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# Unexpected Migration and Oxidative Cyclization of Substituted 2-Acetophenone Triflates under Basic Conditions: Synthetic and Mechanistic Insights

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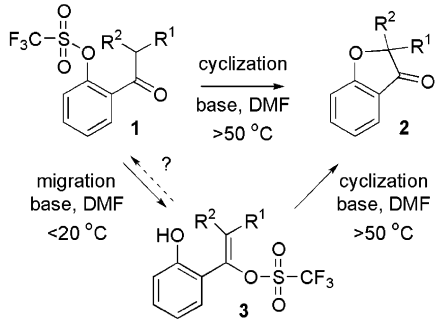
Oxidative ring closure of alkyl-substituted 2-hydroxyacetophenone trifluoromethanesulfonate esters (triflates) occurs upon exposure to base in anaerobic DMF at 20−90 °C. Alkyl substitution is required for ring closure. A migrated enol triflate product forms at lower temperature in high yield via migration of the trifluoromethanesulfonate in the unsubstituted and monoalkyl-substituted cases. The alkyl-substituted enol triflates also enter into the benzofuran-3-one ring-forming process under thermal cyclization conditions. Potential mechanistic pathways are evaluated.

## Introduction

While studying the chemistry of alkyl-substituted 2-hydroxyacetophenone trifluoromethanesulfonic esters (triflates) **1**, we observed an unexpected yet facile conversion of mono- and dialkyl-substituted ketones **1** to 2-substituted benzofuran-3-ones **2** (Scheme 1). The conversion is thermally induced in polar solvents such as DMF and $CH_3CN$ under anaerobic conditions in the presence of base. In addition, unsubstituted and monosubstituted ketones yield their corresponding enol triflate isomers **3** at low temperatures. When warmed under basic anaerobic conditions (50−90 °C), monosubstituted enol isomers **3**, but not unsubstituted substrates, are also readily converted to the corresponding benzofuran-3-ones **2**.

The reactions yielding isomers **3** and benzofuran-3-ones **2** are useful alternatives to existing methods for synthesizing both 2-hydroxyacetophenone enol triflates and substituted benzofuran-3-ones.[1] Indeed, the ability to control trifluoromethanesulfonate ester (triflate) regiochemistry on bifunctional molecules of this type significantly impacts subsequent transition-metal-mediated synthetic protocols. For instance, we have found that Heck reactions of ketones **1** are possible,[2] and Heck carbonylation reactions with substrates such as **3** are also known to proceed without triflate migration.[3] The success

**SCHEME 1**




of these transformations hinges on maintaining the regiochemical integrity of the substrate under the chosen reactions conditions. This issue, and our interest in better understanding the nature of the benzofuranone formation process, prompted us to study both processes. We have observed profound substitution effects ($R^1$ and $R^2$) on the ability of **1** to cyclize to **2** or migrate to **3**. Our initial experiments define the scope and limitations of these processes and form the basis for a proposed hypervalent trifluoromethane sulfur intermediate common to both the migration and the oxidative cyclization pathways.

## Results

**Triflate Migrations.** Triflate migrations **1** → **3** are influenced by ketone substitution and conditions as shown in Table 1. The parent ketone **1a** and monoalkyl-substituted substrates rapidly generated migrated products upon exposure to 1.1 equiv of *t*-BuOK in THF at 0−20 °C (Table 1, substrates a−c). As indicated, several bases induce migration, with base strength and temperature affecting rate; however, neither migration nor benzofuranone formation was observed under any condi-

(1) For leading references to benzofuran-3-one syntheses, see: (a) Jung, M. E.; Abrecht, S. *J. Org. Chem.* **1988**, *53*, 423−425. (b) Smith, A. B., III; Koft, E. R. *J. Am. Chem. Soc.* **1982**, *104*, 2659−2661. (c) Kanvinde, M. N.; Kelkar, R. M.; Paradkar, M. V. *Synth. Commun.* **1993**, *23*, 961−969. (d) Garanti, L.; Zecchi, G.; Pagnoni, U. M. *J. Heterocycl. Chem.* **1977**, *14*, 445−448. (e) Prakash, O.; Goyal, S. *Synthesis* **1992**, 628−629. (f) Pirrung, M. C.; Werner, J. A. *J. Am. Chem. Soc.* **1986**, *108*, 6060−6062. (g) Powers, L. J.; Mertes, M. P. *J. Med. Chem.* **1970**, *13*, 1102−1105.

(2) Results to be published at a later time.

(3) (a) Louie, J.; Driver, M. S.; Hamann, B. C.; Hartwig, J. F. *J. Org. Chem.* **1997**, *62*, 1268−1273 and references therein. (b) Gilbertson, S. R.; Fu, Z.; Xie, D. *Tetrahedron Lett.* **2001**, *42*, 365−368 and references therein.

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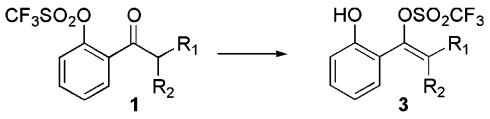
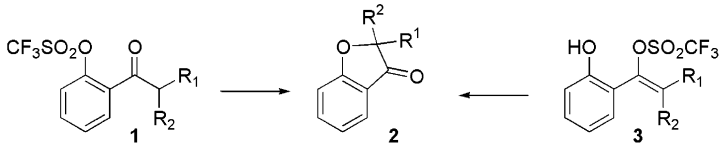
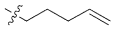
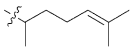
**TABLE 1. Triflate Migrations**




| entry | substrate | $R^1$ | $R^2$ | base (equiv) | T (°C) | time (h) | solvent | yield (%) |
|---|---|---|---|---|---|---|---|---|
| 1 | 1a | H | H | *t*-BuOK (1.1) | 0 - 20 | 0.5 | THF | 97 |
| 2 | 1b | $CH_3$ | H | *t*-BuOK (1.1) | 0 - 20 | 0.5 | THF | 96 |
| 3 | 1b | $CH_3$ | H | LHMDS (1.1) | -78 | 1.5 | THF | 93 |
| 4 | 1b | $CH_3$ | H | KOAc (3.0) | 0 - 20 | 18 | DMF | 93 |
| 5 | 1c |  | H | *t*-BuOK (1.1) | 0 - 20 | 0.5 | DMF | 88 |
| 6 | 1f | $-(CH_2)_4-$ | | -- | -- | -- | -- | 0 |

**TABLE 2. Benzofuran-3-one Cyclizations**




| entry | substrate | $R^1$ | $R^2$ | base (equiv) | T (°C) | time (h) | solvent | yield (%) |
|---|---|---|---|---|---|---|---|---|
| 1 | 1a | H | H | DBU (2.5) | 90 - 140 | 18 | DMF | 0 |
| 2 | 3a | H | H | DBU (2.5) | 90 - 140 | 18 | DMF | 0 |
| 3 | 1b | $CH_3$ | H | KOAc (3.0) | 90 | 4 | DMF | 92 |
| 4 | 1b | $CH_3$ | H | DBU (2.5) | 90 | 4 | DMF | 90 |
| 5 | 1b | $CH_3$ | H | DBU (2.5) | 90 | 4 | $CH_3CN$ | 90 |
| 6 | 3b | $CH_3$ | H | DBU (2.5) | 90 | 4 | DMF | 92 |
| 7 | 1d |  | H | KOAc (3.0) | 90 | 4 | DMF | 80 |
| 8 | 1e |  | H | KOAc (3.0) | 90 | 4 | DMF | 83 |
| 9 | 1f | $-(CH_2)_4-$ | | KOAc (3.0) | 50 | <1 | DMF | 85 |
| 10 | 1g |  | | DBU (2.5) | 20 | 0.2 | DMF | 19-25 |
| 11 | 1h | $CH_3$ | $CH_3$ | DBU (2.5) | 20 | 0.2 | DMF | 85 |

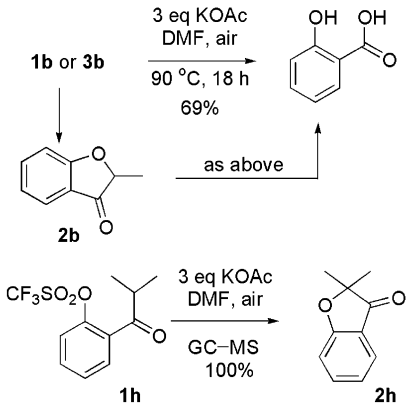
tion studied in the absence of base or with $Et_3N$ alone.[4] $^1H$ NMR studies (NOE**)** reveal that ketone **1b** is converted to the *Z*-(O)-enol triflate **3b** exclusively under all of these conditions. Finally, dialkyl substitution impedes migration. For example, **1f**−**h** do not give isolable migration products; instead, conversion to benzofuranones proceeds at room temperature with disubstituted examples (vide infra).[5]

**Benzofuran-3-one Cyclizations.** The cyclization to benzofuran-3-ones is most facile with dialkyl substitution (Table 2). At room temperature, dialkyl-substituted acetophenones **1f** and **1h** convert rapidly and cleanly to the corresponding benzofuranones **2f** and **2h** in excellent yield (Table 2, entries 9 and 11). Potassium acetate (KOAc) readily promotes the conversion in <1 h at 50 °C (Table 2, entry 9); however, the preferred base for

(4) Interestingly, 1.1 equiv of LiBr/1.5 equiv of TEA/DMF catalyzes the migration, whereas TEA alone does not. This catalysis is consistent with previous results involving closely related starting materials under similar conditions. See: (a) Ciattini, P. G.; Mastropietro, G.; Morera, E.; Ortar, G. *Tetrahedron Lett.* **1993**, *34*, 3763−3766. (b) Farina, V.; Baker, S. R.; Benigni, D. A.; Hauck, S. I.; Sapino, C., Jr. *J. Org. Chem.* **1990**, *55*, 5833−5847. The role of LiBr is unclear, but it presumably facilitates ketone ionization by triethylamine.

(5) We have detected product of the same mass as starting material **1f** with *t*-BuOK in DMF at 0 °C by GC−MS. This material has been preliminarily assigned the structure **3f**, but it has eluded isolation.

**SCHEME 2**

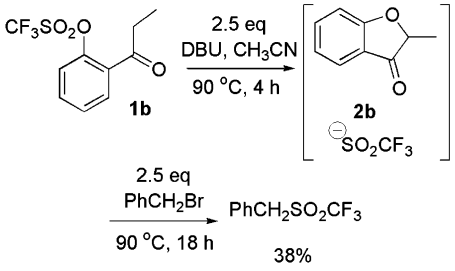



these conversions is DBU. Partial triflate cleavage has been observed with KOAc generating the corresponding phenols. No reaction occurs in the absence of base even under thermal conditions. Monosubstituted ketones **1** and their corresponding enol isomers (e.g., **3b**) require elevated temperatures and longer reaction times to convert to their corresponding benzofuranone in anaerobic reaction media (Table 2, entries 3−8).[6] In stark contrast to alkyl-substituted examples, unsubstituted parent compound **1a** and enol triflate **3a** do not cyclize to give benzofuranone **2a** even under forcing conditions (Table 2, entries 1 and 2). Enol triflate **3a** was formed from **1a** under these conditions.

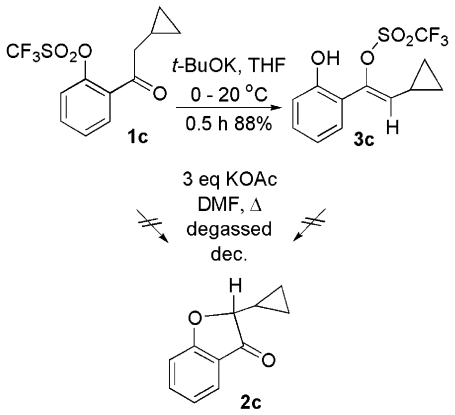
**Mechanistic Considerations.** Disubstituted cyclopentenyl ketone **1h** readily converts to benzofuranone **2h** in both anaerobic *and* aerated reaction media. This result contrasts with those obtained with substrate **1b**, which readily migrates as described above but requires degassed conditions for successful cyclization to **2b**. In this case and in other monoalkyl-substituted examples, the benzofuranones (e.g., **2b**) react with air and ultimately convert to salicylic acid (Scheme 2).[7] We suspect that the acidity of these substrates results in ready peroxide formation following the cyclization process and that subsequent oxidative cleavage produces salicylic acid.[8,9]

The conversion to a benzofuran-3-one (**1** → **2** or **3** → **2**) is an oxidative sequence and requires that the triflate group be reduced to trifluoromethanesulfinic acid ion ($CF_3SO_2^-$, Scheme 3). To confirm its formation, a solution of **1b** in $CH_3CN$ (0.5 M) was cyclized under the described conditions (Table 2, entry 5), and the reaction mixture was then treated with 2.5 equiv of benzyl bromide. The sulfinate ion derivative $PhCH_2SO_2CF_3$ was isolated via flash chromatography in 38% yield, providing support for the oxidation/reduction pathway to **2** from **1**.[10]

**SCHEME 3**




**SCHEME 4**




Cyclopropane derivative **1c** was prepared[11] as a mechanistic probe (Scheme 4).[12] Although **1c** readily converts at or below room temperature to the migrated enol triflate **3c** (Table 1, entry 5), on warming to 50−90 °C under cyclization conditions both **1c** and **3c** were completely consumed with the formation of polar unidentified materials. Benzofuranone **2c** was not observed, and $^1$H NMR analysis of the crude reaction product indicated that cyclopropane moieties were absent.[13]

To gain further insight into cyclopropane cleavage, we studied anisole derivatives **4** and **5**[14] to ascertain the stability of the isolated cyclopropylmethyl ketone and its corresponding enol triflate (Scheme 5). On exposure to cyclization conditions, ketone **4** was recovered unchanged

(6) Both mono- and dialkyl-substituted examples become brown upon treatment with DBU in DMF and darken slightly on warming. Success of these reactions is unimpaired when performed in the absence of light.

(7) The conversion of **1b** to salicylic acid is facile (3 equiv of KOAc, DMF, air, 90 °C, 18 h, 69%). Compound **3b** is also converted to salicylic acid under these conditions in an air atmosphere.

(8) See: (a) Doering, W. von E.; Chanley, J. D. *J. Am. Chem. Soc.* **1946**, *68*, 586−589. (b) Doering, W. von E.; Haines, R. M. *J. Am. Chem. Soc.* **1954**, *76*, 482−486. (c) Sawaki, Y.; Ogata, Y. *J. Am. Chem. Soc.* **1977**, *99*, 5412−5416. For a discussion of photooxygenation of 2-methylbenzofuran-3-one silyl ethers, see: (d) Adam, W.; Kades, E.; Wang, X. *Tetrahedron Lett.* **1990**, *31*, 2259−2262.

(9) While it might be unnecessary in some cases, as such it is advisable to deoxygenate all of these reactions.

(10) For sulfonate to sulfinate conversions, see: (a) Ley, S. V.; Lygo, B.; Wonnacott, A. *Tetrahedron Lett.* **1985**, *26*, 535−538. (b) Netscher, T.; Bohrer, P. *Tetrahedron Lett.* **1996**, *37*, 8359−8362. (c) Creary, X. *J. Org. Chem.* **1985**, *50*, 5080−5084. (d) Creary, X. *J. Org. Chem.* **1980**, *45*, 2727−2729. (e) Binkley, R. W.; Ambrose, M. G. *J. Org. Chem.* **1983**, *48*, 1777−1779.

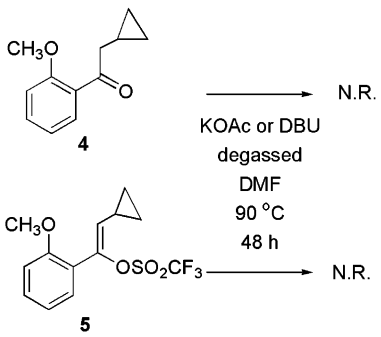
(11) Syntheses of substrates **1** follow straightforward methods. For Weinreb amide formation conditions, see: (a) Nitz, T. J.; Volkots, D. L.; Aldous, D. J.; Oglesby, R. C. *J. Org. Chem.* **1994**, *59*, 5828−5832. (b) For halogen metal exchange conditions, see: Parham, W. E.; Bradsher, C. K. *Acc. Chem. Res.* **1982**, *15*, 300−305. (c) For demethylation of 2-methoxyacetophenones, see: Nagaoka, H.; Schmid, G.; Iio, H.; Kishi, Y. *Tetrahedron Lett.* **1981**, *22*, 899−903. (d) For triflate formation, see: Su, T. M.; Sliwinski, W. F.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1969**, *91*, 5386-5389. (e) For a review of the Fries rearrangement, see: Blatt, A. H. in *Organic Reactions*; Wiley: New York, 1942; Vol. 1, pp 342−369. March, J. *Advanced Organic Chemistry*, 4th ed.; Wiley: New York, 1992; pp 555−556. See the Experimental Section and Supporting Information.

(12) For examples of cyclopropanes as mechanistic radical probes, see: (a) He, M.; Dowd, P. *J. Am. Chem. Soc.* **1997**, *119*, 1133−1137. (b) Corey, E. J.; Nagata, R. *J. Am. Chem. Soc.* **1987**, *109*, 8107−8108. (c) Waldemar, A.; Finzel, R. *J. Am. Chem. Soc.* **1992**, *114*, 4563−4568. (d) Nonhebel, D. C. *Chem. Soc. Rev.* **1993**, 347−359.

(13) Structures from these crude reactions remain to be determined.

(14) Structure **5** was prepared by alkylation of **3c** (NaH, DMF, MeI, 0−20 °C).

**SCHEME 5**




after heating at 90 °C for 48 h (>98%). Enol triflate **5** proved equally stable, although a small amount of ketone **4** was recovered due to cleavage of the triflate group upon prolonged exposure to KOAc. These results demonstrate that the isolated cyclopropyl group is stable under the cyclization conditions; however, the presence of the triflate in **1c** or the phenol in **3c** leads to cyclopropane instability under cyclization conditions.

These results are consistent with reaction pathways involving reactive radical[12] or cationic[15] intermediates. Accordingly, we tested for radical chain mechanisms under inhibition and initiation conditions.[16,17] Under standard degassed reaction conditions with substrate **1b**, the radical inhibitor styrene (1 equiv) did not influence the reaction. Stoichiometric BHT slowed but did not completely inhibit the reaction (50% completion at 8 h). Further attempts to initiate and catalyze the reaction with $BEt_3/O_2$[18] as a source of ethyl radical with both **1b** and **3b** in the presence of KOAc provided only recovered starting materials in both reactions. Substrate **1g** cyclized equally well in the presence of hydroquinone and TEMPO (1 equiv, DBU/DMF conditions). Although reasonable radical chain mechanisms involving trifluoromethanesulfinate and $CF_3$ radicals as chain propagators have been described by Fuchs,[19] our results and the formation of $CF_3SO_2^-$ do not support the involvement of radical *chain* processes.

In our studies of substrate **1g**, the only product detected by TLC and GC−MS after 15 min at room temperature was spiro-benzofuranone **2g** (Table 2, entry 10); however, the isolated yield was reproducibly poor on repeated attempts. Polar material was also observed, which we suspect was a result of side reactions involving reactive intermediates. In contrast, the saturated dialkyl-substituted example provided rapid and clean conversion to products (Table 2, entries 9 and 11).

Finally, tethered olefinic examples **1d** and **1e** were studied as additional mechanistic probes (Table 2, entries 7 and 8). Under cyclization conditions, high yields of benzofuranone products were obtained with no evidence of olefinic radical trapping. Upon prolonged heating, **2e** slowly converts to a spiro-product we believe is derived via Conia reactions (<10% at 18 h).[20]

## Discussion

Substrates **1** and **3** contain functionality with hybridization states that present stereoelectronic challenges to conventional nucleophilic $S_N2$ or $S_N2'$ displacement mechanisms leading to benzofuranones **2**.[21,22] Although the overall process has $S_N2$ characteristics ($CF_3SO_2^-$ formation, base induction, temperature dependence), the observed substitution effects on substrate reactivity are opposite of those expected for $S_N2$ pathways. The reaction also appears to be neither accelerated or initiated by radical initiators nor fully retarded with radical traps, including tethered olefinic traps. It is, however, incompatible with neighboring cyclopropane or proximal olefinic substitution. How does such a reaction proceed?

The mechanistic proposals in Scheme 6 are in accord with the results and observations detailed herein. Consistent with the requirement for base in the reaction, we propose that ionization is required. Base treatment results in sulfur transesterification whereby the initial ionization of **1** transfers charge via 1,2-addition/elimination at the triflate center, leading to migrated products **3** upon reprotonation. This ligand exchange is mediated via sulfur intermediate **6** (10-S-5).[23] Parent compound **1a** ($R_1 = R_2 = H$) forms thermodynamically favored isomer **3a** exclusively. Presumably, the favored product-side equilibrium in this case prevents both a return to ketone **1a** via intermediate **6** and entry into cyclization modes. Mono- and dialkyl-substituted examples also access intermediate **6**, and the product distributions at low temperature no doubt reflect the thermodynamic stability of the products. Interactions of the alkyl substitution and triflate ester in the Z(O)-enol triflates in mono- and disubstituted examples (TfO with $R^1$) and alkyl−aryl interactions in the disubstituted examples ($R^2$ with aryl) destabilize enol(ate) isomers **3** and regulate triflate

(15) For cyclopropanes designed for ready ionization, see: Carpino, L. A.; Chao, H. G.; Ghassemi, S.; Mansour, E. M. E.; Riemer, C.; Warrass, R.; Sadat-Aalaee, D.; Truran, G. A.; Imazumi, H.; El-Faham, A.; Ionescu, D.; Ismail, M.; Kowaleski, T. L.; Han, C. H.; Wenschuh, H.; Beyermann, M.; Bienert, M.; Shroff, H.; Albericio, F.; Triolo, S. A.; Sole, N. A.; Kates, S. A. *J. Org. Chem.* **1995**, *60*, 7718−7719.

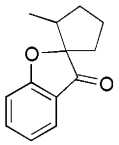
(16) For a discussion of radical chain mechanisms and substituent effects, see: March, J. *Advanced Organic Chemistry*, 4th ed.; Wiley: New York, 1992; pp 186−195 and 683−686.

(17) For references to the $S_{RN}1$ mechanism, see: (a) Kim, J. K.; Bunnett, J. F. *J. Am. Chem. Soc.* **1970**, *92*, 7466−7464. (b) Rossi, R. A.; Pierini, A. B.; Palacios, S. M. *J. Chem. Educ.* **1989**, *66*, 720−722. (c) Bunnett, J. F. *Tetrahedron* **1993**, *49*, 4477−4484.

(18) For radical initiation with $BEt_3/O_2$ and leading references, see: Miyabe, H.; Ueda, M.; Maito, T. *J. Org. Chem.* **2000**, *65*, 5043−5047. Yamada, K.; Fujihara, H.; Yamamoto, Y.; Miwa, Y.; Taga, T.; Tomioka, K. *Org. Lett.* **2002**, *4*, 3509−3511.

(19) For radical chain reactions involving trifluoromethane sulfonate radicals ($CF_3SO_2^{\bullet} \rightarrow CF_3^{\bullet} + SO_2$), see: Gong, J.; Fuchs, P. L. *J. Am. Chem. Soc.* **1996**, *118*, 4486-4487. Xiang, J. S.; Mahadevan, A.; Fuchs, P. L. *J. Am. Chem. Soc.* **1996**, *118*, 4284−4290.

(20) Pattenden, G.; Teague, S. J. *J. Chem. Soc., Perkin.Trans. 1* **1988**, 1077−1083 and references therein.

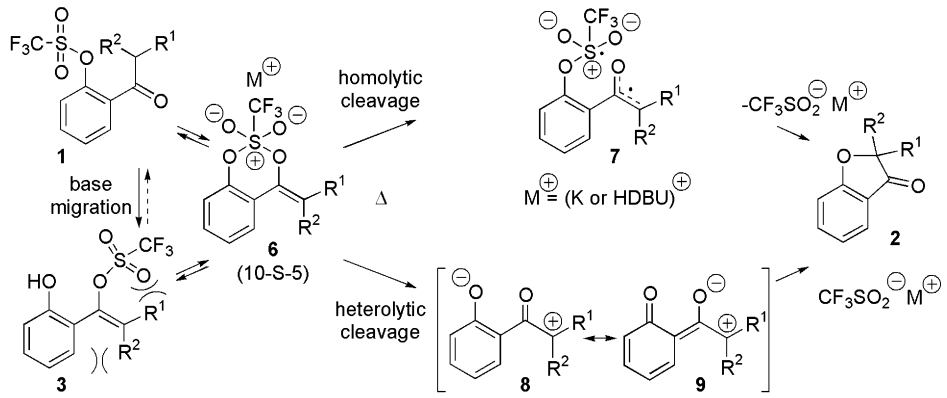


(21) For a discussion of $S_N2$ displacement mechanisms, see: March, J. *Advanced Organic Chemistry*, 4th ed.; Wiley: New York, 1992; pp 294−298.

(22) An examination of models suggests that ideal 180° alignment of an enol(ate) nucleophile and sulfinate leaving group cannot be achieved.

(23) For extensive discussion regarding related transition structures, see: Perkins, C. W.; Wilson, S. R.; Martin, J. C. *J. Am. Chem. Soc.* **1985**, *107*, 3209−3218 and references therein.

**SCHEME 6**




isomerism between ketones **1** and enol triflates **3**.[24] Thus, at lower temperature, alkyl substitution governs the collapse of intermediates **6** to give the observed preference of phenolic products **3** for **a**, **b**, and **c** but keto-side preference **1** for **f** and **g**.

The facility of dialkyl-substituted examples to cyclize to benzofuranones **2** below 50 °C requires the involvement of species stabilized by such substitution. The homolytic cleavage pathway of an S−O bond in intermediate **6** is consistent with this postulate. Two such cleavages are reasonable; however, we consider the enol−sulfur O−S bond of **6** as most labile.[25] The resulting diradical anion intermediate **7** would be greatly stabilized at both radical centers. The electron-deficient trifluoromethane group stabilizes the sulfur-centered radical, yet interestingly, less electron-deficient groups or ones that delocalize this radical are insufficiently stabilizing to promote entry into the ring closure event.[26] The enol radical center of **7** is stabilized by alkyl substitution, and in the case of **c** appears to result in cyclopropane cleavage. The departure of trifluoromethanesulfinic ester ion ($CF_3SO_2^-$) from **7** leads to benzofuranone bond formation. This conversion may be a concerted single-electron reductive bond-forming transfer, or it may involve the formation of a diradical intermediate via homolytic cleavage of the remaining sulfur−ether S−O bond followed by ring closure.[27]

An alternative mechanistic pathway involves heterolytic S−O bond cleavage from **6** to form trifluoromethane sulfinate ion and zwitterionic intermediate **8**. Tautomeric intermediate **9** illustrates attainable quinone methide vinylogous cation oxide stabilization. These intermediates could also lead to facile cyclopropane cleavage[15,28] and are reminiscent of alleneoxide/methylenecyclopropanone rearrangements that have a parallel atomic arrangement.[29] Related isoelectronic vinylic oxyallyl cations have been shown by extensive calculations to be important in prostaglandin biosynthesis and exhibit electrocyclic conrotatory ring closure from intermediates such as **8** and **9** or their rotational isomers.[30] Related oxyallyl cations have been implicated in the reactions of α-amino α′-fluoro ketones.[31]

In either the homolytic or heterolytic pathway, the fact that only trifluoromethane sulfonate successfully enters the reactive pathway is attributable to the superior ionization potential of triflate compared to that of tosylate, which migrates but does not enter the cyclization pathway.[26,32] Both pathways from **6** are consistent with the data obtained and provide plausible mechanistic pathways.

The conditions described herein for the formation of monosubstituted enol triflates and mono- and dialkyl-substituted benzofuran-3-ones is efficient and easily operated. Further, the results described herein are consistent with the proposed pathways and not $S_N2$ or radical chain mechanisms. Discrimination among zwitterionic, concerted, or diradical(oid) mechanisms in cyclization events is of great importance to the physical organic chemistry community, and we believe these results lay the groundwork for further investigations of this novel reaction pathway.

(24) In enol triflate **3a**, the triflate is not destabilized by a neighboring and cis substituent. We postulate that in highly substituted cases the equilibrium favors the starting ketones (**1f**, **1g**) due to severe steric interactions encountered in the corresponding fully substituted enolic forms. The enol form, however, appears to be thermodynamically favored in the mono- and unsubstituted examples at low temperature.

(25) The phenolsulfonate O−S cleavage is similarly stabilized; however, alkyl substitution in intermediates derived from this cleavage stabilize the phenol radical through extended vinylogous conjugation.

(26) The triflate (or a similarly electron-deficient group) is required. We have found that other sulfonates migrate (KOAc/DMF or DBU) but fail to cyclize. When exposed to KOAc/DMF at 90 °C, mesyl-, tosyl-, and nosylates provided mixtures of products, including starting phenol (sulfonyl hydrolysis) and a product derived from the resulting mixed anhydride ($AcOSO_2CF_3$). The $AcOSO_2CF_3$ apparently serves to acylate the phenol and dehydrate via aldol processes to provide (in the case of derivative **b**) 2,3-dimethylchromen-4-one (e.g., Wittig, G. *Chem. Ber.* **1926**, *59*, 117). Furthermore, aryl-substituted ketones ($R^1 = C_6H_5$) take a different course and generate complex mixtures but do not produce benzofuranones. Migration occurs in 42% yield (*t*-BuOK/THF, 0−20 °C).

(27) For studies of SET mechanisms, see: (a) Newcomb, M. *Act. Chem. Scand.* **1990**, *44*, 299−310. (b) Newcomb, M.; Curran, D. P. *Acc. Chem. Res.* **1988**, *21*, 206−214. (c) Ashby, E. C. *Acc. Chem. Res.* **1988**, *21*, 414−421.

(28) In an attempt to trap an intermediate of this type, the reaction of **1g** was carried out in the presence of triethylsilane (1 equiv). It proceeded as without triethylsilane. See ref 15.

(29) (a) Crandall, J. K.; Conover, W. W.; Konim, J. B.; Machlender, W. H. *J. Org. Chem.* **1974**, *39*, 1723−1729. (b) Camp, R. O.; Greene, F. D. *J. Am. Chem. Soc.* **1973**, *90*, 7349. (c) Crandall, J. K.; Conover, W. W. *J. Chem. Soc., Chem. Commun.* **1973**, *10*, 340−341.

(30) Hess, B. A., Jr.; Smentek, L.; Brash, A. R.; Cha, J. K. *J. Am. Chem. Soc.* **1999**, *112*, 5603−5604.

(31) Myers, A. G.; Barbay, J. K. *Org. Lett.* **2001**, *3*, 425−428.

(32) The solvolysis rate for trifluoromethane sulfonates has been demonstrated to be 40 000 times greater than that of tosylates. See: Crossland, R. K.; Wells, W. E.; Shiner, V. J., Jr. *J. Am. Chem. Soc.* **1971**, *88*, 4217−4220. Also see: Stang, P. J.; Hanack, M.; Subramanian, L. R. *Synthesis* **1982**, 85−126.

## Experimental Section

**General Method for the Preparation of Substituted 2-Trifluoromethanesulfonyl Acetophenones. Preparation of Trifluoromethanesulfonic Acid 2-(Cyclopent-3-enecarbonyl)phenyl Ester (1g).** Cyclopent-3-enyl(2-hydroxyphenyl)methanone (564 mg, 3.0 mmol) and pyridine (475 mg, 6.0 mmol) were stirred in $CH_2Cl_2$ (15 mL) at −78 °C under $N_2$. To this solution was added trifluoromethane sulfonic anhydride (1.02 g, 3.6 mmol) in $CH_2Cl_2$ (10 mL) dropwise over 0.5 h. The mixture was allowed to warm to ambient temperature, stirred for 2 h, and then poured into 1 N aqueous HCl solution (25 mL). The mixture was shaken, the layers were separated, and the organic layer was washed with 1 N aqueous HCl solution (2 × 15 mL), $H_2O$ (2 × 30 mL), saturated aqueous $NaHCO_3$ solution (20 mL), and finally, saturated aqueous NaCl solution (20 mL). The organic layer was dried through a cotton plug and concentrated to an oil, which was purified by chromatography on silica gel plug eluting with 10%EtOAc/hexanes to afford an oil after concentration (808 mg, 84%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.74 (dd, $J$ = 7.8, 1.7 Hz, 1H), 7.56 (ddd, $J$ = 8.3, 7.4, 1.7 Hz, 1H), 7.45 (dd, $J$ = 7.8, 1.2 Hz, 1H), 7.30 (d, $J$ = 8.3 Hz, 1H), 5.62 (br s, 2H), 3.95 (m, 1H), 2.77−2.58 (m, 4H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 201.1, 147.1, 133.5, 132.2, 130.6, 128.9, 128.7, 123.5, 123.1, 120.4, 117.2, 47.3, 36.0; GC−MS $m/z$ 320 ($M^+$, 100); HRMS calcd 321.0408 for $C_{13}H_{12}O_4F_3S$, obsd $m/z$ 321.0405 $(M + 1)^+$.

**Trifluoromethanesulfonic acid 2-acetylphenyl ester (1a):** $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.81 (dd, $J$ = 7.9, 1.7 Hz, 1H), 7.59 (m, 1H), 7.48 (m, 1H), 7.33 (d, $J$ = 8.3 Hz, 1H), 2.63 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 196.9, 147.5, 133.9, 132.3, 131.0, 128.8, 123.0, 29.7; GC−MS $m/z$ 268 ($M^+$, 100).

**Trifluoromethanesulfonic acid 2-propionylphenyl ester (1b):** $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.76 (dd, $J$ = 7.7, 1.7 Hz, 1H), 7.57 (ddd, $J$ = 8.3, 7.7, 1.7 Hz, 1H), 7.46 (ddd, $J$ = 7.7, 7.5, 1.0 Hz, 1H), 7.32 (d, $J$ = 8.3 Hz, 1H), 2.96 (q, $J$ = 7.1 Hz, 2H), 1.21 (t, $J$ = 7.1 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 201.0, 146.8, 133.3, 132.7, 130.2, 128.5, 122.8, 126.3, 123.1, 119.9, 116.7, 35.0, 7.9; IR ($cm^{-1}$) 3381.9, 3082.2, 2983.5, 2942.6, 2910.2, 1700.5, 1605.8, 1482.2, 1425.9, 1350.1, 1247.9, 1211.6, 1140.4, 1078.1, 956.8, 886.7, 783.7, 789.1; GC−MS $m/z$ 282 ($M^+$); HRMS calcd 283.0252 for $C_{10}H_{10}O_4F_3S$, obsd $m/z$ 283.0252 ($M^+$, 100).

**Trifluoromethanesulfonic acid 2-(2-cyclopropylacetyl)-phenyl ester (1c):** $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.73 (dd, $J$ = 7.7, 1.8 Hz, 1H), 7.56 (ddd, $J$ = 8.3, 7.4, 1.8 Hz, 1H), 7.45 (ddd, $J$ = 8.0, 7.4, 1.0 Hz, 1H), 7.32 (d, $J$ = 8.3 Hz, 1H), 2.83 (d, $J$ = 6.8 Hz, 2H), 1.10 (m, 1H), 0.57 (m, 2H), 0.15 (dd, $J$ = 10.6, 4.8 Hz, 2H); GC−MS $m/z$ 252 ($M^+$, 100).

**Trifluoromethanesulfonic acid 2-hept-6-enoylphenyl ester (1d):** $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.75 (dd, $J$ = 7.7, 1.7 Hz, 1H), 7.57 (ddd, $J$ = 8.3, 7.3, 1.9 Hz, 1H), 7.47 (br t, $J$ = 8.0 Hz, 1H), 7.32 (d, $J$ = 8.3 Hz, 1H), 5.79 (m, 1H), 5.00 (dd, $J$ = 17.1, 1.4 Hz, 1H), 4.94 (dd, $J$ = 10.2, 1.0 Hz, 1H), 2.94 (t, $J$ = 7.4 Hz, 2H), 2.06 (m, 2H), 1.74 (m, 2H), 1.45 (m, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 146.4, 138.4, 133.3, 130.3, 130.3, 128.5, 128.5, 122.7, 114.8, 41.6, 33.5, 28.3, 23.3; $CF_3$ and carbonyl residues not observed; IR ($cm^{-1}$) 2934.0, 1698.5, 1605.5, 1426.7, 1216.6, 1141.1, 888.1, 769.9; GC−MS $m/z$ 267 ($M - CF_3^+$, 100).

**Trifluoromethanesulfonic acid 2-(3,7-dimethyloct-6-enoyl)phenyl ester (1e):** $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.72 (dd, $J$ = 7.7, 1.5 Hz, 1H), 7.56 (br t, $J$ = 8.3 Hz, 1H), 7.45 (br dd, $J$ = 7.7, 7.5 Hz, 1H), 7.30 (d, $J$ = 8.1 Hz, 1H), 5.04 (m, 1H), 2.91 (dd, $J$ = 16.7, 5.3 Hz, 1H), 2.72 (dd, $J$ = 16.7, 8.1 Hz, 1H), 2.12 (m, 1H), 1.97 (m, 2H), 1.64 (s, 3H), 1.56 (s, 3H), 1.36 (m, 1H), 1.24 (m, 1H), 0.94 (d, $J$ = 6.7 Hz, 3H); GC−MS $m/z$ 378 ($M^+$, 100).

**Trifluoromethanesulfonic acid 2-cyclopentanecarbonylphenyl ester (1f).** $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.74 (dd, $J$ = 7.7, 1.7 Hz, 1H), 7.56 (ddd, $J$ = 8.3, 7.5, 1.5 Hz, 1H), 7.46 (ddd, $J$ = 7.7, 7.5, 1.1 Hz, 1H), 7.32 (dd, $J$ = 8.3, 1.1 Hz, 1H), 3.56 (quint, $J$ = 8.0 Hz, 1H), 1.88 (m, 4H), 1.71 (m, 2H), 1.61 (m, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 146.8, 133.0, 132.6, 130.4, 128.4, 122.7, 122.6, 120.1, 118.6, 116.1, 49.5, 29.6, 26.1; IR ($cm^{-1}$) 2957.9, 2871.6, 1693.5, 1604.7, 1480.9, 1425.4, 1211.4, 1140.9, 999.1, 902.6, 864.2, 779.5; GC−MS $m/z$ 322 ($M^+$, 100).

**Trifluoromethanesulfonic acid 2-methyl-2-propionylphenyl ester (1h):** $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.69 (dd, $J$ = 7.9, 1.6 Hz, 1H), 7.56 (m, 1H), 7.45 (m, 1H), 7.34 (dd, $J$ = 8.3, 0.8 Hz, 1H), 3.34 (m, 1H), 1.18 (d, $J$ = 6.6 Hz, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 146.9, 133.2, 132.2, 130.3, 128.7, 122.9, 39.2, 18.6; GC−MS $m/z$ 296 ($M^+$, 100).

**Migration Reaction (1 → 3) *t*-BuOK/THF Conditions. Preparation of Trifluoromethanesulfonic Acid 1-(2-Hydroxyphenyl)propenyl Ester (3b).** A solution of trifluoromethanesulfonic acid 2-propionylphenyl ester (282 mg, 1.0 mmol) was stirred in anhydrous THF (5 mL) at 0 °C under $N_2$ and treated with *t*-BuOK (247 mg, 2.2 mmol). After 30 min, the reaction was judged complete, poured into 1 N aqueous HCl solution (25 mL) at 0 °C, and extracted with ethyl acetate (3 × 25 mL). The organic layer was washed with $H_2O$ (2 × 25 mL), saturated aqueous $NaHCO_3$ solution (25 mL), and saturated aqueous NaCl solution (20 mL). The organic layer was dried through a cotton plug and concentrated to an oil, which was purified by chromatography on silica gel plug eluting with 10%EtOAc/hexanes to afford an oil after concentration (271 mg, 96%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 11.09 (s, O*H*), 7.66 (dd, $J$ = 8.2, 1.4 Hz, 1H), 7.59 (ddd, $J$ = 7.7, 7.0, 1.4 Hz, 1H), 7.05 (dd, $J$ = 8.5, 1.1 Hz, 1H), 6.99 (dd, $J$ = 8.5, 7.3 Hz, 1H), 5.32 (dd, $J$ = 7.0 Hz, 1H), 1.86 (dd, $J$ = 7.0, 0.8 Hz, 3H), NOE difference experiment: irradiation of $\delta$ 5.32 (vinyl proton) causes 14% enhancement of $\delta$ 7.66; IR ($cm^{-1}$) 3055.8, 2985.9, 1639.7, 1615.8, 1576.2, 1488.3, 1452.2, 1365.0, 1309.5, 1267.8, 1209.9, 1180.7, 1117.2, 1072.9, 1035.0, 985.0, 948.6, 828.8, 782.8, 718.3, 677.2; GC−MS $m/z$ 282 ($M^+$, 100).

**Trifluoromethanesulfonic acid 2-acetylphenyl ester (3a):** $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 11.41 (s, O*H*), 7.63 (m, 2H), 7.04 (m, 2H), 4.84 (s, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 163.8, 139.1, 131.7, 120.2, 119.7, 56.7; APCI MS $m/z$ 267 (M − 1); GC−MS $m/z$ 268$^+$, 100).

**Trifluoromethanesulfonic acid 2-cyclopropyl-1-(2-hydroxyphenyl)vinyl ester (3c):** $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 11.68 (s, O*H*), 7.58 (dd, $J$ = 8.4, 7.3 Hz, 1H), 7.53 (d, $J$ = 8.3 Hz, 1H), 7.06 (dd, $J$ = 8.5, 1.0 Hz, 1H), 6.97 (ddd, $J$ = 8.1, 7.3, 1.0 Hz, 1H), 4.50 (d, $J$ = 10.7 Hz, 1H), 1.78 (m, 1H), 1.03 (m, 1H), 0.81 (m, 2H), 0.38 (m, 1H); LC−MS $m/z$ 120 (M − 188$^+$, 100).

**Cyclization Reaction (1 → 2). Preparation of 2,2-Dimethylbenzofuran-3-one (2h).** Trifluoromethanesulfonic acid 2-methyl-2-propionylphenyl ester (**1h**, 498 mg, 1.68 mmol) was dissolved in DMF (8.0 mL) and stirred under a $N_2$ atmosphere. DBU (1,8-diazabicyclo[5.4.0]undec-7-ene, 0.63 mL, 4.20 mmol) was added dropwise causing the reaction solution to become fluorescent green. After being stirred for 12 min, the reaction was judged complete, poured into 1 N aqueous HCl solution (25 mL) at 0 °C, and extracted with ethyl acetate (3 × 25 mL). The organic layer was washed with $H_2O$ (2 × 25 mL), saturated aqueous $NaHCO_3$ solution (25 mL), and saturated aqueous NaCl solution (20 mL). The organic layer was dried through a cotton plug and concentrated to an oil, which was purified by chromatography on silica gel plug eluting with 10% EtOAc/hexanes to afford an oil after concentration (222 mg, 81%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.65 (dd, $J$ = 7.5, 1.1 Hz, 1H), 7.59 (m, 1H), 7.06−7.02 (m, 2H), 1.44 (s, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 171.5, 138.3, 125.1, 121.9, 119.8, 113.8, 88.1, 23.2; GC−MS $m/z$ 162 ($M^+$, 83%, see SI).

**Preparation of 2-Methylbenzofuran-3-one (2b).** Trifluoromethanesulfonic acid 2-propionylphenyl ester (**1b**) (282 mg, 1.0 mmol) was dissolved in DMF (5.0 mL), degassed (3 $N_2$/vacuum cycles), and stirred under a $N_2$ atmosphere. DBU

(380 mg, 2.5 mmol) was added dropwise causing the reaction solution to become brown. The mixture was warmed to 90 °C with stirring for 1 h and then worked up as above to provide product as an oil (253 mg, 90%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.64 (dd, $J$ = 7.7, 1.3 Hz, 1H), 7.58 (ddd, $J$ = 8.5, 7.3, 1.5 Hz, 1H), 7.08 (d, $J$ = 8.5 Hz, 1H), 7.05 (dd, $J$ = 7.7, 7.3 Hz, 1H), 4.61 (q, $J$ = 7.3 Hz, 1H), 1.50 (d, $J$ = 7.3 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 172.4, 138.0, 124.4, 121.8, 120.4, 113.5, 81.8, 16.38; IR ($cm^{-1}$) 3200.5, 3062.6, 2927.5, 1643.7, 1588.0, 1484.8, 1374.1, 1302.4, 1210.9, 1117.5, 990.4, 829.9, 739.6, 817.2; GC−MS $m/z$ 148 ($M^+$, 100).

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**Supporting Information Available:** Experimental conditions and spectral data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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