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Superacid-Promoted Reactions of α-Ketoamides and Related Systems

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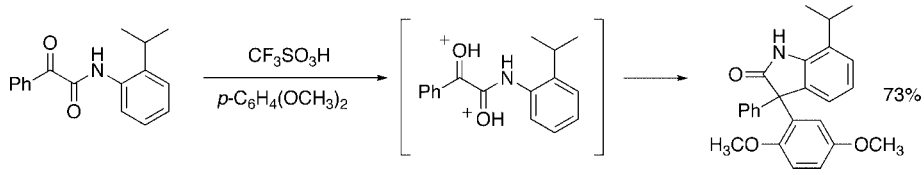
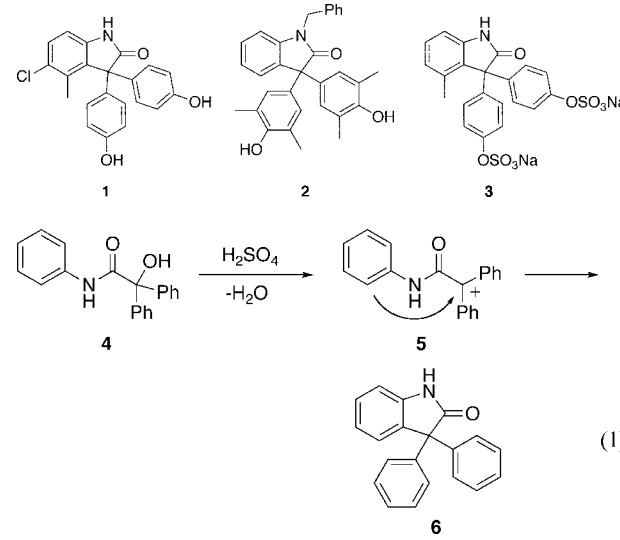


The superacid-promoted reactions of α-hydroxy and α-ketoamides have been studied. Ionization of these compounds leads to varied aryl-substituted oxyindole products. In some cases, electrocyclization can lead to substituted fluorene products. Dicationic, superelectrophilic intermediates are proposed as intermediates leading to the products from α-hydroxy and α-ketoamides.

Introduction

Substituted oxyindoles are known to have a variety of biological activities. The aryl-substituted oxyindole substructure is present in natural products and in several potent therapeutic agents, such as anticancer drugs (**1**),[1] cardiovascular drugs (**2**),[2] and laxatives (**3**).[3] The aryl-substituted oxyindoles may be prepared by a number of synthetic routes,[4] including the condensation of isatins with arenes in an acid-promoted conversion.[5] The cyclizations of mandelic and benzilic acid derivatives (i.e., **4**) have also been studied, and in H_2SO_4-catalyzed reactions, for example, the aryl-substituted oxyindoles are produced (eq 1).[6]



(1)

Recently, we described our studies of the superacid-promoted cyclizations of β-ketoamides to quinolin-2-ones (Knorr cyclization).[7] Experimental and theoretical evidence strongly suggested the involvement of diprotonated, superelectrophilic intermediates

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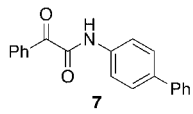
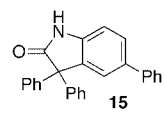
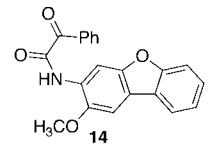
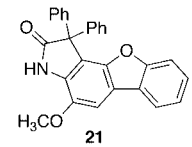
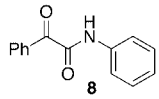
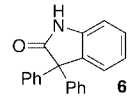
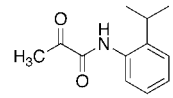
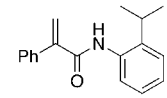
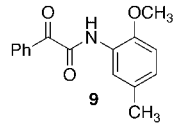
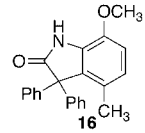
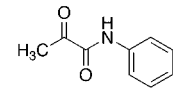
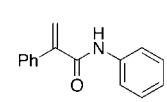
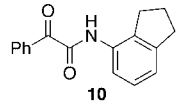
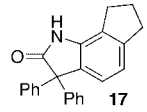
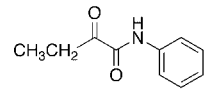
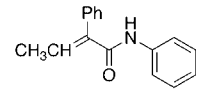
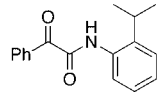
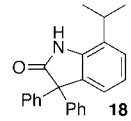
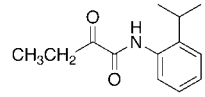
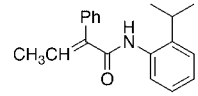
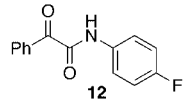
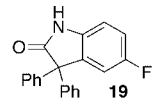
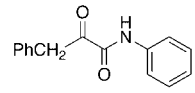
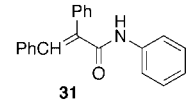
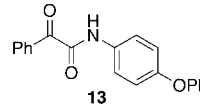
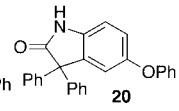
TABLE 1. Products and Yields from the Reactions of α-Ketoamides with CF_3SO_3H and C_6H_6 at 50 °C[a]

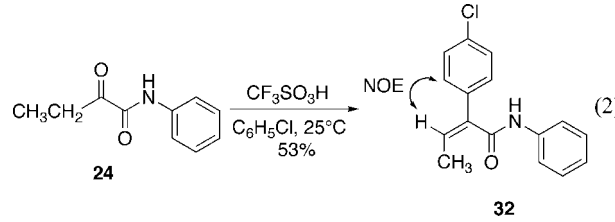
entry	α-ketoamide	product	yield	entry	α-ketoamide	product	yield
(1)	 **7**	 **15**	73%	(8)	 **14**	 **21**	52%
(2)	 **8**	 **6**	94%	(9)	 **22**	 **27**	52%
(3)	 **9**	 **16**	81%	(10)	 **23**	 **28**	44%
(4)	 **10**	 **17**	76%	(11)	 **24**	 **29**	65%
(5)	 **11**	 **18**	74%	(12)	 **25**	 **30**	66%
(6)	 **12**	 **19**	72%	(13)	 **26**	 **31**	40%
(7)	 **13**	 **20**	44%				

[a] Reaction conditions: 0.1 mmol of α-ketoamide, 1 mL of C_6H_6, 23 mmol of CF_3SO_3H, 50 °C, 18 h.

leading to the cyclization products.[8] The *β*-ketoamides are protonated at the two carbonyl oxygens in superacid, giving dicationic intermediates. A number of 1,2-dicarbonyl compounds have likewise been shown to form diprotonated superelectrophilic species in strongly acidic media.[9] In this regard, we considered the possibility that the 1,2-dicarbonyl groups of α-ketoamides could form superelectrophiles capable of undergoing cyclizations to the aryl-substituted oxyindoles. Herein, we report the results of these studies, describing a new route to aryl-substituted oxyindoles and proposing a superelectrophilic mechanism.

Results and Discussion

A series of α-ketoamides (**7**−**14** and **22**−**26**) are reacted with C_6H_6 in the presence of CF_3SO_3H, and the aryl-substituted oxyindoles (**6** and **15**−**21**) are formed in good to fair yields (Table 1). The α-ketoamides are prepared by DCC-promoted coupling reactions between the appropriate anilines and phenylglyoxylic acid or other α-ketoacids.[10] With the use of benzene in the condensation reactions, the *gem*-diphenyl group is produced (entries 1−8). With the alkyl- and benzyl-substituted α-ketoamides (**22**−**26**), the expected oxyindole products are not obtained from CF_3SO_3H and benzene, but rather the α,*β*-unsaturated amides (**27**−**31**; entries 9−13) are formed. Even with forcing conditions (50 or 80 °C), only the α,*β*-unsaturated amides (or decomposition products) are obtained. Although the stereochemistry of the double bond has not been definitively established for products **29**, **30**, and **31**, it assumed to be syn on the basis of structural studies of the chlorobenzene product (**32**) from α-ketoamide **24** (eq 2). Strong NOE enhancements are observed between the olefinic hydrogen and the *ortho*-hydrogens in **32**, while only a weak enhancement is detected between the methyl group and the *ortho*-hydrogens. Unsymmetrically substituted oxyindole products may be formed by the reactions of α-ketoamides with varied arene nucleophiles, as shown in the conversion with *p*-dimethoxybenzene (eq 3). Likewise, reaction of the α-hydroxyamide (**34**) with superacid gives 7-isopropyl-3-phenylindolin-2-one (**35**, eq 4). In the case of the naphthyl system (**36**), the cyclization does not produce the 5-member ring, but rather, cyclization to the benzo[*de*]quinolin-2(3*H*)-one (**37**) is preferred (eq 5).



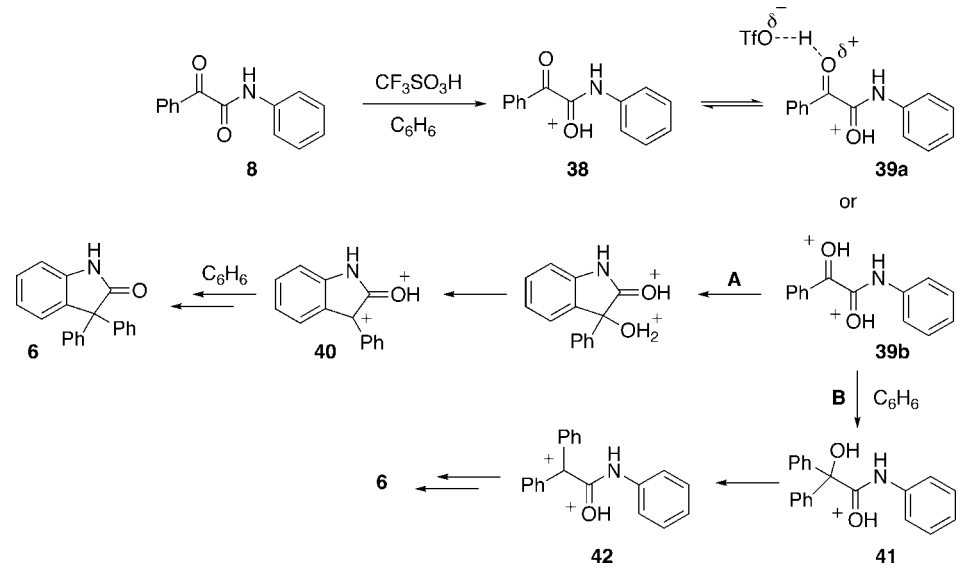
24 **32**

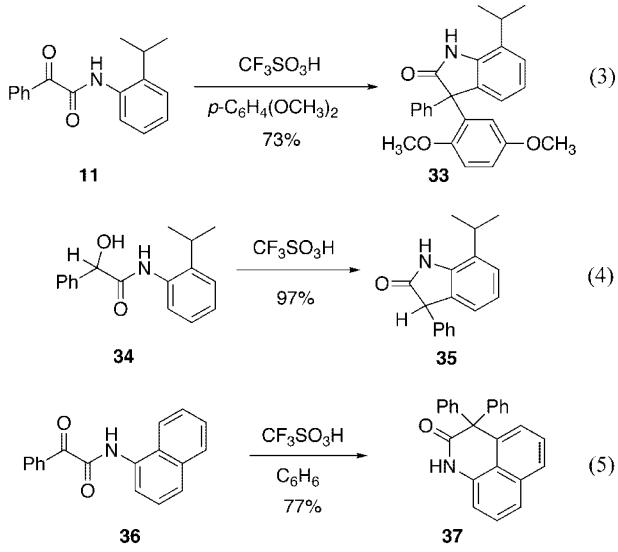
(8) For a general reference on superelectrophiles, see: Olah, G. A.; Klumpp, D. A. *Superelectrophiles and Their Chemistry*; Wiley & Sons: New York, 2008.

(9) (a) Yamazaki, T.; Saito, S.; Ohwada, T.; Shudo, K. *Tetrahedron Lett* **1995**, *36*, 5749–5752. (b) Klumpp, D. A.; Yeung, K. Y.; Prakash, G. K. S.; Olah, G. A. *Synlett* **1998**, 918–919. (c) Klumpp, D. A.; Zhang, Y.; Do, D.; Kartika, R. *Appl. Catal. A: Gen.* **2008**, *336*, 128–132.

(10) Tani, K.; Suwa, K.; Tanigawa, E.; Ise, T.; Yamagata, T.; Tatsuno, Y.; Otsuka, S. *J. Organomet. Chem.* **1989**, *370* (1−3), 203–221.

SCHEME 1. Proposed superelectrophilic mechanism for the preparation of oxyindole 6 from α-ketoamide 8 and C_6H_6 in CF_3SO_3H





Although the condensation reactions (α-ketoamides to oxyindoles) have not been fully optimized, the effects of acid strength and quantities have been studied. In the reaction of α-ketoamide **8** with C_6H_6 (0.88 mmol **8**, 2 mL C_6H_6, 50 °C, 14 h), product **6** may be obtained in yields of 80% or more with as little as 5 mmol of CF_3SO_3H (7 equiv). When less CF_3SO_3H or weaker Brønsted acids are used, the condensation reaction is much less efficient. Even with a large excess of concentrated sulfuric acid (86 equiv), product **6** can only be isolated in 7% yield. Similar reactions of **8** with C_6H_6 in phosphoric acid, or CF_3CO_2H, gave only unreacted starting material **8**. Likewise, solid acids (sulfated zirconia, montmorillonite K10, or acidic alumina) exhibited no catalytic activity in the condensation.[11] Triflic acid (CF_3SO_3H, H_o −14.1) is 1000 times more strongly acidic than 98% H_2SO_4 (H_o −10), and it is roughly 10^{11} times stronger than CF_3CO_2H (H_o −2.7).[12] Thus, the yields of product **6** are proportional to acid strength and good conversions are only observed in superacidic media.

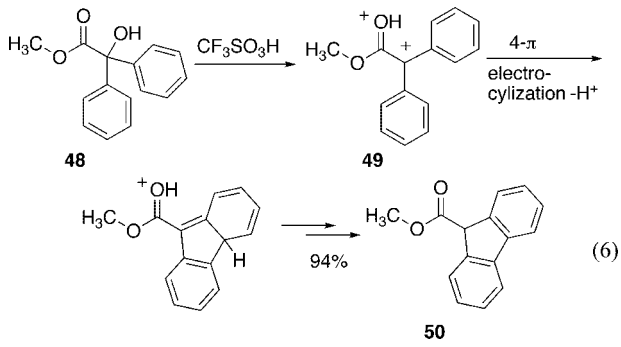
In the superacid-promoted conversions of α-ketoamides to oxyindoles, a mechanism is proposed which involves superelectrophilic species (Scheme 1). Protonation of the amide carbonyl leads to the carboxonium cation (**38**), which itself should have no tendency to cyclize or react with benzene at the ketone group. Partial or complete protonation at the ketone gives the superelectrophilic species (**39a** or **39b**), and cyclization then leads to the carbenium−carboxonium dication (**40**, route **A**). Dication **40** then reacts with benzene to give the final aryl-substituted oxyindole (**6**). The proposed mechanism is also consistent with the observed need for superacidic conditions. Weaker acids such as H_2SO_4 and CF_3CO_2H are less capable of protonating the monocationic species (**38**) and forming the superelectrophile (**39a** or **39b**). Based on the earlier results with benzilic acid derivatives (eq 1), it is conceivable that the α-ketoamides could initially react with benzene and then undergo cyclization to the oxindole **6** (route **B**). However in contrast to the earlier results from H_2SO_4-promoted reactions, we have found that benzilic acid derivatives (**4**, **43**, **44**) do not provide the oxyindoles from CF_3SO_3H, but rather the fluorene ring system (i.e., **45**−**47**) is produced (Scheme 2). None of the expected aryl-substituted oxindoles are formed in reactions of compounds **4**, **43**, or **44**. This observation argues against the involvement of either **41** or **42** in the formation of oxyindoles (route **B**, Scheme 1).

The formation of products **6**, **46**, and **47** can be understood in light of Shudo's and Ohwada's earlier studies of ester **48** and its superacid-promoted conversion to **50** (eq 6).[13] In this study, kinetic and spectroscopic evidence demonstrated the involvement of superelectrophile **49** in a concerted, 4-π electrocyclization leading to the fluorene ring system. It was suggested that electrostatic repulsive effects lead to a significant degree of charge delocalization into the phenyl rings (of dication **49**) and this facilitates the 4-π electrocyclization. A similar reaction is likely occurring in the case of **42** and the related superelectrophiles from benzilic acid derivatives **43** and **44**.

(11) Commercial grade solid acid catalysts were used in these reactions: compound **8** (0.1 g), benzene (3 mL), and the solid acid (1.0 g) were stirred at 50 °C for 12 h.

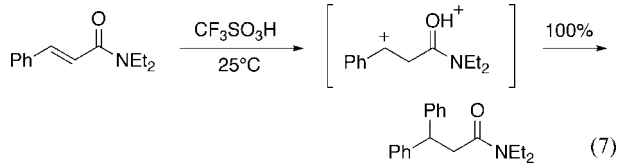
(12) Olah, G. A.; Prakash, G. K. S.; Sommer, J. In *Superacids*; Wiley: New York, 1985.

(13) (a) Ohwada, T.; Shudo, K. *J. Am. Chem. Soc.* **1989**, *111*, 34–40. (b) Ohwada, T.; Suzuki, T.; Shudo, K. *J. Am. Chem. Soc.* **1998**, *120*, 4629–4637.



48 **49** **50** (6)

Interestingly, the alkyl- and benzyl-substituted α-ketoamides give the α,β-unsaturated amides (**27**−**31**) in reactions with benzene in CF_3SO_3H (entries 9−13, Table 1), suggesting that (in these systems) the initial electrophilic reaction is with benzene, rather than the phenyl group in a cyclization step. This may be due to high electrophilic reactivities of the *O*,*O*-diprotonated intermediates from the alkyl-substituted α-ketoamides (**22**−**26**). Presumably, the methyl, ethyl, and benzyl groups are less capable of stabilizing the adjacent carboxonium ion (compared to the phenyl group of superelectrophile **39**), and this results in an enhanced reactivity toward benzene and a deactivation of the amidophenyl group (thus suppressing intramolecular reaction). Under the reaction conditions, there was little or no tendency for the α,β-unsaturated amides (**27**−**31**) to react further with benzene or the adjacent phenyl group. In contrast, the superelectrophilic reactivity of a number of α,β-unsaturated amides has been previously demonstrated (eq 7).[14] The sluggish reactivity of amides **27**−**31** may reflect a tendency to form (primarily) monocationic species in CF_3SO_3H.

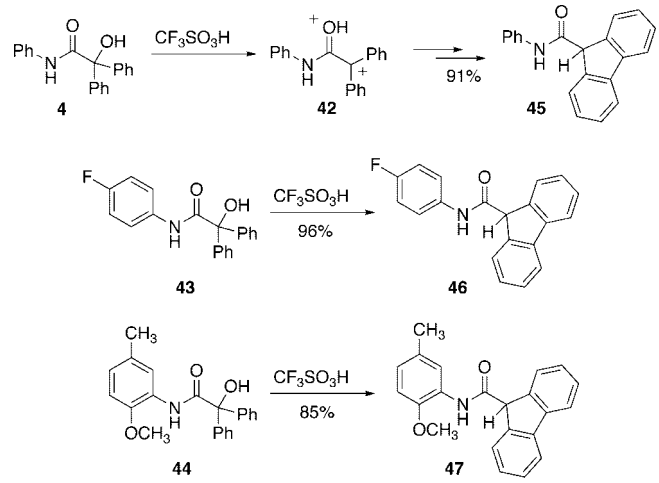


(7)

In order to further gain insights into the chemistry of the α-ketoamides, DFT calculations were done on the possible monocationic and dicationic intermediates (Scheme 3).[15] At the MP2(FC)/6-311++G(d,p) level, the energies of the monoprotonated products from **8** were studied, and it was shown that protonation at the amide carbonyl (i.e., **38**) is favored by about 8 kcal·mol^{-1} over protonation at the ketone. With the diprotonated products, several structures were located at energy minima, including **39b**, **52**, and **53**. Among these structures, **39b** is found to be the most stable superelectrophile, located 12 and 55 kcal·mol^{-1} below **52** and **53**, respectively. If it is assumed that cyclization of **8** requires protonation of the ketone group, then these results are evidence for the involvement of superelectrophile **39b** or the protosolvated species **39a**.

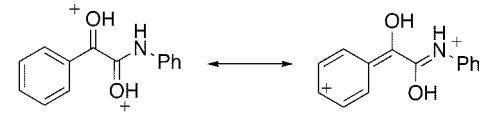
Compounds **8** and **4** were also studied using NMR spectroscopy and stable ion conditions (superacidic solution and low temperature; Table 2). Ionization of α-ketoamide **8** in $FSO_3H-SbF_5-SO_2ClF$ leads to a significant downfield shift of the phenyl ring carbons, and the two carbonyl ^{13}C resonances are shifted slightly upfield in the superacid (compared to $CDCl_3$). The protonated amide and ketone groups are assigned to the

SCHEME 2. Superacid-Promoted Reactions of Benzilic Acid Derivatives 4, 43, and 45



4 **42** **45** **43** **46** **44** **47**

resonances at δ 157.5 and 186.7, respectively. The upfield shifts of the carboxonium groups can be understood to involve charge delocalization involving the amide nitrogen and the phenyl group (keto). Charge−charge repulsive effects will lead to an increasing contribution from the delocalized resonance forms, such as **39b′** (eq 8).[16] Similar observations were made by Shudo and Ohwada in their studies of protonated methyl benzoylformate: with increasing acidity the benzoyl group is shifted upfield due to charge delocalization in the dication **54** (Scheme 4).[17] The amide carboxonium ion resonance at δ 157.5 (from **8**) is also consistent with a dicationic species, as diprotonated oxamide (**55**) exhibits a carboxonium resonance at δ 157.9 in magic acid solution.[18] Although the NMR data suggests the formation of **39** in superacidic media, it is not possible to determine the extent of protonation.



39b **39b'** (8)

In the case of compound **4**, ionization in $FSO_3H-SbF_5-SO_2ClF$ gives a ^{13}C NMR spectrum with several notable features (Table 2). The hydroxylic carbon resonance at δ 82.0 ($CDCl_3$) has disappeared and the phenyl ring carbons are (on the average) shifted significantly downfield in the superacidic media. The

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(15) Gaussian 03, Revision B.04: 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.

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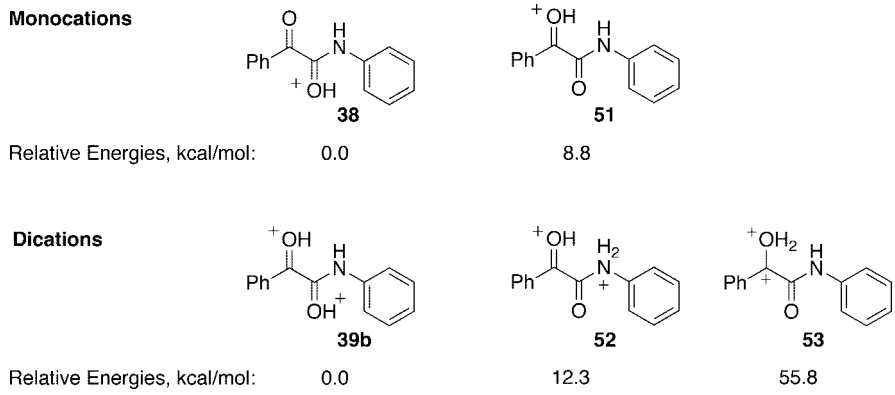
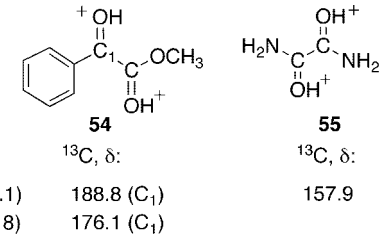
(17) (a) Ohwada, T.; Shudo, K. *J. Org. Chem.* **1989**, *54*, 5227–5237. (b) See also: Olah, G. A.; Westerman, P. W. *J. Org. Chem.* **1973**, *38*, 1986–1992.

(18) Olah, G. A.; Bausch, J.; Rasul, G.; George, H.; Prakash, G. K. S. *J. Am. Chem. Soc.* **1993**, *115*, 8060–8065.

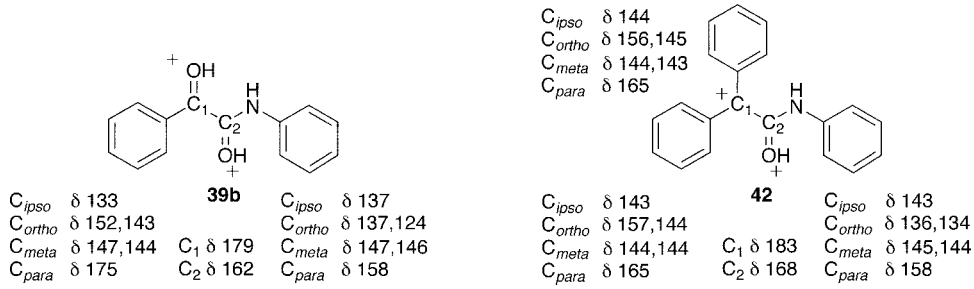
SCHEME 3. Calculated Relative Stabilities of Plausible Monocationic (38 and 51) and Dicationic Intermediates (39b, 52, and 53; MP2/6-311++G(d,p) level)



SCHEME 4. ^{13}C NMR Data from the Ionizations of Benzoyl Formate and Oxamide in Superacids[17,18]



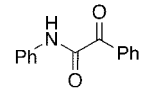
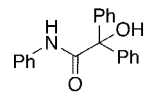
SCHEME 5. Calculated ^{13}C NMR Chemical Shift Values for Dications 39b and 42 (GIAO-B3LYP/6-311++G(d,p)//B3LYP/6-31+G(d) Level)



number of ^{13}C resonances also increases from 10 signals in compound **4** to 13 signals from the ionized product in superacid. It is not presently clear if these signals arise from a static species or a mixture of equilibrating products, including dication **42**. When the solution of **4** in FSO_3H-SbF_5−SO_2ClF is carefully quenched at low temperature, the starting material is recovered. If the same solution is warmed to room temperature and then quenched, only decomposition products are obtained. Interestingly, Shudo and Ohwada observed that the α-hydroxyester **48** and related systems tend to form superelectrophiles that are too reactive for direct observation by low temperature NMR (i.e., **49**).[13]

For comparison, the calculated ^{13}C chemical shifted of superelectrophiles **39b** and **42** were also determined (Scheme 5). Geometry optimizations of dications **39b** and **42** were done using DFT calculations at the B3LYP/6-31+G(d) level.[15] The calculated NMR shifts were then determined (relative to tetramethylsilane) from the optimized structures at the GIAO-B3LYP/6-311++G(d,p) level. For dication **39b**, the calculated gas-phase ^{13}C NMR shifts are in reasonably good agreement with the experimentally determined values. For example, the calculated ^{13}C resonances for the keto and amido carboxonium ions are δ 179 and 162, respectively, while compound **8** in FSO_3H−SbF_5−SO_2ClF solution exhibits resonances at δ 186.7 and 157.5. The calculations also show deshielded aromatic ring carbons, likely a consequence of charge delocalization in **39b**. In the case of dication **42**, there are similarities between the calculated ^{13}C NMR and the spectrum obtained from ionization of **4** in FSO_3H−SbF_5−SO_2ClF solution. However, even with comparison to the computed spectrum, it is not clear if com-

TABLE 2. ^{13}C NMR Spectral Data from Ionizations of Compounds 8 and 4 in FSO_3H−SbF_5−SO_2ClF and Data from $CDCl_3$ Solution

	solvent		^{13}C signals, δ
 **8**	$CDCl_3$	25°C	120.0, 125.3, 128.6, 129.2, 131.5, 133.1, 134.6, 136.7, 159.0, 187.5
	FSO_3H-SbF_5-SO_2ClF (1:1:1)	-70°C	123.5, 124.7, 129.5, 130.3, 133.0, 133.7, 140.1, 154.8, 157.5, 186.7
 **4**	$CDCl_3$	25°C	82.0, 119.8, 124.7, 127.6, 128.3, 128.5, 129.0, 137.2, 142.6, 171.1
	FSO_3H-SbF_5-SO_2ClF (1:1:1)	-70°C	123.3, 129.9, 132.4, 132.8, 133.1, 133.6, 136.0, 141.5, 150.2, 153.2, 165.0, 181.7, 186.6

pound **4** ionizes cleanly to dication **42** in $FSO_3H-SbF_5-SO_2ClF$ solution.

In conclusion, we have found that aryl-substituted oxyindoles may be prepared in good to excellent yields by the reactions of α-hydroxy and α-ketoamides with an arene in superacidic CF_3SO_3H. In some cases, α-hydroxyamides may undergo a cyclization to the fluorene-type ring system. Mechanisms are proposed for these conversions involving dicationic superelectrophiles.

Experimental Section

General Methods. Triflic acid was purchased from a commercial supplier and distilled prior to its use. The α-ketoamides were prepared by dicyclohexylcarbodiimide (DCC) promoted coupling reactions between α-ketoacids and anilines according to a published method,[10] while compound **34** was prepared similarly from mandelic acid. Compounds **4**, **44**, and **45** were prepared by reactions of the appropriate α-ketoamides with PhMgBr solution using standard procedures. Benzene was dried over 4 Å sieves prior to its use. Low-temperature NMR experiments were done using stable ion conditions;[19] FSO_3H and SbF_5 were obtained from commercial suppliers while SO_2ClF was prepared according to a published procedure.[20] Other reagents and solvents were used as received from commercial suppliers.

Preparation of Aryl-Substituted Oxyindoles (6, 15−21, and 33) and Compounds 27−32 and 37. The α-ketoamide (1 mmol) with the arene nucleophile (i.e., 1 mL of C_6H_6) was dissolved in $CHCl_3$ (5 mL), and CF_3SO_3H (2 mL, 23 mmol) was slowly added. The resulting solution was stirred overnight (ca. 18 h) at 50 °C. The mixture was then poured over ca. 15 g of ice and extracted twice with $CHCl_3$. The organic phase was then washed once with water andtwice with brine and dried over anhydrous Na_2SO_4. If necessary, the product was further purified by column chromatography (hexane/ether).

Cyclization to Products 35 and 45−47. The substrate (1 mmol) and $CHCl_3$ (5 mL) were combined, and CF_3SO_3H (2 mL, 23 mmol) was slowly added. The resulting solution was stirred overnight (ca. 18 h) at 50 °C. The mixture was then poured over ca. 15 g of ice and extracted twice with $CHCl_3$. The organic phase was then washed once with water and twice with brine and dried over anhydrous Na_2SO_4. If necessary, the product was further purified by column chromatography (hexane:ether).

3,3,5-Triphenyl-1,3-dihydroindol-2-one (15): white solid; mp 288−291 °C; ^{1}H NMR (DMSO-d_6) δ 10.88 (s, 1H), 7.26 (d, 1H, J = 7 Hz), 7.52 (s, 1H), 7.58 (t, 3H, J = 15 Hz), 7.41 (t, 2H, J = 15 Hz), 7.24−7.36 (m, 10H), 7.09 (d, 1H, J = 7 Hz); ^{13}C NMR (DMSO-d_6) δ 178.6, 142.3, 141.4, 140.4, 134.8, 134.3, 129.3, 128.9, 128.5, 127.5, 127.4, 127.3, 126.8, 124.6, 111.0, 62.9; EI MS (low res) 361 (M^+), 332, 254, 165; HRMS calcd for $C_{26}H_{19}NO$ 361.1467, found 361.1465.

7-Methoxy-4-methyl-3,3-diphenyl-1,3-dihydroindol-2-one (16): white solid; mp 192−197 °C; ^{1}H NMR ($CDCl_3$) δ 7.76 (s, 1H), 7.36−7.28 (m, 10 H), 6.83 (d, 1H, J = 8 Hz), 6.79 (d, 1H, J = 8 Hz), 3.9 (s, 3H), 1.85 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 179.2, 142.3, 138.4, 132.3, 129.1, 129.0, 128.3, 128.2, 127.4, 125.0, 110.0, 70.1, 55.7, 18.31; EI MS (low res) 329 (M^+), 300, 285, 165; HRMS calcd for $C_{22}H_{19}NO$ 329.1416, found 329.1416.

Compound 17: white solid; mp 275−279 °C; ^{1}H NMR ($CDCl_3$) δ 8.38 (s, 1H), 7.33−7.26 (m, 10 H), 7.03 (d, 1H, J = 7.6 Hz), 6.97 (d, 1H, J = 7.6 Hz), 2.96 (t, 2H, J = 14 Hz), 2.88 (t, 2H, J = 14 Hz), 2.17 (pent, 2H, J = 14 Hz); ^{13}C NMR ($CDCl_3$) δ 180.3, 145.8, 142.1, 136.0, 131.0, 128.4, 128.3, 127.1, 125.4, 124.2, 118.5, 63.1, 32.8, 29.4, 25.5; EI MS (low res) 325 (M^+), 296, 248, 220, 165; HRMS calcd for $C_{23}H_{19}NO$, 325.1467, found 325.1467.

7-Isopropyl-3,3-diphenyl-1,3-dihydroindol-2-one (18): yellow solid; mp 225−229 °C; ^{1}H NMR ($CDCl_3$) δ 9.24 (s, 1H), 7.35−7.28 (m, 10 H), 7.18 (d, 2H, J = 7 Hz), 7.09 (dd, 1H, J = 7 Hz), 2.99 (sept, 1H, J = 8 Hz), 1.29 (d, 6H, J = 8 Hz); ^{13}C NMR ($CDCl_3$) δ 180.4, 143.6, 141.9 (two carbons), 137.7, 133.2, 130.5, 128.5, 128.3, 127.2, 124.8, 123.7, 122.8, 63.2, 28.9, 22.5; EI MS (low res) 327 (M^+), 300, 285, 165; HRMS calcd for $C_{23}H_{21}NO$ 327.1623, found 327.1624.

5-Fluoro-3,3-diphenyl-1,3-dihydroindol-2-one (19): white solid; mp 220−223 °C; ^{1}H NMR ($CDCl_3$) δ 8.99 (s, 1H), 7.36−7.32 (m, 6H), 7.30−7.28 (m, 4H), 6.98 (d, 1H, J = 8 Hz), 6.94 (s, 1H), 6.92 (d, 1H, J = 8 Hz); ^{13}C NMR ($CDCl_3$) δ 180.4, 159.2 (d, J_{C-F} = 159 Hz), 141.1, 136.3, 135.2, 128.7, 128.3, 127.7, 114.8 (d, J_{C-F} = 24 Hz), 114.0 (d, J_{C-F} = 25 Hz), 111.2 (d, J_{C-F} = 8 Hz), 63.7; EI MS (low res) 303 (M^+), 274, 198, 165; HRMS calcd for $C_{20}H_{14}FNO$ 303.1059, found 303.1058.

5-Phenoxy-3,3-diphenyl-1,3-dihydroindol-2-one (20): white solid; mp 196−200 °C; ^{1}H NMR ($CDCl_3$) δ 7.68 (s, 1H), 7.34−7.30 (m, 12H), 7.07−7.10 (m, 1H), 7.03 (s, 1H), 6.95 (d, 2H, J = 8 Hz), 6.93−6.94 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 179.1, 162.9, 141.3, 135.6, 129.7, 128.5, 128.3, 127.5, 122.8, 119.2, 118.8, 117.7, 110.5, 65.8; EI MS (low res) 377(M^+), 348, 254, 165; HRMS calcd for $C_{26}H_{19}NO_2$ 377.1416, found 377.1418.

4-Methoxy-1,1-diphenyl-1,3-dihydro-10-oxa-3-azacyclopenta[*a*]fluoren-2-one (21): yellow solid; mp 279−282 °C; ^{1}H NMR ($CDCl_3$) δ 7.88 (s, 2H), 7.50−7.46 (m, 5H), 7.41−7.28 (m, 10H), 4.04 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 177.6, 156.4, 146.4, 141.1, 140.0 (two carbons), 128.7, 128.4, 128.2, 127.5, 126.1, 124.6, 122.7, 119.9, 119.5, 116.3, 111.9, 102.3, 56.3; EI MS (low res) 405(M^+), 376, 361, 285; HRMS (ESI, M + 1 ion) calcd for $C_{27}H_{20}NO_3$ 406.1443, found 406.1441.

***N*-(2-Isopropylphenyl)-2-phenylacrylamide (27):** white solid; mp 101−104 °C; ^{1}H NMR ($CDCl_3$) δ 7.99 (d, 1H, J = 2.0 Hz), 7.45−7.51(m, 4H),7.34 (s, 1H), 7.18−7.19 (m, 2H), 7.16−7.17 (m, 1H), 6.44 (s, 1H), 5.74 (s, 1H) 2.66 (sept, 1H, J = 6.8 Hz), 1.16 (d, 6H, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$) δ 164.8, 145.0, 139.1, 137.0, 134.2, 128.9, 128.8, 128.5, 126.5, 125.6, 125.4, 123.9, 123.3, 28.0, 22.6; MS 265 (M^+), 222, 162, 103; HRMS (ESI, M+1 ion) calcd for $C_{18}H_{20}NO$ 266.1545, found 266.1532.

***N*,2-Diphenylbut-2-enamide (29):** white solid; mp 205−209 °C; ^{1}H NMR ($CDCl_3$) δ 7.50−7.53 (m, 2H), 7.42−7.47 (m, 4H), 7.31−7.27 (m, 4H), 7.07−7.10 (m, 1H), 7.05 (s, 1H), 1.74 (d, 3H, J = 4.5 Hz); ^{13}C NMR ($CDCl_3$) δ 164.6, 137.8, 137.5, 137.0, 135.1, 129.9, 129.2, 128.8, 128.4, 124.2, 119.8, 15.3; EI MS (low res) 237 (M^+), 145, 117, 91; HRMS (ESI, M+1 ion) calcd for $C_{16}H_{16}NO$ 238.1232, found 238.1220.

***N*-(2-isopropylphenyl)-2-phenylbut-2-enamide (30):** white solid; mp 110−115 °C; ^{1}H NMR ($CDCl_3$) δ 7.99 (d, 1H, J = 2.0 Hz), 7.45−7.51 (m, 4H),7.34 (s, 1H), 7.18−7.19 (m, 2H), 7.16−7.17 (m, 1H), 6.44 (s, 1H), 5.74 (s, 1H) 2.66 (sept, 1H, J = 6.8 Hz), 1.16 (d, 6H, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$) δ 166.9, 139.7, 138.7, 137.9, 134.0, 131.9, 128.8, 128.0, 127.2, 126.4, 125.8, 125.5, 123.9, 27.9, 22.8, 15.7; MS 279 (M^+), 264, 117, 91; HRMS (ESI, M + 1 ion) calcd for $C_{19}H_{22}NO$ 280.1701, found 280.1688.

***N*,2,3-Triphenylacrylamide (31):** white solid; mp 138−141 °C; ^{1}H NMR ($CDCl_3$) δ 7.643−7.62 (m, 2H), 7.56−7.55 (m, 2H), 7.46−7.41 (m, 4H), 7.39−7.29 (m, 6H), 7.18−7115 (m, 1H), 7.12 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 167.7, 138.3, 137.5, 137.1, 135.1, 130.8, 129.5, 129.0, 128.8, 128.7, 128.6, 128.5, 126.5, 124.8, 120.2; EI MS (low res) 299(M^+), 207, 179; HRMS (ESI, M + 1 ion) calcd for $C_{21}H_{18}NO$ 300.1388, found 300.1382.

(*Z*)-2-(4-Chlorophenyl)-*N*-phenylbut-2-enamide (32): white solid; mp 144−147 °C; ^{1}H NMR ($CDCl_3$) δ 7.58 (d, 2H, J = 8 Hz), 7.38−7.31 (m, 6H), 7.18−7.14 (m, 1H), 6.23 (q, 1H, J = 7 Hz), 2.08 (d, 3H, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 166.5, 138.0, 137.5, 135.6, 133.9, 130.6, 129.1, 129.0, 127.9, 124.7, 119.8, 15.8; EI MS (low res) 273 (M^+), 271, 151, 115.

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3-(2,5-Dimethoxyphenyl)-7-isopropyl-3-phenyl-1,3-dihydroindol-2-one (33): brown solid; mp 210−214 °C; ^{1}H NMR ($CDCl_3$) δ 8.88 (s, 1H), 7.53 (s, 1H), 7.34−7.28 (m, 2H), 7.17 (d, 2H, J = 8 Hz), 7.02−6.99 (m, 1H), 6.92 (d, 2H, J = 8 Hz), 6.77 (s, 2H), 6.53 (s, 1H), 3.67 (s, 3H), 3.35 (s, 3H), 2.98 (septet, 1H, J = 7 Hz), 1.30 (d, 6H, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 180.8, 153.84, 152.0, 139.0, 138.9, 134.0, 132.6, 129.5, 129.2, 128.0, 127.4, 124.4, 123.4, 121.9, 117.3, 113.9, 112.7, 60.3, 56.3, 55.6, 29.0, 22.7, 22.1; EI MS (low res) 387 (M^+), 356, 133, 91; HRMS calcd for $C_{25}H_{25}NO_3$ 387.1834, found 387.1833.

7-Isopropyl-3-phenyl-1,3-dihydroindol-2-one (34): white solid; mp 138−141 °C; ^{1}H NMR ($CDCl_3$) δ 8.89 (s, 1H), 7.38 (d, 2H, J = 7 Hz), 7.32 (d, 1H, J = 7.5 Hz), 7.28−7.26 (mult, 3H), 7.19 (d, 1 H, J = 7.5 Hz), 7.04−7.02 (m, 1H), 4.68 (s, 1H), 2.96 (sept, 1 H, J = 6 Hz), 1.28 (d, 6H, J = 6 Hz); ^{13}C NMR ($CDCl_3$) δ 178.7, 139.1, 136.6, 130.1, 129.3, 128.8, 128.5, 127.5, 124.9, 122.8, 122.7, 52.8, 28.9, 22.5, 22.3; EI MS (low res) 251 (M^+), 208, 180, 152; HRMS calcd for $C_{17}H_{17}NO$ 251.1310, found 251.1312.

3,3-Diphenyl-1*H*-benzo[*de*]quinolin-2(3*H*)-one (36): white solid; mp 240−244 °C; ^{1}H NMR ($CDCl_3$) δ 10.88 (s, 1H), 8.01 (d, 1H, J = 8 Hz), 7.90 (d, 1H, J = 8 Hz), 7.64 (d, 2H, J = 8 Hz), 7.55−7.52 (m, 2H), 7.45−7.25 (mult, 10H); ^{13}C NMR ($CDCl_3$) δ 182.1, 141.6, 136.5, 133.5, 128.6, 128.5, 128.5, 128.1, 127.4, 126.4, 126.3, 126.3.2, 122.7, 121.9, 120.0, 64.3; EI MS (low res) 335 (M^+), 306, 258, 230, 152; HRMS calcd for $C_{24}H_{17}NO$ 335.1310, found 335.1313.

***N*-(4-Fluorophenyl)-9*H*-fluorene-9-carboxamide (46):** white solid; mp 261−264 °C; ^{1}H NMR ($CDCl_3$) δ 7.86 (d, 2H, J = 7.5 Hz), 7.79 (d, 2H, J = 7.5 Hz), 7.52 (t, 2 h, J = 15 Hz), 7.43 (t, 2H, J = 15 Hz), 7.33−7.28 (mult, 2H), 6.95 (t, 2H, J = 15 Hz), 6.82 (s, 1H), 4.95 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 168.8, 159.4 (d, J_{C-F} = 243 Hz), 141.2 (d, J_{C-F} = 69 Hz), 133.3, 128.7, 128.0, 125.4, 121.8 (d, J_{C-F} = 8 Hz), 120.5, 115.5 (d, J_{C-F} = 22 Hz), 56.9; EI MS (low res) 303 (M^+), 160, 139, 110; HRMS calcd for $C_{20}H_{14}FNO$ 303.1059, found 303.1063.

***N*-(2-Methoxy-5-methylphenyl)-9*H*-fluorene-9-carboxamide (47):** yellow solid; mp 143−146 °C; ^{1}H NMR ($CDCl_3$) δ 8.19 (s, 1H), 7.85−7.81 (mult, 4H), 7,75 (s, 1H), 7.49 (t, 2H, J = 15 Hz), 7.41 (t, 2H, J = 15 Hz), 6.78 (d, 1H, J = 8 Hz), 6.64 (d, 1H, J = 8 Hz), 4.95 (s, 1H), 3.58 (s, 3H), 2.30 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 168.3, 146.1, 141.4, 141.2, 130.5, 128.4, 127.7, 127.1, 125.5, 124.0, 120.3, 109.9, 57.1, 55.7, 20.9; EI MS (low res) 329 (M^+), 166, 149, 122; HRMS calcd for $C_{22}H_{19}NO_2$ 329.1416, found 329.1414.

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Supporting Information Available: ^{1}H and ^{13}C spectra of new compounds, representative experimental procedures, and computational data. This material is available free of charge via the Internet at http://pubs.acs.org.

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