

无金属催化烯烃自由基环化合成多氟取代吲哚酮

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摘要 一种无金属催化的活泼烯烃与全氟碘代丁烷自由基环化合成含氟吲哚酮的反应被发展。在廉价易得的偶氮二异丁腈(AIBN)介导下,多种 *N*-芳基丙烯酰胺类化合物与全氟碘代丁烷发生自由基串联环化反应,以53%~85%的产率合成了一系列的潜在生理活性的多氟取代吲哚酮。此工作为潜在药用价值的多氟取代吲哚酮合成提供了一条高效、廉价、绿色的新途径。

关键词 无金属催化;偶氮二异丁腈;C—H环化;自由基;多氟吲哚酮

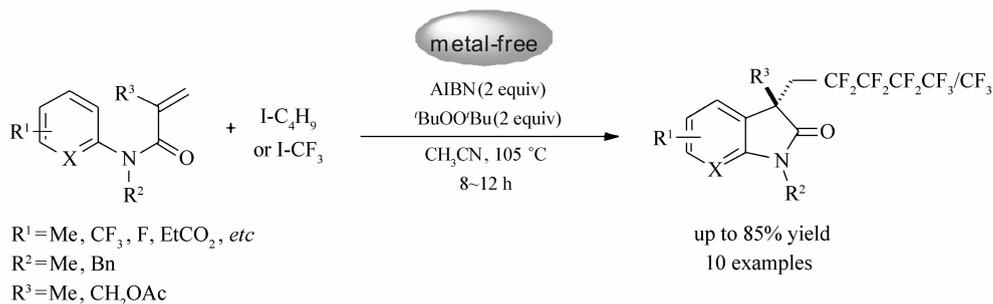
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含氟化合物已在医药、农药和材料等领域得到广泛应用^[1]。据统计,目前20%的医药和30%农药中至少含有一个氟原子。最近,在有机分子中,特别是在一些杂环架中引入含氟基团的方法研究吸引了众多化学家兴趣。吲哚酮及其衍生物广泛分布在自然界中,是许多潜在生理活性化合物的重要构建骨架^[2-3]。*N*-芳基丙烯酰胺的串联自由基环化反应是目前合成吲哚酮最便捷、有效的方法^[4]。基于含氟分子潜在的药用价值,近年来通过 *N*-芳基丙烯酰胺自由基环化来构建含氟吲哚酮也得到了一些文献报道。但是,这些报道的大部分局限于在吲哚酮骨架中引入三氟甲基基团^[5-10]。因此,增加在吲哚酮骨架引入的含氟基团(如多氟基团)的多样性目前仍然有重要的意义。据我们所知,目前国内外只有两例在吲哚酮骨架中引入全氟基团的报道^[11-12],但这种方法需要贵重的钪或铪光催化剂,且所采用的氟试剂 R_fSO_2Cl 价格不菲。全氟碘代试剂是有机氟化学常用的试剂,价格相对较便宜,商业渠道很容易买到。以全氟碘代试剂代替 R_fSO_2Cl ,同时采用无任何金属参与的途径在吲哚酮骨架中引入多氟基团不但经济,而且“绿色”,因此将具有重要的合成意义。基于我们在吲哚酮合成研究兴趣的拓展^[13-16],本文发展了一种无金属催化 AIBN 介导的活泼烯烃与全氟碘代丁烷环化反应合成多氟取代吲哚酮的方法(Scheme 1)。此方法底物适应范围广,操作简单,催化体系廉价,且产率高达85%。



Scheme 1 Synthesis of perfluorinated oxindoles

1 实验部分

1.1 仪器和试剂

所用的芳基胺、草酰氯、和碘代全氟丁烷购自阿拉丁试剂公司或百灵威试剂公司,其它试剂除标明

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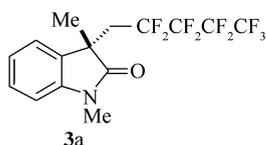
通讯联系人:唐石,教授;Tel/Fax:0743-8563911;E-mail:stang@jssu.edu.cn;研究方向:有机催化与合成

外均为分析纯。实验中所需的原料 *N*-芳基丙烯酰胺 (**1a** ~ **1j**) 参照相关文献[6]报道方法合成得到。AV ANCE 400 MHz 型超导傅里叶数字化核磁共振仪(瑞士 Bruker 公司);GC-MS-QP2010 型质谱仪(日本岛津公司);RE-52AA 型旋转蒸发器(上海亚荣生化仪器厂);XT5A 型显微熔点仪(北京市科仪电光学仪器厂)。

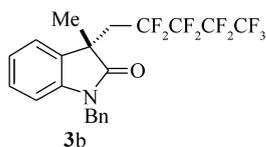
1.2 目标产物 **3** 的合成

以产物 **3a** 合成为例,取 52.5 mg(0.3 mmol)原料 *N*-苯基-*N*-甲基丙烯酰胺 **1a** 溶于 1.5 mL 乙腈中,加入 AIBN 98.4 mg(0.6 mmol)和全氟碘代丁烷 207.5mg(0.6 mmol),然后加入 87.6 mg(0.6 mmol)的二叔丁基过氧化物,在 105 °C 温度下搅拌 8 ~ 12 h。经 TLC 检测反应完全后,经柱层析分离,石油醚-乙酸乙酯梯度洗脱,得到最终目标产物 **3a**,为一种淡黄色固体。

1.3 产物的表征数据

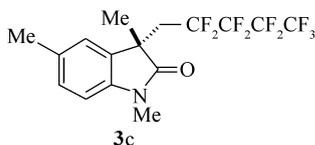


1,3-Dimethyl-3-(2,2,3,3,4,4,5,5,5-nonafluoropentyl) indolin-2-one (**3a**): $^1\text{H NMR}$ (400 MHz, CDCl_3), δ : 7.36 ~ 7.22 (m, 2H), 7.08 (t, $J = 7.5$ Hz, 1H), 6.88 (d, $J = 8.0$ Hz, 1H), 3.23 (s, 3H), 2.97 ~ 2.43 (m, 2H), 1.41 (s, 3H)。



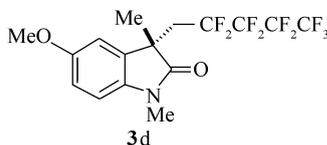
1-Ethyl-3-methyl-3-(2,2,3,3,4,4,5,5,5-nonafluoropentyl) indolin-2-one (**3b**): Yellowish oil. $^1\text{H NMR}$ (400 MHz, CDCl_3), δ : 7.34 ~ 7.13 (m, 7H), 7.04 (t, $J = 8.4$ Hz, 1H), 6.75 (d, $J = 8.0$ Hz, 2H), 4.94 (d, $J = 3.6$ Hz, 2H), 2.93 (dd, $J = 35.6, 14.4$ Hz, 1H), 2.65 (dd, $J = 31.2, 15.2, 8.0$ Hz, 1H), 1.48 (s, 3H); $^{13}\text{C NMR}$ (101 MHz, CDCl_3), δ : 178.6, 141.9, 135.7, 131.2, 127.3, 123.6, 122.6, 126.0 ~ 114.3 (m),

109.5, 44.3, 44.0, 36.6 (t, $J = 20.4$ Hz), 26.5; $^{19}\text{F NMR}$ (376 MHz, CDCl_3), δ : -81.1 (t, $J = 8.1$ Hz, 3F), -107.6 (d, $J_{\text{F-F}} = 264$ Hz, 1F), -114.3 (d, $J_{\text{F-F}} = 270$ Hz, 1F), -124.5 (br, 2F), -125.4 ~ -126.1 (m, 2F)。



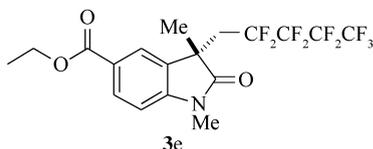
1,3,5-Trimethyl-3-(2,2,3,3,4,4,5,5,5-nonafluoropentyl) indolin-2-one (**3c**): Yellowish solid, mp 62 ~ 63 °C. $^1\text{H NMR}$ (400 MHz, CDCl_3), δ : 7.12 ~ 7.05 (m, 2H), 6.76 (d, $J = 8.4$ Hz, 1H), 3.21 (s, 3H), 2.85 (dd, $J = 35.2, 15.6$ Hz, 1H), 2.56 (ddd, $J = 31.2, 15.2, 8.0$ Hz, 1H), 2.34 (s, 3H), 1.40 (s, 3H); $^{13}\text{C NMR}$ (101 MHz, CDCl_3), δ : 178.5,

140.4, 132.2, 131.3, 128.8, 124.4, 125.0 ~ 114.1 (m), 108.1, 44.2, 36.9 (t, $J = 23$ Hz), 26.5, 25.9, 21.1; $^{19}\text{F NMR}$ (376 MHz, CDCl_3), δ : -81.0 (t, $J = 8.0$ Hz, 3F), -108.9 (d, $J_{\text{F-F}} = 272$ Hz, 1F), -114.7 (d, $J_{\text{F-F}} = 273$ Hz, 1F), -124.6 (br, 2F), -125.0 ~ -126.2 (m, 2F)。



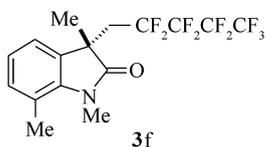
5-Methoxy-1,3-dimethyl-3-(2,2,3,3,4,4,5,5,5-nonafluoropentyl) indolin-2-one (**3d**): Yellowish oil. $^1\text{H NMR}$ (400 MHz, CDCl_3), δ : 6.92 ~ 6.74 (m, 3H), 3.79 (s, 3H), 3.21 (s, 3H), 2.86 (dd, $J = 35.0, 15.6$ Hz, 1H), 2.56 (ddd, $J = 30.8, 15.6, 8.4$ Hz, 1H), 1.41 (s, 3H); $^{13}\text{C NMR}$ (101 MHz, CDCl_3), δ : 178.2, 156.4, 136.3, 132.7, 125.0 ~ 114.1 (m),

112.5, 111.3, 108.7, 55.8, 44.6, 36.6 (t, $J = 31.1$ Hz), 26.5, 25.9; $^{19}\text{F NMR}$ (376 MHz, CDCl_3), δ : -81.0 (t, $J = 8.0$ Hz, 3F), -108.8 (d, $J_{\text{F-F}} = 268$ Hz, 1F), -114.9 (d, $J_{\text{F-F}} = 273$ Hz, 1F), -124.6 (br, 2F), -125.2 ~ -126.3 (m, 2F)。



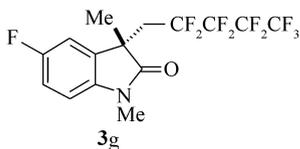
Ethyl 1,3-dimethyl-3-(2,2,3,3,4,4,5,5,5-nonafluoropentyl)-2-oxoindoline-5-carboxylate (**3e**): Yellowish oil. $^1\text{H NMR}$ (400 MHz, CDCl_3), δ : 8.06 (dd, $J = 8.4, 1.6$ Hz, 1H), 7.93 (s, 1H), 6.91 (d, $J = 8.4$ Hz, 1H), 3.27 (s, 3H), 4.36 (q, $J = 7.2$ Hz, 2H), 2.91 (dd, $J = 35.2, 15.6$ Hz, 1H), 2.64 (ddd, $J = 30.8, 15.6, 8.4$ Hz, 1H), 1.44 (s,

3H), 1,39(t, $J = 7.2$ Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3), δ : 178.8, 166.2, 146.8, 131.1, 125.0, 124.8, 125.0 ~ 114.0 (m), 108.0, 61.0, 43.9, 36.2 (t, $J = 20.2$ Hz), 26.5, 25.8, 14.4; ^{19}F NMR (282 MHz, CDCl_3), δ : -81.0 (t, $J = 8.0$ Hz, 3F), -108.7 (d, $J_{\text{F-F}} = 265$ Hz, 1F), -114.7 (d, $J_{\text{F-F}} = 268$ Hz, 1F), -124.5 (br, 2F), -125.2 ~ -126.9 (m, 2F)。



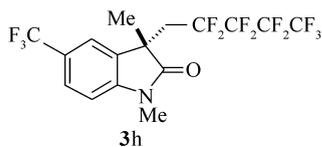
3f

ethyl 1,3,7-trimethyl-3-(2,2,3,3,4,4,5,5,5-nonafluoropentyl)indolin-2-one (**3f**): Yellowish solid, mp 115 ~ 116 °C. ^1H NMR (500 MHz, CDCl_3), δ : 7.10 (d, $J = 7.5$ Hz, 1H), 7.04 (d, $J = 7.5$ Hz, 1H), 6.96 (t, $J = 7.5$ Hz, 1H), 3.52 (s, 3H), 2.89 (dd, $J = 35.2, 15.6$ Hz, 1H), 2.65 ~ 2.50 (m, 4H), 1.40 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3), δ : 179.2, 140.4, 132.0, 131.7, 125.0 ~ 114.0 (m), 122.3, 121.3, 119.9, 43.3, 36.0 (t, $J = 20.3$ Hz), 29.7, 26.3, 18.9; ^{19}F NMR (470 MHz, CDCl_3), δ : -81.1 (t, $J = 8.0$ Hz, 3F), -109.0 (A-B, $J_{\text{F-F}} = 269$ Hz, 1F), -114.7 (A-B, $J_{\text{F-F}} = 272$ Hz, 1F), -124.6 (br, 2F), -125.2 ~ -126.7 (m, 2F)。



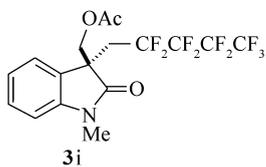
3g

5-fluoro-1,3-dimethyl-3-(2,2,3,3,4,4,5,5,5-nonafluoropentyl)indolin-2-one (**3g**): yellowish solid, mp 78 ~ 79 °C. ^1H NMR (400 MHz, CDCl_3), δ : 7.06 ~ 6.95 (m, 2H), 6.93 ~ 6.75 (m, 1H), 3.22 (s, 3H), 2.87 (dd, $J = 34.8$ Hz, 15.2 Hz, 1H), 2.56 (ddd, $J = 30.8, 15.6, 8.0$ Hz, 1H), 1.42 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3), δ : 178.2, 159.3 (d, $J = 241.9$ Hz), 138.8, 132.9, 125.0 ~ 114.2 (m), 114.8 (d, $J = 27.6$ Hz), 111.8 (d, $J = 25.5$ Hz), 109.0 (d, $J = 8.2$ Hz), 44.6, 36.9 (t, $J = 20.2$ Hz), 26.6, 25.7; ^{19}F NMR (376 MHz, CDCl_3), δ : -81.0 ~ -81.0 (t, $J = 8.0$ Hz, 3F), -108.7 (d, $J_{\text{F-F}} = 273$ Hz, 1F), -114.6 (d, $J_{\text{F-F}} = 266.9$ Hz, 1F), -120.4 (s, 1F), -124.6 (br, 2F), -125.2 ~ -126.2 (m, 2F)。



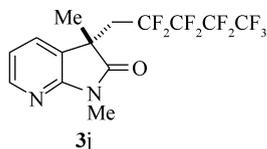
3h

1,3-dimethyl-3-(2,2,3,3,4,4,5,5,5-nonafluoropentyl)-5-(trifluoromethyl)indolin-2-one (**3h**): Yellowish solid, mp 92 ~ 93 °C. ^1H NMR (400 MHz, CDCl_3), δ : 7.59 (d, $J = 8.4$ Hz), 7.50 (s, 1H), 6.96 (d, $J = 8.4$ Hz, 1H), 3.27 (s, 3H), 2.92 (dd, $J = 35.2$ Hz, 15.6 Hz, 1H), 2.63 (ddd, $J = 30.8, 15.6, 8.4$ Hz, 1H), 1.45 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3), δ : 178.4, 145.8, 131.7, 126.3 (q, $J = 3.8$ Hz), 124.0 (q, $J = 32.9$ Hz), 124.4 (q, $J = 272.8$ Hz), 124.0 ~ 114.0 (m), 109.5, 44.1, 36.9 (t, $J = 20.1$ Hz), 26.6, 25.7; ^{19}F NMR (282 MHz, CDCl_3), δ : -61.3 (t, $J = 8.0$ Hz, 3F), -81.0 (t, $J = 8.0$ Hz, 3F), -108.5 (d, $J_{\text{F-F}} = 274$ Hz, 1F), -114.7 (d, $J_{\text{F-F}} = 272$ Hz, 1F), -124.6 (br, 2F), -125.3 ~ -127.0 (m, 2F)。



3i

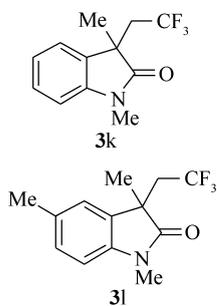
1,3-methyl-3-(2,2,3,3,4,4,5,5,5-nonafluoropentyl)-2-oxoindolin-3-yl methyl acetate (**3i**): Yellowish oil. ^1H NMR (400 MHz, CDCl_3), δ : 7.38 ~ 7.24 (m, 2H), 7.07 (d, $J = 7.6$ Hz, 1H), 6.86 (d, $J = 8.0$ Hz, 1H), 4.38 (d, $J = 10.8$ Hz, 1H), 4.07 (d, $J = 10.8$ Hz, 1H), 2.99 ~ 2.69 (m, 2H), 1.97 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3), δ : 175.2, 170.0, 143.5, 129.3, 126.9, 124.8 ~ 114.0 (m), 122.7, 108.6, 67.4, 47.9, 33.1 (t, $J = 20.0$ Hz), 36.5, 20.5; ^{19}F NMR (376 MHz, CDCl_3), δ : -81.1 (t, $J = 3.4$ Hz, 3F), -108.1 (A-B, $J_{\text{F-F}} = 272$ Hz, 1F), -114.1 (A-B, $J_{\text{F-F}} = 276$ Hz, 1F), -124.4 (br, 2F), -125.2 ~ -126.8 (m, 2F)。



3j

1,3-dimethyl-3-(2,2,3,3,4,4,5,5,5-nonafluoropentyl)-1H-pyrrolo[2,3-b]pyridin-2-one (**3j**): Yellowish solid, mp 83 ~ 84 °C. ^1H NMR (400 MHz, CDCl_3), δ : 8.23 (dd, $J = 4.8, 1.2$ Hz, 1H), 7.23 ~ 7.09 (m, 2H), 3.25 (s, 3H), 2.94 ~ 2.77 (m, 2H), 1.46 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3), δ : 176.9, 152.2, 143.0, 137.9, 114.0 ~

125.0 (m), 123.2, 114.7, 46.2, 36.1 (t, $J = 20.3$ Hz), 26.2, 24.1; ^{19}F NMR (282 MHz, CDCl_3), δ : -81.0 (t, $J = 8.0$ Hz, 3F), -109.8 (A-B, $J_{\text{F-F}} = 274$ Hz, 1F), -113.5 (A-B, $J_{\text{F-F}} = 261$ Hz, 1F), -124.5 (br, 2F), -125.2 ~ -126.7 (m, 2F)。



1,3-Dimethyl-3-(2,2,2-trifluoroethyl) indolin-2-one (**3k**)^[11]: ^1H NMR (500 MHz, CDCl_3), δ : 7.36 ~ 7.26 (m, 2H), 7.11 (t, $J = 7.5$ Hz, 1H), 6.90 (d, $J = 7.5$ Hz, 1H), 3.26 (s, 3H), 2.90 ~ 2.78 (m, 1H), 2.72 ~ 2.63 (m, 1H), 1.42 (s, 3H)。

1,3,5-Trimethyl-3-(2,2,2-trifluoroethyl) indolin-2-one (**3l**)^[6]: ^1H NMR (500 MHz, CDCl_3), δ : 7.15 ~ 7.08 (m, 2H), 6.79 (d, $J = 8.0$ Hz, 1H), 3.23 (s, 3H), 2.87 ~ 2.77 (m, 1H), 2.70 ~ 2.58 (m, 1H), 2.37 (s, 3H), 1.41 (s, 3H)。

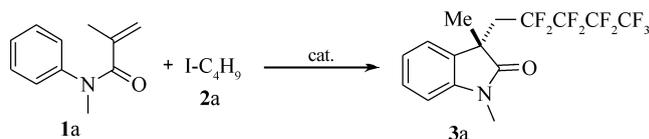
2 结果与讨论

2.1 反应条件探索

最佳反应条件筛选以 *N*-苯基-*N*-甲基丙烯酰胺 **1a** 全氟碘代丁烷的环化反应为模板反应,探索最佳反应条件(表 1)。首先对催化剂/引发基进行了摸索,常用的金属类自由基引发剂,如 FeBr_2 、 CuI 、 AgNO_3 ,对此环化反应基本无效,仅仅痕量的目标产物 **3a** 被检测到(entries 1 ~ 3)。然后,我们尝试了 CuI/AIBN 组合催化体系,目标产物 **3a** 的产率提高到 38%,另外还得到一种由 AIBN 分解得到 α -氰异丙基自由基参与环化而生成的含氰吲哚副产物(entry 4)。撤掉 CuI 后,单独使用 AIBN 作为引发剂能使反应产率提高到 81%(entry 5)。AIBN 的用量对反应影响也较大,当降低用量至 1 equiv 时,反应产率也随之下降到 70%(entry 6)。我们还考察了一些还原类或强碱类全氟烷基自由基引发剂,如 $\text{Na}_2\text{S}_2\text{O}_3$ 、 Cs_2CO_3 ,实验结果表明,这些试剂对反应无效(entries 7 ~ 8)。氧化剂筛选结果表明使用叔丁基过氧化物(DTBP)时的反应效果最好,其它氧化剂,如 TBPB 、 $\text{K}_2\text{S}_2\text{O}_8$,效果明显不如 DTBP(entries 9 ~ 11)。撤去了氧化剂,几乎没有目标产物生成(entry 11)。溶剂筛选发现乙腈作为溶剂反应效果最好,当以甲苯或二氯乙烷替换乙腈时,反应产率明显下降(entries 12 ~ 13)。最后还摸索了温度对反应的影响,当温度降低到 80 $^\circ\text{C}$ 时,产率也相应下降到 26%。升高温度同样不利用反应进行,当温度升至 120 $^\circ\text{C}$ 以上时,DTBP 将分解产生甲基自由基参与反应生成一种副产物^[17],严重影响反应产率(entries 14 ~ 15)。

表 1 优化反应条件摸索

Table 1 Screening of optimal reaction conditions^a



Entry	Initiator	Oxidant	Yield of 3a / % ^b
1	FeBr_2	DTBP	trace
2	CuI	DTBP	trace
3	AgNO_4	$\text{K}_2\text{S}_2\text{O}_8$	trace
4	CuI/AIBN	DTBP	38
5	AIBN	DTBP	81
6c	AIBN	DTBP	70
7	$\text{Na}_2\text{S}_2\text{O}_3$	DTBP	trace
8	Cs_2CO_3	DTBP	trace
9	AIBN	$\text{K}_2\text{S}_2\text{O}_8$	43
10	AIBN	TBPB	56

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Entry	Initiator	Oxidant	Yield of 3a / $\%$ ^b
11	AIBN	none	trace
12 ^d	AIBN	DTBP	22
13 ^e	AIBN	DTBP	45
14 ^f	AIBN	DTBP	26
15 ^g	AIBN	DTBP	37

a. Reaction conditions: compound **1a** (0.3 mmol), C₄F₉I (2 equiv.), metal (10 % molar fraction), initiator (2 equiv.), oxidant (2 equiv.), and solvent (2 mL) at 105 °C for 12 h. DTBP = Di-*tert*-butyl peroxide, AIBN = azodiisobutyronitrile, TBPB = *tert*-butylperoxyl benzoate, DMF = dimethylformamide; b. yield of the isolated product; c. using 1 equiv of AIBN; d. toluene instead of CH₃CN; e. DMF instead of CH₃CN; f. at 80 °C; g. at 120 °C.

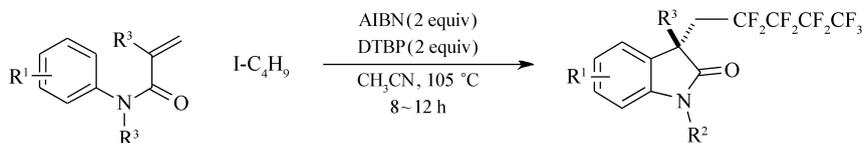
综上所述,最佳反应条件为:*N*-苯基-*N*-甲基丙烯酰胺 **1a** (0.3 mmol), C₄F₉I (2 equiv.), DTBP (2 equiv.), 温度 105 °C, 乙腈溶剂, 反应时间为 12 h。

2.2 反应底物范围

得到最佳反应条件后,我们接着考察了反应底物的适用范围(表 2)。实验结果表明,*N*-芳基丙烯酰胺芳环上带各种取代基团(如 H, Me, CO₂Et), 无论是缺电子还是富电子基团对优化反应条件都表现较好的兼容性,但反应活性方面富电子取代基团明显大于缺电子基团(entries 1~6)。例如,其中甲基取代的 *N*-芳基丙烯酰胺(**1c**)以产率高达 85% 生成目标产物,但由对位 CO₂Et 取代的丙烯酰胺(**1e**)生成产物产率下降到 53%。我们也考察了 *N*-芳基丙烯酰胺 *N*-取代基团反应影响,当甲基换成苄基时,产率有所下降(entry 2)。我们很高兴看到一些氟取代基团,如 CF₃ 和 F 对反应条件也表现较好的兼容性,这为多氟取代的吡啶酮制备提供了更丰富途径(entries 7~8)。优化反应条件对 *N*-芳基丙烯酰胺碳-碳双键上的基团有较好兼容性,例如当甲基换成酯基 CH₂OAc 基团时,反应仍保持较高的活性(entry 9)。

表 2 环化反应的底物范围

Table 2 Scope of substrates in cyclization^a

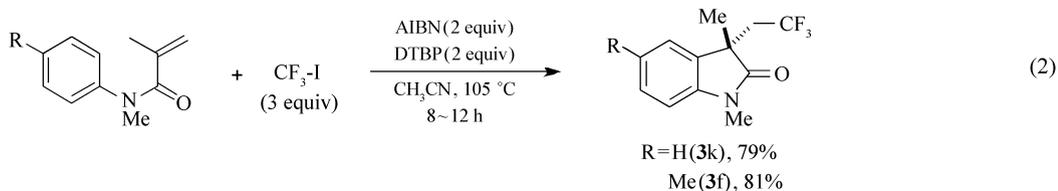
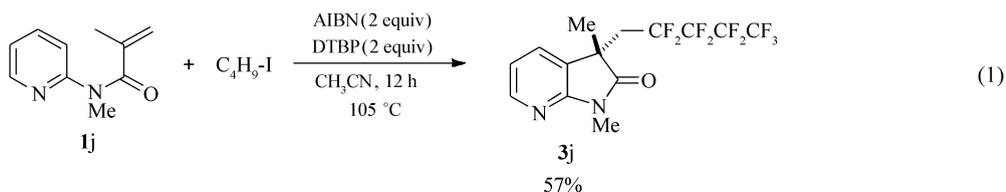


Entry	Substrate 1	Product 3	Yield of product 3 / $\%$ ^b
1	R ¹ = H, R ² = R ³ = Me (1a)	3a)	81
2	R ¹ = H, R ² = Bn, R ³ = Me (1b)	3b)	62
3	R ¹ = 4-Me, R ² = R ³ = Me (1c)	3c)	85
4	R ¹ = 4-OMe, R ² = R ³ = Me (1d)	3d)	76
5	R ¹ = 4-CO ₂ Et ₃ , R ² = R ³ = Me (1e)	3e)	53
6	R ¹ = 2-Me, R ² = R ³ = Me (1f)	3f)	75
7	R ¹ = 4-F, R ² = R ³ = Me (1g)	3g)	73
8	R ¹ = 4-CF ₃ , R ² = R ³ = Me (1h)	3h)	62
9	R ¹ = H, R ² = Me, R ³ = CH ₂ OAc (1i)	3i)	69

a. Reaction conditions: compound **1** (0.3 mmol), C₄F₉I (2 equiv.), DTBP (2 equiv.), and CH₃CN (1.5 mL) at 105 °C for 8~12 h;

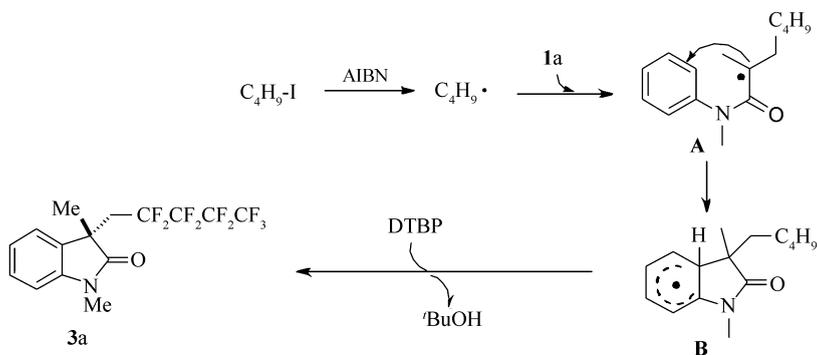
b. yield of the isolated product.

此方法还可以用来合成含吡啶环的多氟取代吡啶酮。例如,*N*-芳基丙烯酰胺(**1j**) 在优化条件下顺利发生串联反应,最后成环以 57% 的产率得到多氟取代的吡啶酮 **3j**(式(1))。此外,三氟甲基碘也能做为氟源参与反应,其与 *N*-芳基丙烯酰胺 **1a** 和 **1c** 高效地发生自由基环化反应,分别以 79% 和 81% 的产率得到相应的吡啶酮产物 **3k** 和 **3l**(式(2))。值得提出的是,此反应中需适量增加三氟甲基碘的用量(3 equiv)以保障较高的反应产率。



2.3 反应机理

根据以前相关的报道以及我们实验结果^[3-6],提出了可能的反应机理过程(Scheme 1): AIBN 受热均裂,在释放 N_2 气的同时生成了含氰自由基引发 $\text{C}_4\text{F}_9\text{I}$ 生成自由基 $\text{C}_4\text{F}_9\cdot$ 。生成的自由基 $\text{C}_4\text{F}_9\cdot$ 对 N -丙烯酰胺的双键进行加成生成自由基中间体 A,紧接着自由基关环生成中间体 B。最后反应中间体 B 被 DTBP 氧化脱去一个质子,最终得到目标产物多氟取代吲哚酮 3a。



Scheme 1 Proposed mechanism for the formation of fluorinated oxindoles

3 结论

本文发展了一种无金属催化条件下烯烃与全氟碘代丁烷环化合成多氟取代吲哚酮的方法。该方法以 AIBN 为自由基引发剂,叔丁基过氧化物(DTBP)作为氧化剂,催化 N -芳基丙烯酸酰胺能高效发生自由基环化反应得到了多种多氟取代吲哚酮。此方法底物适应范围广,反应操作简单、原料易得、催化体系廉价,其将为合成含氟吲哚酮,特别是多氟取代吲哚,提供了一条高效、廉价、“绿色”的新途径。

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Metal-free Cyclization of Alkenes Toward Perfluorinated Oxindoles

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Abstract A metal-free cyclization reaction of activated alkenes with nonafluorobutyl iodide toward perfluorinated oxindoles was developed. In the presence of azodiisobutyronitrile (AIBN), various *N*-arylacrylamide underwent radical cyclization smoothly to afford a series of synthetically important perfluorinated oxindoles in 53% ~ 85% yields. This work provides a novel high efficient, cheap and green route for the synthesis of perfluorinated oxindoles having potential medicinal values.

Keywords metal-free; azodiisobutyronitrile; C—H cyclization; radical; perfluorinated oxindole

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