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Fluoroquinolones from Imidoylketenes and Iminopropadienones, R–N=C=C=C=O

Belinda E. Fulloon[A] *and Curt Wentrup*[A,B]

[A]School of Chemistry and Molecular Biosciences, The University of Queensland, Brisbane, Qld 4072, Australia.

[B]Corresponding author. Email: wentrup@uq.edu.au

3-Fluoro-, 4-fluoro-, and 2,3,4-trifluorophenyliminopropadienones have been generated by flash vacuum thermolysis (FVT) of 5-[(fluoroarylamino)methoxymethylene]-2,2-dimethyldioxan-4,6-dione (Meldrum's acid) derivatives. Their reaction with methanol affords interconverting imidoylketenes and oxoketenimines, which are employed in a synthesis of fluoroquinolones. The same quinolones are obtained from methyl 1-fluoroaryl-1,2,3-triazole-4-carboxylates, which on FVT eliminate N_2 to generate oxoketenimines. Rearrangement of the oxoketenimines to imidoylketenes and cyclization afford the quinolones.

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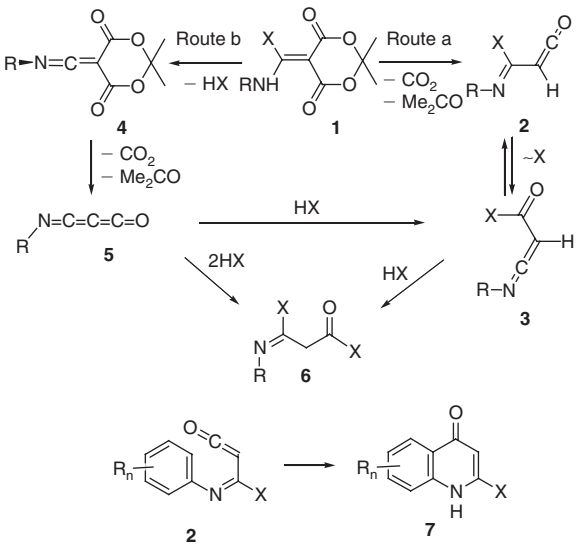
Introduction

Quinolones form an important class of biologically active compounds, especially well known for their antibiotic properties.[1] Because of a dwindling approval rate for new antibiotics,[2] and a rapid rise in microbial resistance, there is an urgent need for research into the development of new types of antibiotics, including new syntheses of quinolones, particularly fluoroquinolones. It was shown in previous work that certain quinolones can be synthesized by flash vacuum thermolysis (FVT) of Meldrum's acid derivatives,[3] 1,2,3-triazoles,[4] and pyrrole-2,3-diones.[5]

The mechanism of thermolysis of 5-aminomethylene derivatives of Meldrum's acid **1** has been elucidated previously.[3,6] There are two routes, a and b (Scheme 1). Briefly, FVT results in fragmentation of **1** to an imidoylketene **2**, which interconverts thermally with an oxoketenimine **3**. Owing to a favourable lone pair–lowest unoccupied molecular orbital (LUMO) interaction, the barrier for this 1,3-shift is very low for X = OMe, SMe, NMe_2, and halogens.[7] The formation of **2** and **3** (route a) takes place in competition with elimination of HX (X = OMe, SMe, or NMe_2) and formation of a transient but detectable ketenimine **4** (route b).

Further fragmentation of **4** by elimination of acetone and CO_2 leads to the iminopropadienone **5**. Usually, **2** and **3** can be observed spectroscopically and trapped chemically using FVT temperatures of ~400–500°C. Increasing proportions of iminopropadienone **5** are formed as the FVT temperature is increased and, above 500–700°C, this becomes the only product.[3,6a,8] Iminopropadienones **5** can be observed spectroscopically, usually at temperatures below −100° to −50°C, but a few examples of stable, isolable iminopropadienones have been reported,[3,9] namely the neopentyl, mesityl, *o-tert*-butylphenyl, 1-naphthyl, and pentafluorophenyl derivatives.

The iminopropadienones **5** react with nucleophiles (e.g. the HX formed in the elimination step, or with added nucleophile) to afford the same ketenimines **3** and ketenes **2** as were formed in route a. These ketenimines and ketenes may react further with HX to generate malonic imide esters **6**.[3]



Scheme 1. Imidoylketene **2**, oxoketenimine **3**, and iminopropadienone **5** formation from Meldrum's acid derivatives **1**.

When R is an aromatic group with at least one unsubstituted *ortho* position, the ketenes **2** can undergo an electrocyclic reaction, resulting in the formation of quinolones **7**. Both reaction routes, a and b, lead to ketenimines **3**, which interconvert rapidly with ketenes **2**. Thus, this system can be employed as a synthesis of quinolones **7**. For preparative purposes, it is advantageous to use high FVT temperatures, e.g. 700°C, where the iminopropadienones **5** are the exclusive primary reaction products. Subsequent addition of nucleophile and warm-up generate the quinolones.

Here, we report the use of the Meldrum's acid and triazole routes to generate fluoroquinolones.

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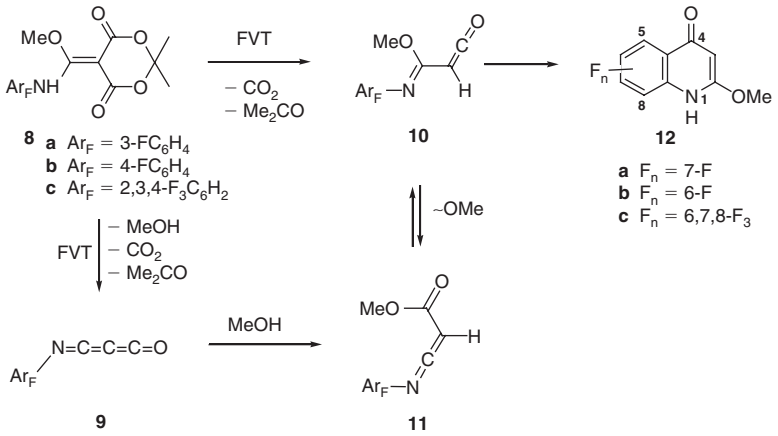


Scheme 2. Fluorophenyliminopropadienone and fluoroquinolone formation.

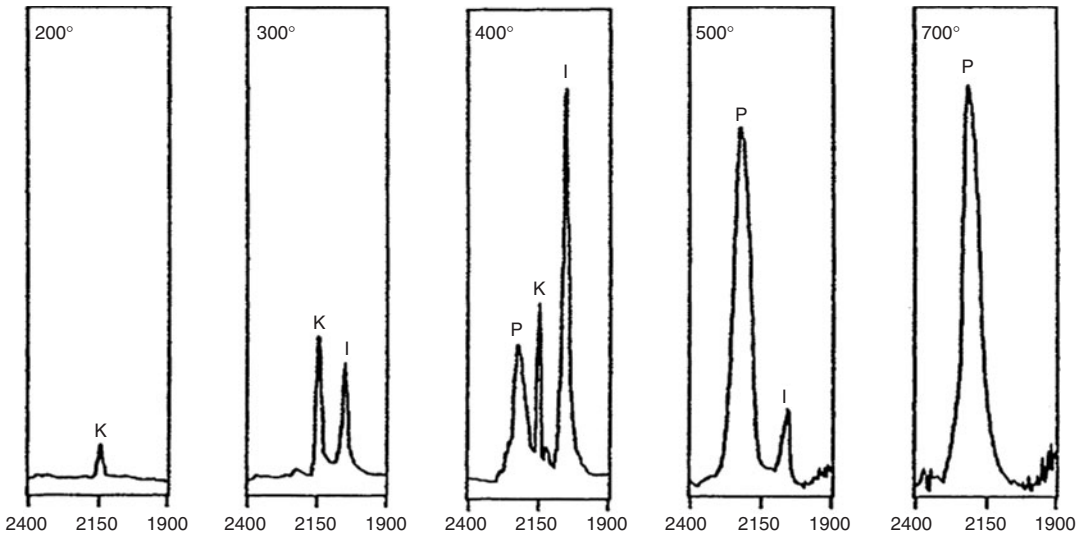


Fig. 1. Flash vacuum thermolysis (FVT) of 2,2-dimethyl-5-[2,3,4-trifluorophenylamino(methoxy)]-1,3-dioxan-4,6-dione **8c** at 200–700°C. IR spectra of the products at 77 K. K = ketene **10c**, I = ketenimine **11c**. P = iminopropadienone **9c**. Abscissae in wavenumbers (cm^{-1}).

Results and Discussion

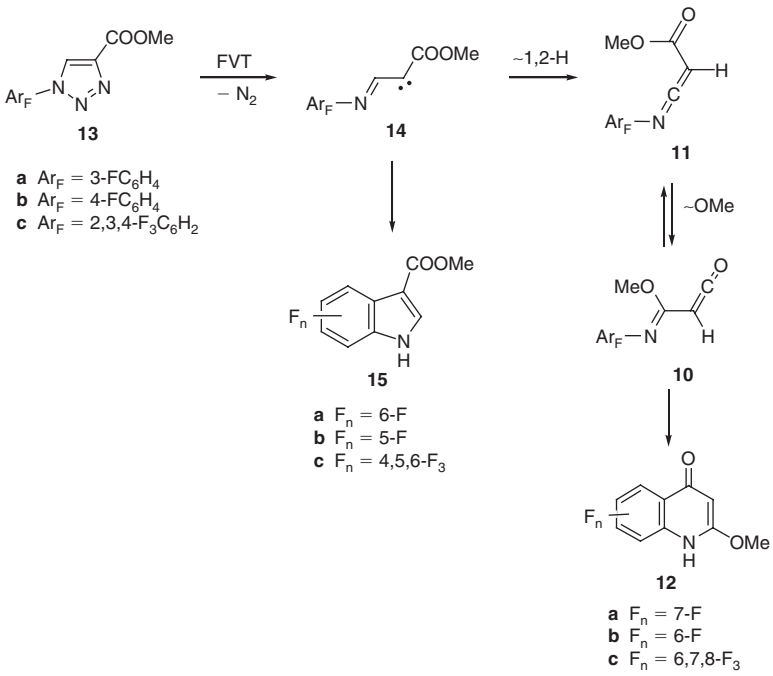
Quinolones from Meldrum's Acids

The Meldrum's acid derivatives **8** (Scheme 2) were prepared from 5-[(bismethylthio)methylene]-2,2-dimethyldioxan-4,6-dione by first displacing one methylthio group with the requisite fluoroaniline, and then displacing the second one with methanol using $HgO/HgCl_2$ as a catalyst. The ^{13}C NMR spectra of **8** reveal only one C=O peak for each compound. X-ray structures of a series of similar compounds[10] revealed considerable twisting about the central $C_5{=}C_7$ bond due to the push–pull effect, which also results in low rotational barriers about this bond and an averaging of the two C=O resonances.

The cumulenes formed by FVT of the dioxans **8a**–**c** over the temperature range 150–700°C were examined by isolation of the products as neat films at 77 K for IR spectroscopy. An example is illustrated in Fig. 1, and results for the three dioxans are shown in Figs S1–S3 (Accessory Publication).

At an FVT temperature of 150°C, no reactions took place. In each case, at 200°C, the spectrum revealed the presence of a ketene (**10**; IR (77 K) ~2138 cm^{-1}). At 300°C, a ketenimine (**11**; IR (77 K) ~2044w cm^{-1}) appeared as well. At 400°C, a third intermediate, the fluorophenyliminopropadienone **9** appeared, giving rise to a very strong absorption at ~2224 cm^{-1}. At 500°C, the iminopropadienone **9** was almost the only species, and by 700°C, **9** was the only product observed in the IR spectrum. These observations are illustrated in Figs S1–S3 (Accessory Publication). Compounds **9** were relatively long-lived, remaining observable on the deposition window until ~10°C. We reported recently that pentafluorophenyliminopropadienone is stable in solution at room temperature for extended periods, so that its ^{13}C NMR spectrum can be obtained easily.[9] All these results suggest a stabilizing 'fluorine effect' (see also below).

The dioxans **8** were subjected to preparative FVT at 700°C with isolation of the products on a coldfinger (77 K) coated with methanol. On completion of the pyrolysis, the coldfinger was warmed to room temperature, allowing the methanol to thaw and react with the iminopropadienones **9**. The resulting 2-methoxyfluoroquinolones **12** were isolated in ~50% yields. Each of the isolated quinolones was free of other isomers. Thus, **8a** and **8b** yielded only **12a** and **12b**, respectively, as evidenced by the ^{13}C NMR spectra as well as comparison of the ^{1}H NMR spectra with those of known quinolones.[11]



Scheme 3. The triazole route to quinolones and indoles.

Quinolones and Indoles from Triazoles

The imidoylketenes **10** and oxoketenimines **11** can also be generated from 1,2,3-triazoles **13** via a 1,2-H shift in the intermediate iminocarbene **14** (Scheme 3). Hence, FVT of triazoles can also be employed as a synthesis of quinolones **12**. However, a competing reaction leading to indoles **15** via an electrocyclization of imidoylcarbenes **14** diminishes the yield of quinolone. The best yield of quinolone (~60%) is obtained by FVT at high temperature (700°C), where cyclization of the imidoylketene **10** is complete in the gas phase.

The cumulenes formed by FVT of the triazoles were monitored by low-temperature IR spectroscopy in the same way as described for the Meldrum's acids above. An example is shown in Fig. 2, and data for the three triazoles are in Fig. S4 (Accessory Publication).

The ketenimines **11** are observed as the principal products, but smaller amounts of ketenes **10** are also observed at temperatures below 600–700°C; they disappear at high temperature because of rapid cyclization to quinolone. No traces of iminopropadienones **9** were detectable in the FVT reactions of the triazoles. It is noted that the ketene peak (K, Figs 1 and 2) is particularly strong in the case of the trifluorophenylimidoylketene **10c**, thus again suggesting a 'fluorine effect' that stabilizes ketenes. A stabilizing effect of fluorine was also obtained for other fluorinated ketenes of the type C_2F_5–CO–$C(CF_3)$=C=O, the first isolable α-oxoketene.[12] α-Oxoketenes and α-imidoylketenes are not usually isolable at room temperature in the absence of steric protection or the fluorine effect. α-Oxoketenimines are more stable and can be isolated in several instances (see below).

Preparative FVT of the triazoles at 700°C afforded quinolones **12** in yields of ~60%, together with indoles **15** (~10%). When FVT is carried out at lower temperatures (500°C), the oxoketenimines **11** can be isolated in yields of ~30%. They are distillable liquids and can be kept for a few hours at room temperature but hydrolyze by addition of water to the C=N double bond, forming malonic amide esters. FVT of the isolated ketenimines **11** at 400°C with isolation of the product at 77 K for IR spectroscopy reveals that the ketenimine–ketene equilibrium **11**⇌**10** is set up anew: typical ketene-to-ketenimine ratios are seen in the IR spectra, and quinolone **12** starts forming (Figs S5–S7, Accessory Publication).

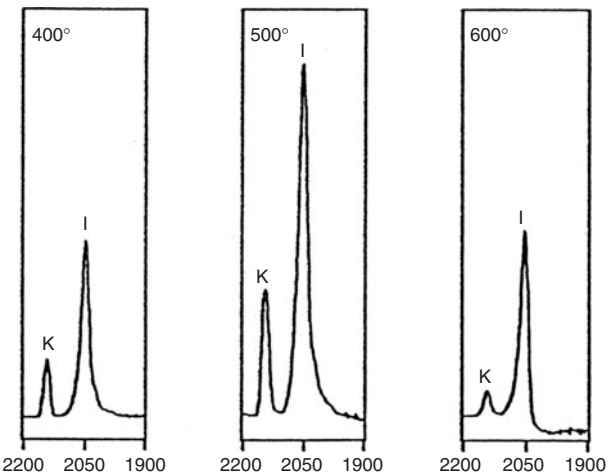


Fig. 2. IR spectra (cumulene region) of the products of flash vacuum thermolysis (FVT) of 1-(trifluorophenyl)-4-carbomethoxy-1,2,3-triazoles **13c** at various temperatures. Abscissae in wavenumbers (cm^{-1}). K = imidoylketene **10**; I = oxoketenimine **11**. The ketenes K and ketenimines I are identical with the ones recorded in Fig. 1.

Conclusion and Outlook

Fluorinated quinolones have been obtained by FVT of Meldrum's acid derivatives. Fluorinated quinolones and indoles are obtained by FVT of 1,2,3-triazoles. There is a significant stabilizing effect of fluorine on aryliminopropadienones **5** (**9**) and arylimidoylketenes **10**. The nature of this fluorine effect will be investigated by means of theoretical calculations.

Experimental

Procedures for preparative FVT and Ar matrix isolation have been published.[13] ^{1}H and ^{13}C NMR spectra of quinolones and indoles were assigned by comparison with data for structurally similar compounds.[3,4a,5,6,11]

5-[3-Fluoroanilino(methylthio)methylene]-2,2-dimethyl-1,3-dioxan-4,6-dione

This compound was prepared by adaptation of a method described by Huang et al.[14] A mixture of bismethylthiomethylene-Meldrum's acid[9] (1.24 g, 5.0 mmol), 3-fluoroaniline (0.55 g, 5.0 mmol), and ethanol (5 mL) was refluxed for 2 h. The solvent was then evaporated, and the residue recrystallized from THF/hexane to afford white crystals (1.35 g; 87%), mp 131–133°C. δ_H ($CDCl_3$) 1.74 (s, 6H, CH_3), 2.28 (s, 3H, SCH_3), 7.04–7.31 (m, 4H), 11.35 (s, 1H, NH). δ_C ($CDCl_3$) 18.96 (SCH_3), 26.36 (CH_3), 87.06, 103.26, 112.47, 114.71, 120.96, 130.66, 138.85, 163.83, 166.13 (C–F, d, *J* 235), 178.13 (C=O). ν_{max}(KBr)/cm^{-1} 2956, 1708, 1653, 1549, 1392, 1375, 1205, 1023. *m/z* (electron ionization mass spectrometry (EIMS)) 311 (M^+), 253, 206, 161, 134, 107, 95, 75, 43. (Found: C 54.1, H 4.52, N 4.40. Calc. for $C_{14}H_{14}NO_4FS$: C 54.01, H 4.53, N 4.50%.)

5-[3-Fluoroanilino(methoxy)methylene]-2,2-dimethyl-1,3-dioxan-4,6-dione ***8a***

To a solution of the above dioxan (0.156 g, 0.5 mmol) in methanol (5 mL) was added HgO (yellow, 0.109 g, 0.5 mmol) and $HgCl_2$ (0.135 g, 0.5 mmol), and the mixture was refluxed for 20 min. The mixture was filtered and the filtrate evaporated. Water (10 mL) was added to the residue to precipitate the product, which was isolated and recrystallized from THF/hexane. Yield 0.10 g (70%), mp 148–150°C. δ_H ($CDCl_3$) 1.76 (s, 6H, CH_3), 4.18 (s, 3H, OCH_3), 6.57–7.04 (m, 4H), 11.28 (s, 1H, NH). δ_C ($CDCl_3$) 26.37 (CH_3), 62.35 (OCH_3), 75.42, 103.27, 111.10, 113.12, 119.34, 129.91, 137.58, 159.21, 162.35 (C–F, d, *J* 257), 166.74 (C=O). ν_{max}(KBr)/cm^{-1} 3072, 1719, 1675, 1600, 1497, 1392, 1365, 1269, 1089, 1018. (Found: C 57.11, H 4.91, N 4.59. Calc. for $C_{14}H_{14}NO_5F$: C 56.93, H 4.78, N 4.75%.)

5-[4-Fluoroanilino(methylthio)methylene]-2,2-dimethyl-1,3-dioxan-4,6-dione

This compound was prepared by adaptation of the method described above and obtained as white crystals; yield 1.20 g (78%), mp 168–170°C. δ_H ($CDCl_3$) 1.75 (s, 6H, CH_3), 2.29 (s, 3H, SCH_3), 7.06–7.30 (m, 4H), 11.41 (s, 1H, NH). δ_C ($CDCl_3$) 18.91 (SCH_3), 26.33 (CH_3), 86.01, 103.18, 116.26, 116.73, 127.29, 133.10, 161.61 (C–F, d, *J* 252), 178.52 (C=O). ν_{max}(KBr)/cm^{-1} 2958, 1715, 1658, 1552, 1508, 1402, 1376, 1271, 1214, 1020. *m/z* (EIMS) 311 (M^+), 253, 209, 161, 134, 107, 59, 75, 58, 43. (Found: C 54.03, H 4.56, N 4.36. Calc. for $C_{14}H_{14}NO_4FS$: C 54.01, H 4.53, N 4.50%.)

5-[4-Fluoroanilino(methoxy)methylene]-2,2-dimethyl-1,3-dioxan-4,6-dione ***8b***

Prepared by adaptation of the method described above and obtained as white crystals; yield 0.11 g (74%), mp 190–191°C. δ_H 1.76 (s, 6H, CH_3), 4.13 (s, 3H, OCH_3), 7.04–7.33 (m, 4H), 11.36 (s, 1H, NH). δ_C ($CDCl_3$) 26.17 (CH_3), 62.93 (OCH_3), 75.68, 103.19, 116.35, 125.20, 127.52, 131.02, 164.13 (C–F, d, *J* 254), 171.40 (C=O). ν_{max}(KBr)/cm^{-1} 3071, 1721, 1654, 1618, 1582, 1511, 1373, 1270, 1206, 1084, 1019. *m/z* (EIMS) 295 (M^+), 237, 192, 161, 137, 109, 95, 75, 58, 43. (Found: C 57.01, H 4.74, N 4.86. Calc. for $C_{14}H_{14}NO_5F$: C 56.93, H 4.78, N 4.75%.)

5-[2,3,4-Trifluoroanilino(methylthio)methylene]-2,2-dimethyl-1,3-dioxan-4,6-dione

Synthesized using the procedure described above. White crystals; yield 1.21 g (69%), mp 135–138°C. δ_H ($CDCl_3$) 1.75 (s, 6H, CH_3), 2.38 (s, 3H, SCH_3), 7.03–7.09 (m, 2H), 12.42 (s, 1H, NH). δ_C ($CDCl_3$) 18.84 (SCH_3), 26.28 (CH_3), 87.62, 103.48, 112.11 (dd), 122.08 (m), 123.45 (dd), 140.56 (C–F, dt, *J* 255), 146.28 (C–F, ddd, *J* 255), 150.89 (C–F, ddd, *J* 254), 159.91, 179.50 (C=O). ν_{max}(KBr)/cm^{-1} 3072, 1712, 1652, 1556, 1496, 1402, 1376, 1271, 1056, 1018. *m/z* (EIMS) 347 (M^+), 289, 242, 198, 170, 143, 131, 119, 99, 84, 69, 43. (Found: C 48.56, H 3.702, N 3.73. Calc. for $C_{14}H_{12}NO_4F_3S$: C 48.41, H 3.48, N 4.03%.)

5-[2,3,4-Trifluoroanilino(methoxy)methylene]-2,2-dimethyl-1,3-dioxan-4,6-dione ***8c***

Synthesized using the procedure adapted described above. Yield 0.10 g (60%), mp 165–167°C. δ_H ($CDCl_3$) 1.77 (s, 6H, CH_3), 4.17 (s, 3H, OCH_3), 6.72–7.20 (m, 2H), 11.49 (s, 1H, NH). δ_C ($CDCl_3$) 26.35 (CH_3), 63.61 (OCH_3), 75.09, 103.49, 119.94 (m), 118.96 (dd), 121.15 (dd), 140.96 (C–F, dt, *J* 246), 147.31 (C–F, ddd, *J* 244), 151.35 (C–F, ddd, *J* 248), 161.09, 172.46 (C=O). ν_{max}(KBr)/cm^{-1} 2952, 1713, 1677, 1583, 1507, 1485, 1409, 1378, 1270, 1043. *m/z* (EIMS) 331 (M^+), 273, 229, 198, 170, 145, 119, 93, 75, 43. (Found: C 50.84, H 3.52, N 4.16. Calc. for $C_{14}H_{12}NO_5F_3$: C 50.75, H 3.65, N 4.23%.)

FVT of Fluoroarylmethylene-Meldrum's Acids ***8***

The dioxans **8** were subjected to analytical FVT over the temperature range 150–700°C, subliming at ~110°C at a vacuum of $\sim 3 \times 10^{-1}$ Pa. The products were collected on a KBr deposition disk at 77 K for IR spectroscopy. The results are illustrated in Figs 1 and S1–S3. Ketenimines **11** (I) appeared at 2044, 2049, and 2047 cm^{-1} for **11a**, **11b**, and **11c**, respectively. Imidoylketene **10** (K) appeared at 2138, 2139, and 2140 cm^{-1}, respectively, for **11a**, **11b**, and **11c**. Iminopropadienones **9** (P) appeared at 2224s and 2190w, 2221s and 2184w, and 2219s and 2187w cm^{-1}, respectively, for **9a**, **9b**, and **9c**. At FVT temperatures of 500°C and above, the corresponding fluoroquinolone **12** also appeared in the IR spectra (1637, 1675, and 1634 cm^{-1}, respectively, for **12a**, **12b**, and **12c**; not shown). The fluoroquinolones **12** were isolated and characterized in the preparative FVT experiments at 700°C as described below.

*2-Methoxy-7-fluoro-4(1*H*)-quinolone* ***12a***

The dioxan **8a** (65 mg) was subjected to preparative FVT at 700°C, subliming at ~105°C in the course of 4 h. Methanol was used as a trapping agent by coating onto the coldfinger before and after pyrolysis. On completion of pyrolysis, the coldfinger was warmed to room temperature. The resulting yellow solid (21 mg; 50% yield) was identified as 2-methoxy-7-fluoroquinolone **12a**, mp 311–312°C. δ_H ([D_6]DMSO) 3.49 (s, 3H, CH_3), 5.82 (s, 1H), 7.08 (ddd, 1H, H-6, $J_{6,8}$ 2.4, $J_{6,F}$ 8.6), 7.33 (dd, 1H, H-8, $J_{8,F}$ 11.5), 7.90 (dd, 1H, H-5, $J_{5,6}$ 9.1, $J_{5,F}$ 6.6), 11.45 (s, 1H, NH). δ_C ([D_6]DMSO) 28.75 (CH_3), 97.03, 101.40 (d), 108.81 (d), 112.84, 125.59 (d), 141.73 (d), 161.76 (C–F, d, *J* 253), 162.91, 164.87 (C=O). ν_{max}(KBr)/cm^{-1} 3391, 3098, 2954, 1641 (C=O), 1600, 1559, 1512, 1374, 1334, 1243, 1148, 1064.

m/z (EIMS) 193 (M^+), 163, 150, 135, 123, 107, 95, 75, 57. (Found: C 61.88, H 3.98, N 7.15. Calc. for $C_{10}H_8NO_2F$: C 62.18, H 4.17, N 7.25%.)

*2-Methoxy-6-fluoro-4(1*H*)-quinolone* ***12b***

The dioxan **8b** was subjected to FVT at 700°C and workup as described for **8a** above. The resulting yellow solid (17 mg; 49%) was identified as 2-methoxy-6-fluoroquinolone **12b**, mp 188–190°C. δ_H ([D_6]DMSO) 3.52 (s, 3H, CH_3), 5.90 (s, 1H, CH), 7.47–7.49 (dd, 1H), 7.54–7.56 (m, 1H), 7.61–7.64 (dd, 1H), 11.50 (s, 1H, NH). δ_C ([D_6]DMSO) 28.71 (CH_3), 98.83, 108.25 (d), 116.71 (d), 117.13 (d), 118.79 (d), 136.72, 156.83 (C–F, d, *J* 239), 160.55, 162.68 (C=O). ν_{max}(KBr)/cm^{-1} 3360 (N–H), 2989, 1635, 1611, 1599, 1559, 1498, 1478, 1417, 1328, 1244, 1199, 1097, 1063. *m/z* (EIMS) 193 (M^+), 163, 150, 135, 123, 107, 95, 75, 57. (Found: C 61.97, H 3.95, N 7.49. Calc. for $C_{10}H_8NO_2F$: C 62.18, H 4.17, N 7.25%.)

*2-Methoxy-6,7,8-trifluoro-4(1*H*)-quinolone* ***12c***

The dioxan **8c** (85 mg) was subjected to FVT at 700°C and workup as above. The resulting yellow solid (16 mg; 47%) was analyzed as 2-methoxy-6,7,8-trifluoroquinolone **12c**, mp 302–304°C. δ_H ([D_6]DMSO) 3.67 (d, 3H, OCH_3), 5.91 (s, 1H), 7.66 (t, 1H), 11.86 (s, 1H, NH). δ_C ([D_6]DMSO) 31.01 (OCH_3), 98.81, 105.71 (m), 113.19 (m), 127.65, 139.68 (C–F, ddd, *J* 253), 141.77 (C–F, dt, *J* 267), 144.85 (C–F, ddd, *J* 264), 159.83, 163.41 (C=O). ν_{max}(KBr)/cm^{-1} 3390, 3087, 2959, 1639, 1617, 1527, 1490, 1396, 1325, 1244, 1076, 1007. *m/z* (EIMS) 229 (M^+), 200, 186, 158, 143, 113, 99, 81, 75. (Found: C 52.53, H 2.46, N 6.07. Calc. for $C_{10}H_5NO_2F_3$: C 52.65, H 2.23, N 6.14%.)

*Methyl 1-(3-Fluorophenyl)-1*H*-1,2,3-triazole-4-carboxylate* ***13a***

Synthesized using a procedure adapted from Abu-Orabi et al.[15] 3-Fluorophenyl azide[16] (2.30 g, 0.017 mol) was dissolved in ethanol (110 mL). Methyl propiolate (1.43 g, 0.015 mol) was added to the solution, and the mixture was refluxed for 18 h. The solvent was removed by rotary evaporation and the remaining solid recrystallized from ethanol/diethyl ether to produce white crystals. Yield 2.40 g (65%), mp 132–134°C. δ_H ($CDCl_3$) 3.97 (s, 3H, OCH_3), 7.15–7.55 (m, 4H), 8.52 (s, 1H). δ_C ($CDCl_3$) 52.37, 108.61, 116.05, 116.48, 125.51, 131.46, 137.37, 140.67, 160.79 (C=O), 163.02 (C–F, d, *J* 251.7). ν_{max}(KBr)/cm^{-1} 3142, 2952, 1710, 1616, 1508, 1443, 1349, 1218, 1164, 1040. *m/z* (EIMS) 221 (M^+), 190, 162, 148, 134, 107, 95, 75, 59, 44. (Found: C 54.34, H 3.61, N 18.98. Calc. for $C_{10}H_8N_3O_2F$: C 54.28, H 3.65, N 19.00%.)

*Methyl 1-(4-Fluorophenyl)-1*H*-1,2,3-triazole-4-carboxylate* ***13b***

Prepared according to the literature.[17]

2,3,4-Trifluorophenyl Azide

Prepared from 2,3,4-trifluoroaniline by adaptation of a method reported by Dyall et al.[18] for naphthyl azides. It was obtained as a brown oil in a yield of 3.53 g (75%) on a 17-mmol scale and purified by Kugelrohr distillation at 40°C/10^{-2} Pa. δ_H ($CDCl_3$) 6.79–6.99 (m, 2H). δ_C ($CDCl_3$) 112.10 (d), 114.21 (d), 125.52 (d), 140.56 (C–F, dt, *J* 252.2), 143.74 (C–F, ddd, *J* 248.6), 148.65 (C–F, ddd, *J* 241.3). ν_{max}(CCl_4)/cm^{-1} 2979, 2119, 1599, 1506, 1303, 1235, 1129, 1098, 1014. *m/z* (EIMS) 173 (M^+), 145, 116, 97, 70, 52, 39. (Found: C 41.44, H 1.09, N 24.21. Calc. for $C_6H_2N_3F_3$: C 41.61, H 1.16, N 24.28%.)

*Methyl 1-(2,3,4-Trifluorophenyl)-1*H*-1,2,3-triazole-4-carboxylate* ***13c***

Prepared from 2,3,4-trifluorophenyl azide as described for **13a** above. Yield 1.39 g (59%), mp 119–121°C. δ_H ($CDCl_3$) 3.99 (s, 3H, OCH_3), 7.18–7.23 (m, 1H), 7.73–7.78 (m, 1H), 8.56 (d, 1H). δ_C ($CDCl_3$) 52.46 (OCH_3), 113.14 (m), 118.91 (m), 122.02 (m), 128.23 (d), 140.56 (C–F, dt, *J* 251.2), 140.68, 143.75 (C–F, ddd, *J* 245.6), 151.15 (C–F, ddd, *J* 239.5), 160.55 (C=O). ν_{max}(KBr)/cm^{-1} 3128, 2954, 1732, 1529, 1513, 1443, 1348, 1274, 1213, 1159, 1041, 1018. *m/z* (EIMS) 257 (M^+), 226, 198, 170, 143, 119, 81, 69, 53. (Found: C 46.49, H 2.31, N 16.29. Calc. for $C_{10}H_6N_3O_2F_3$: C 46.69, H 2.35, N 16.34%.)

General Procedure for FVT of Triazoles ***13***

(a) The triazole (~10 mg) was subjected to analytical FVT over the temperature range 300–700°C, subliming at ~95°C. The system was operated at a vacuum of $\sim 3 \times 10^{-3}$ Pa, and the products were collected on a KBr deposition disk cooled to 77 K. Neat-film IR spectra were recorded for various FVT temperatures as illustrated in Figs 2 and S4. The ketenimines **11** (I) and ketenes **10** (K) were identical to those derived from the Meldrum's acid derivatives as described above. Iminopropadienones **5** or **9** (P) were absent in these spectra. Solid material that had condensed in the quartz tube between the oven and the cold deposition window at FVT temperatures $\geq$400°C was washed out with ethanol and identified as mixtures of the corresponding quinolone and indole by comparison with the characterization data described above and below.

(b) The triazole (100–120 mg) **13** was subjected to FVT at 500°C, subliming at ~95°C for 2 h. The pyrolysate was collected in a U-tube cooled to 77 K. On completion, the system was pressurized to 101.3 kPa with N_2 and warmed to room temperature. An oil collected in the U-tube, was rinsed into a receiving flask with CCl_4, and the mixture was subjected to Kugelrohr distillation (~55°C, 4.0×10^{-1} Pa), affording a clear oil, identified as the methyl *N*-(fluorophenyl)ketenimine-1-carboxylate **11**, in yields of 20–33 mg (21–30%). The remaining material, after the fluorophenyloxoketenimine **11** had distilled, was composed of the corresponding quinolone (32–36 mg; 31–35% yield) and indole (21–26 mg; 20–25%), which were separated by column chromatography on silica gel, eluting with $CHCl_3$/hexane 2:3 and identified by comparison with the characterization data described above and below.

(c) The triazole **13** (100–110 mg) was subjected to preparative FVT at 700°C, subliming at ~95°C for 2 h. A yellow-pink solid was collected on the 77 K coldfinger. This material was separated by column chromatography on silica gel as described above to afford methyl fluoroindolecarboxylate **15** (9–13%) and 2-methoxyfluoroquinolone **12** (60–63%).

Methyl N*-(3-Fluorophenyl)ketenimine-1-carboxylate* ***11a***

ν_{max}/cm^{-1} 2955, 2046 (C=C=N), 1718 (C=O), 1607, 1439, 1348, 1254, 1148, 1080. δ_H ($CDCl_3$) 3.72 (s, 3H, CH_3), 4.65 (s, 1H), 7.00–7.34 (m, 4H). δ_C ($CDCl_3$) 51.92 (OCH_3), 53.10, 111.75 (d), 115.73 (d), 120.17, 130.81 (d), 138.20 (d), 162.99 (C–F, d, *J* 148.9), 168.11 (C=O), 178.50 (N=C). *m/z* (EIMS) 193 (M^+), 163, 135, 123, 107, 95, 75, 57. High-resolution (HR) MS calc. for $C_{10}H_8NO_2F$ 193.0539. Found 193.0545.

Methyl N-*(4-Fluorophenyl)ketenimine-1-carboxylate* ***11b***

ν_{max}/cm^{-1} 2953, 2047 (C=C=N), 1721 (C=O), 1506, 1443, 1234, 1149, 1040. δ_H ($CDCl_3$) 3.71 (s, 3H, CH_3), 4.61 (s, 1H), 7.03–7.32 (m, 4H). δ_C ($CDCl_3$) 51.83 (OCH_3), 52.83, 116.65 (d), 126.44 (d), 132.47, 162.42 (C–F, d, *J* 249.5), 168.41 (C=O), 177.15 (N=C). *m/z* (EIMS) 193 (M^+), 162, 134, 107, 95, 75, 57. HRMS calc. for $C_{10}H_8NO_2F$ 193.0539. Found 193.0549.

Methyl N-*(2,3,4-Trifluorophenyl)ketenimine-1-carboxylate* ***11c***

ν_{max}/cm^{-1} 2954, 2046 (C=C=N), 1725 (C=O), 1515, 1440, 1246, 1155, 1013. δ_H ($CDCl_3$) 3.72 (s, 3H, CH_3), 4.67 (s, 1H), 6.93–7.12 (m, 2H). δ_C ($CDCl_3$) 51.99 (OCH_3), 52.50, 111.99 (m), 120.67 (m), 122.05, 140.50 (C–F, dt, *J* 251.5), 146.23 (C–F, ddd, *J* 226.3), 151.83 (C–F, ddd, *J* 220.2), 167.81 (C=O), 181.77 (N=C). *m/z* (EIMS) 229 (M^+), 198, 170, 143, 123, 99, 75. HRMS calc. for $C_{10}H_6NO_2F_3$ 229.0351. Found 229.0334.

Methyl 6-Fluoroindole-3-carboxylate ***15a***

This compound is commercially available and has been synthesized by Kleeman et al.[19] Mp 194–196°C. δ_H ($CDCl_3$) 3.89 (s, 3H, OCH_3), 7.01 (ddd, 1H, H-5, $J_{5,7}$ 2.3, $J_{5,F}$ 8.8), 7.07 (dd, 1H, H-7, $J_{7,F}$ 9.1), 7.87 (d, 1H, H-2), 8.09 (dd, 1H, H-4, $J_{4,5}$ 9.0, $J_{4,F}$ 5.4), 8.61 (bs, 1H, NH). δ_C ($CDCl_3$) 51.14 (OCH_3), 98.02 (d), 109.11, 110.94 (d), 122.29, 122.60 (d), 131.16, 136.02 (d), 160.34 (C–F, d, *J* 240.0), 165.26 (C=O). ν_{max}(KBr)/cm^{-1} 3247, 2947, 1669, 1531, 1143, 1282, 1196, 1141, 1101, 1055, 954. *m/z* (EIMS) 193 (M^+), 162, 134, 107, 81, 57, 39. (Found: C 62.08, H 4.14, N 7.25. Calc. for $C_{10}H_8NO_2F$: C 62.16, H 4.18, N 7.25%.)

Methyl 5-Fluoroindole-3-carboxylate ***15b***

This compound is commercially available and has been synthesized by Karabelas et al.[20] Mp 200–202°C. δ_H ($CDCl_3$) 3.90 (s, 3H, OCH_3), 7.01 (ddd, 1H, H-6, $J_{4,6}$ 2.1, $J_{6,F}$ 9.0, $J_{6,7}$ 8.5), 7.31 (dd, 1H, H-4, $J_{4,6}$ 2.1, $J_{4,F}$ 10.1), 7.82 (dd, 1H, H-7, $J_{6,7}$ 8.5, $J_{7,F}$ 5.3), 7.93 (d, 1H, H-2), 8.55 (bs, 1H, NH). δ_C ($CDCl_3$) 50.94 (OCH_3), 106.70 (d, $J_{3,F}$ 4.9), 109.01 (d, $J_{6,F}$ 24.0), 111.60 (d, $J_{4,F}$ 26.4), 112.01 (d, $J_{7,F}$ 10.1), 126.35 (d, $J_{3a,F}$ 11.3), 131.97, 132.23, 159.11 (C–F, d, $J_{5,F}$ 237.7), 165.00 (C=O). ν_{max}(KBr)/cm^{-1} 3229, 2948, 1674, 1527, 1446, 1364, 1276, 1196, 1148, 1038, 931. *m/z* (EIMS) 193 (M^+), 162, 134, 107, 81, 57, 39. (Found: C 62.06, H 4.10, N 6.99. Calc. for $C_{10}H_8NO_2F$: C 62.16, H 4.18, N 7.25%.)

Methyl 5,6,7-Trifluoroindole-3-carboxylate ***15c***

Mp 219–222°C. δ_H ($CDCl_3$) 3.90 (s, 3H, OCH_3), 7.74 (t, 1H), 7.92 (d, 1H, H-2), 8.78 (bs, 1H, NH). δ_C ($CDCl_3$) 50.87 (OCH_3), 95.71, 102.81 (m), 109.53 (d), 120.77 (d), 128.33 (C–F, dt, *J* 242.5), 131.65, 136.25 (C–F, ddd, *J* 239.3), 147.29 (C–F, ddd, *J* 230.0), 164.11 (C=O). ν_{max}(KBr)/cm^{-1} 3260, 2948, 1697, 1673, 1602, 1545, 1473, 1392, 1330, 1205, 1163, 1081, 1005, 967, 918. *m/z* (EIMS) 229 (M^+), 198, 170, 143, 123, 99, 75, 69. (Found: C 52.21, H 2.58, N 6.12. Calc. for $C_{10}H_6NO_2F_3$: C 52.39, H 2.64, N 6.11%.)

Accessory Publication

IR spectra of the products of FVT of **8a**–**c** and **13a**–**c** at various temperatures (Figs S1–S7) are available from the journal's website.

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