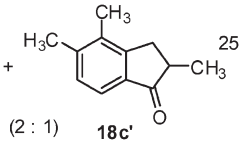
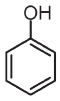
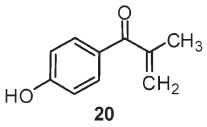


Calculated Structures and Energies of Protonated 2-(Trifluoromethyl)acrylic Acid ($H_2C{=}C(CF_3)COOH$) and Their Comparison with Protonated 2-Methylacrylic Acid ($H_2C{=}C(CH_3)COOH$). To study the mechanistic details and the nature of intermediates involved in the synthetic tranformations in superacid medium, computational studies and calculations on protonated trifluoromethyl as well as methyl acrylic acids (**11**, **17**) were performed using the Gaussian 03 program.[26] The geometry optimizations were performed at the MP2/6-31G** level. Vibrational frequencies at the MP2/6-31G**//MP2/6-31G** level were used to characterize stationary points as minima [number of imaginary frequency (NIMAG) = 0] and to evaluate zero-point vibrational energies (ZPE) which were scaled by a factor of 0.95.[27] For MP2/6-31G** structures further geometry optimizations were carried out at the MP2/cc-pVTZ level. Final energies were computed at the MP2/cc-pVTZ //MP2/cc-pVTZ + ZPE level.

(26) Gaussian 03, Revision C.02: Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. Gaussian, Inc., Wallingford, CT, 2004.

(27) Scott, A. P.; Radom, L. *J. Phys. Chem.* **1996**, *100*, 16502.

TABLE 3. Products of Triflic Acid Catalyzed Reaction of 2-Methylacrylic Acid with Arenes

Entry*	Arene	Temp (°C)	Time (h)	Products	Yield (%)
1		75	24	 **18a**	93
2		RT	4	 **19a** + **18b**	35, 12
3		RT	3	 **19b**	
				 **18c** (2 : 1)  **18c'**	25, 42, 21
4		RT	3	 **20**	72

*Unidentified products were found for entries 2−4.

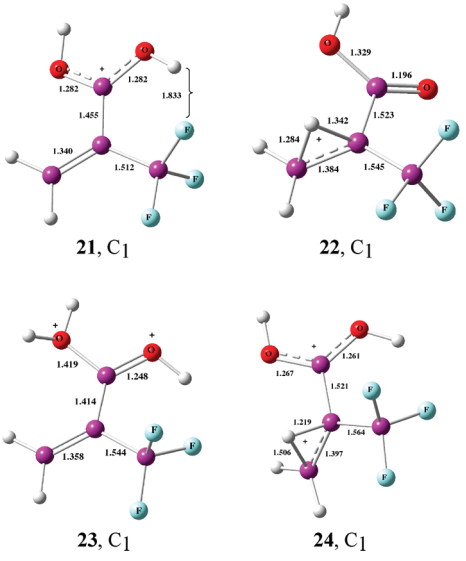


FIGURE 2. MP2/cc-pVTZ-calculated structure of **21**−**24**.

Two structures of protonated 2-(trifluoromethyl)acrylic acid, oxygen protonated **21** and C=C protonated **22**, were found to be minima on the potential energy surface at the MP2/6-31G** and MP2/cc-pVTZ levels (Figure 2). The C_α protonated structure does not correspond to a minimum and converted into **22** upon optimization. Similarly, the C_β protonated structure also does not correspond to a minimum and converted into same **22** upon optimization. The structure **21** is the global minimum being 43.2 kcal/mol more stable than **22** (Table 4). The calculated C_α=C_β and C_α−C-(CO) distances of **21** are 1.340 Å and 1.455 Å, respectively.

TABLE 4. Total Energies (−au), ZPE,[a] and Relative Energies (kcal/mol)[b]

	MP2/6-31G**	ZPE	MP2/cc-pvtz	rel energy
21	602.97091	52.0	603.64129	0.0
22	602.89892	49.2	603.56803	43.2
23	603.02016	56.5	603.68555	0.0
24	603.01807	57.3	603.68490	1.2
25	305.92691	65.8	306.24742	0.0
26	305.88702	63.0	306.20398	24.5
27	306.00374	69.1	306.32034	0.0
28	305.98964	71.4	306.30655	11.0

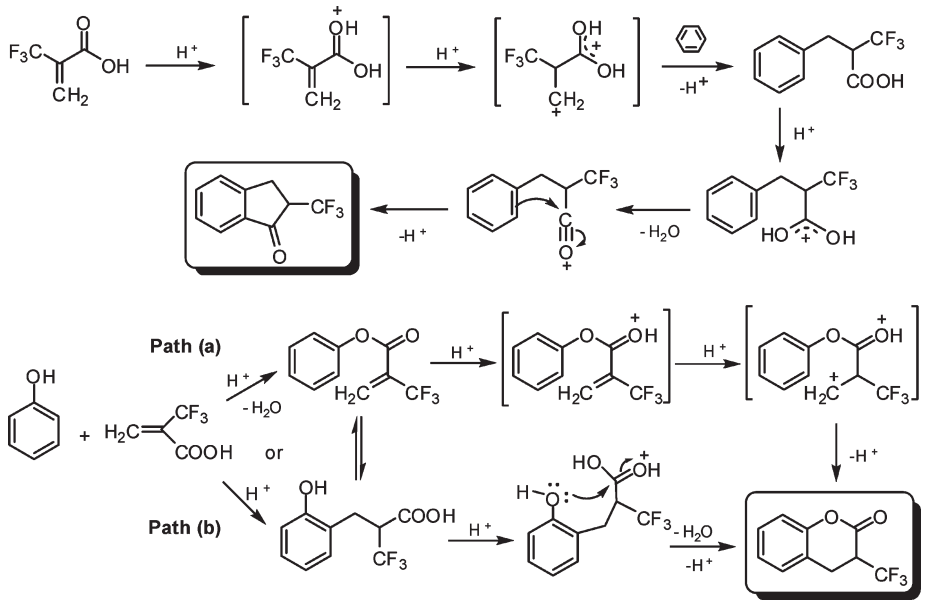
[a]Zero-point vibrational energies (ZPE) at MP2/6-31G**//MP2/6-31G** scaled by a factor of 0.95. [b]Relative energy at MP2/cc-pVTZ//MP2/cc-pVTZ + ZPE level.

The C=C protonated **22** is characterized as a hydrogen-bridged structure involving a 2e−3c bond.

Two isomeric diprotonated 2-(trifluoromethyl)acrylic acid dications, O,O-diprotonated **23** and O- and C=C diprotonated **24** were located as minima (Figure 2). The structure **23** is only 1.2 kcal/mol more stable than **24** (Table 4). The central C−C bond length of 1.414 Å in **23** is significantly shorter than the corresponding central C−C bond length of **21** by about 0.05 Å. This is due to enhanced conjugation between the C_α=C_β double bond and the C=O bond in **23**. The structure **24** contains a carbonium ion adjacent to a carboxonium ion center. Thus, the structure can be considered as a carbonium- carboxonium dication. Thus, both diprotonated 2-(trifluoromethyl)-acrylic acid dications **23** and **24** can be considered as superelectrophiles[28] with greatly increased electrophilic

(28) (a) Olah, G. A. Klumpp, D. A. *Superelectrophiles and Their Chemistry*; Wiley-Interscience: Hoboken, NJ, 2008. (b) Olah, G. A.; Klumpp, D. A. *Acc. Chem. Res.* **2004**, *37*, 211. (c) Olah, G. A. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 767.

SCHEME 4. Suggested Mechanism for the Formation of Indanones and Dihydrocoumarins from 2-(Trifluoromethyl)acrylic Acid and Arenes/Phenols



reactivity compared to their parent monoprotonated monocations.

For comparison, we have also calculated structures of methyl analog of protonated 2-(trifluoromethyl)acrylic acid, i.e., 2-methylacrylic acid at the same level. However, in the latter case, the C_β-protonated structure **26** in addition to the O-protonated **25** were found to be minima on the potential energy surface (Figure 3). The C_α carbon protonated structure does not correspond to a minimum and converted into **25** upon optimization. The structure **25** is 24.5 kcal/mol more stable than **26** (Table 4). The structure **26** is in fact a carboxyl-substituted tertiary carbenium ion.

Two isomeric diprotonated 2-methylacrylic acid dications, O,O-diprotonated **27**, and O- and C_β diprotonated **28** were located as minima (Figure 3). The structure **27** is substantially more stable than the structure **28** by 11.0 kcal/mol (Table 4). The structure **28** contains a carbenium ion adjacent to a carboxonium ion center. Thus, the structure can be considered as a carbenium−carboxonium dication.

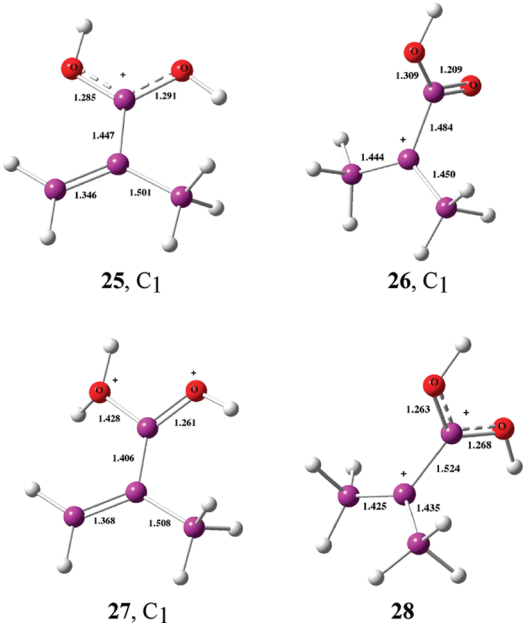


FIGURE 3. MP2/cc-pVTZ-calculated structure of **25**−**28**.

The suggested mechanism for the formation of indanones based on theoretical calculations involves initial protonation of the carbonyl group, which results in the activation of the double bond in the acrylic acid. Further protosolvation would lead to superelectrophilic dications in excess of triflic acid followed by intermolecular Friedel−Crafts alkylation of the arenes to give the corresponding arylpropanoic acids. Further protonation of the resulting arylpropanoic acids lead to cyclization through intramolecular Friedel−Crafts acylation. There are two possible mechanistic pathways for the reaction of phenols. Path (a)[18a] involves the esterification of the phenols with 2-trifluoromethyl acrylic acid to the corresponding vinylic aryl ester, followed by protosolvation and formation of superelectrophilic dicationic intemediates. Subsequent ring closure through intramolecular Friedel−Crafts cyclization (similar to electrocyclization in Nazarov reaction generally catalyzed by excess strong Lewis or Brønsted acids) leads to the coumarin ring.[6c,29] Path (b)[18b,e] involves Friedel−Crafts alkylation at *ortho* position to hydroxyl group to form *β*-(2-hydroxyphenyl)-α-trifluoromethylpropanoic acid, followed by dehydrative cyclization (Scheme 4).

Conclusion

In summary, we have developed a novel and efficient route to trifluoromethylated dihydrocoumarins, indanones, and arylpropanoic acids based on superacid induced Friedel−Crafts-type reaction of 2-(trifluoromethyl)acrylic acid with arenes. This manifests the use of 2-(trifluoromethyl)acrylic

(29) Suzuki, T.; Ohwada, T.; Shudo, K. *J. Am. Chem. Soc.* **1997**, *119*, 6774.

acid as a highly useful synthetic precursor for the synthesis of variety of new biologically important trifluoromethylated heterocycles and carbocycles. Reactivity profiles of both 2-(trifluoromethyl)acrylic acid and 2-methylacrylic acid toward various arenes in triflic acid medium have also been studied using computational methods. Computational studies and calculations suggest the possible involvement of reactive dicationic intermediates formed under superacidic conditions and support the mechanistic pathways involved in these reactions.

Experimental Section

General Procedure A. Triflic Acid Catalyzed Reactions of 2-(Trifluoromethyl)acrylic Acid with Arenes for the Synthesis of 2-Trifluoromethyl-1-indanones and 2-Trifluoromethyl-3-arylpropanoic Acids. 2-(Trifluoromethyl)acrylic acid (0.28 g, 2 mmol) was mixed with excess of arene (10 mmol) in a pressure tube. After the mixture was cooled to 0 °C, triflic acid (3 mL, 34 mmol) was slowly added and the pressure tube was closed. The mixture was stirred for the required period of time at room temperature or higher temperatures (Table 1). Progress of the reaction was monitored by TLC (4:1 hexane/ethyl acetate) and ^{19}F NMR spectroscopy. After the reaction was complete the mixture was poured over ice/water (~25 g) and extracted with CH_2Cl_2 (3 × 15 mL). The organic extracts were combined, washed with water, and dried over anhydrous $MgSO_4$. The solvent was removed by vacuum evaporation, and crude products were purified by column chromatography on silica gel (70−230 mesh) using hexane/ethyl acetate as eluent. The products were characterized by spectral analysis (NMR, GC−MS, and HRMS).

3-Phenyl-2-trifluoromethylpropanoic Acid (12a). Prepared from the reaction of compound **11** and benzene at 45 °C using general procedure A in 68% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.11−3.21 (m, 2H), 3.38−3.50 (m, 1H), 7.17−7.20 (m, 2H), 7.24−7.32 (m, 3H), 9.12 (br, 1H); ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 32.0 (q, $^3J_{(C-F)}$ = 2.29 Hz), 52.2 (q, $^2J_{(C-F)}$ = 27.47 Hz), 124.3 (q, $^1J_{(C-F)}$ = 280.76 Hz), 127.3, 128.7, 128.8, 135.80, 172.1 (q, $^3J_{(C-F)}$ = 3.05 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ −68.64 (d, $J_{(H-F)}$ = 7.63 Hz). HRMS (ESI): m/z calcd for $C_{10}H_8F_3O_2$ (M − 1) 217.0482, obsd 217.0480.

2-Trifluoromethyl-1-indanone (13a). Prepared from the reaction of compound **11** and benzene at 70 °C using general procedure A in 80% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.31−3.50 (m, 3H), 7.44 (t, J = 7.45 Hz, 1H), 7.19 (d, J = 7.90 Hz, 1H), 7.67 (t, J = 7.45 Hz, 1H), 7.82 (d, J = 7.90 Hz, 1H). ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 27.6 (q, $^3J_{(C-F)}$ = 3.00 Hz), 49.7 (q, $^2J_{(C-F)}$ = 27.43 Hz), 124.70, 124.9 (q, $^1J_{(C-F)}$ = 278.60 Hz), 126.4, 128.2, 135.8, 152.1, 196.8. ^{19}F NMR (376 MHz, $CDCl_3$): δ −68.23 (d, $J_{(H-F)}$ = 9.15 Hz). GC−MS (EI): m/z 200.9 (M^+). HRMS (EI): m/z calcd for $C_{10}H_7F_3O$ 200.0449, obsd 200.0448.

General Procedure B. Triflic Acid Catalyzed Reactions of 2-(Trifluoromethyl)acrylic Acid with Phenols for the Synthesis of 3-Trifluoromethyl-3,4-dihydrocoumarins. 2-(Trifluoromethyl)-acrylic acid (0.28 g, 2 mmol) and phenols (2.2 mmol) were dissolved in CH_2Cl_2 (1 mL) in a pressure tube. After the mixture was cooled to 0 °C, triflic acid (3 mL, 34 mmol) was slowly added. The pressure tube was closed, and the mixture was stirred for the required period of time at room temperature or higher temperatures depending on the substrate (Table 2). Progress of the reactions was monitored by TLC (5:3 hexane/ethyl acetate) and ^{19}F NMR spectroscopy. After the reaction was complete the mixture was poured over ice/water (~25 g) and extracted with CH_2Cl_2 (3 × 15 mL). The organic extracts were combined, washed with water, and dried over anhydrous $MgSO_4$. The solvent was removed by vacuum evaporation, and crude products were purified with column chromatography on silica gel (70−230 mesh) using hexane/ethyl acetate as eluent. The products were characterized by spectral analysis (NMR, GC−MS, and HRMS).

6-Methyl-3-trifluoromethyl-3,4-dihydrocoumarin (14b). Prepared by the reaction of **11** with *p*-cresol at room temperature using general procedure B gave **14b** in 91% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.33 (s, 3H), 3.18 (d, J = 9.15 Hz, 2H), 3.35−3.46 (m, 1H), 6.94 (d, J = 8.24 1H), 7.04 (s, 1H), 7.08−7.11 (m, 1H). ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 20.6, 24.3 (q, $^3J_{(C-F)}$ = 2.29 Hz), 43.9 (q, $^2J_{(C-F)}$ = 28.99 Hz), 116.4, 119.3, 123.8 (q, $^1J_{(C-F)}$ = 278.72 Hz), 128.5, 129.5, 134.9, 148.8, 161.8. ^{19}F NMR (376 MHz, $CDCl_3$): δ −69.25 (d, $J_{(H-F)}$ = 8.10 Hz). GC−MS (EI): m/z 230.6 (M^+). HRMS (EI): m/z calcd for $C_{11}H_9F_3O_2$ 230.0555, obsd 230.0546.

General Procedure C. Triflic Acid Catalyzed Reactions of 2-Methylacrylic Acid with Arenes. 2-Methylacrylic acid (0.26 g, 3 mmol) was mixed with an excess of arene (15 mmol) in a pressure tube. After the mixture was cooled to 0 °C, triflic acid (4.5 mL, 51 mmol) was slowly added and the pressure tube was closed. The mixture was stirred for the required period of time at room temperature or higher temperatures (Table 3). Progress of the reaction was monitored by TLC (4:1 hexane/ethyl acetate). After the reaction was complete, the mixture was poured over ice/water (~25 g) and extracted with CH_2Cl_2 (3 × 15 mL). The organic extracts were combined, washed with water, and dried over anhydrous $MgSO_4$. The solvent was removed by vacuum evaporation, and crude products were purified by column chromatography on silica gel (70−230 mesh) using hexane/ethyl acetate as eluent. The products were characterized by spectral analysis (NMR, GC−MS, and HRMS).

2-Methyl-1-indanone (18a). Prepared by the reaction of **17** with benzene at 75 °C using general procedure C in 93% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.30 (d, J = 7.32 Hz, 3H), 2.64−2.73 (m, 2H), 3.34−3.41 (m, 1H),7.34 (td, J = 7.42, 0.73 Hz, 1H), 7.43 (dt, J = 7.69, 0.82 Hz, 1H), 7.56 (td, J = 7.41, 1.10 Hz, 1H), 7.73 (d, J = 7.69 Hz, 1H). ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 16.0, 34.7, 41.7, 123.7, 126.3, 127.1, 134.5, 136.1, 153.2, 209.2. GC−MS (EI): m/z 147.6 (M^+).

1,3-Bis(2,5-dimethylphenyl)-2-methyl-1-propanone (19a). Prepared by reaction of **17** with *p*-xylene at room temperature by using general procedure C in 35% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.16 (d, J = 6.96 Hz, 3H), 2.24 (s, 3H), 2.26 (s, 3H), 2.27 (s, 3H), 2.34 (s, 3H), 2.61 (dd, J = 13.73, 7.87 Hz, 1H), 3.08 (dd, J = 13.73, 6.41 Hz, 1H) 3.47−3.56 (m, 1H), 6.88−6.93 (m, 2H), 7.00 (d, J = 7.69 Hz, 1H), 7.06−7.11 (m, 3H). ^{13}C NMR (100.5 MHz, $CDCl_3$): δ 16.9, 19.0, 20.0, 20.8, 20.8, 36.2, 44.9, 126.9, 128.0, 130.1, 130.6, 131.3, 131.4, 132.8, 134.2, 134.8, 135.1, 137.9, 138.7 208.6. HRMS (EI): m/z calcd for $C_{20}H_{24}O$ 280.1827, observed 280.1823.

Acknowledgment. The support of Loker Hydrocarbon Research Institute is gratefully acknowledged.

Supporting Information Available: Experimental procedures, ^{1}H, ^{13}C, and ^{19}F NMR, and HRMS of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.