JOC*Note*

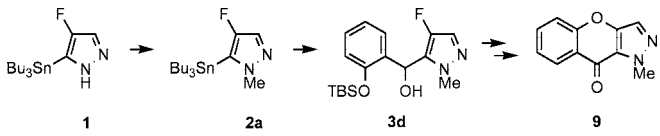
Reaction of *N*-Methyl-5-tributylstannyl-4-fluoro-1*H*-pyrazole and Its Application to *N*-Methyl-chromeno[2,3-*d*]pyrazol-9-one Synthesis

Takeshi Hanamoto,*[,†] Eri Hashimoto,[†] Masayuki Miura,[†] Hiroshi Furuno,[‡] and Junji Inanaga[‡]

Department of Chemistry and Applied Chemistry, Saga University, Honjyo-machi 1, Saga 840-8502, Japan, and Institute for Materials Chemistry and Engineering (IMCE), Kyushu University, Hakozaki, Higashi-ku, Fukuoka 812-8581, Japan

hanamoto@cc.saga-u.ac.jp

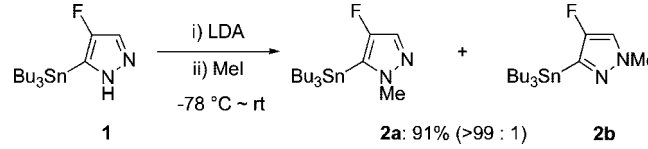
Received March 5, 2008



N-Methylation by sequential treatment of 5-tributylstannyl-4-fluoro-1*H*-pyrazole **1** with LDA and iodomethane regioselectively afforded the compound **2a** in high yield. The addition reaction of 5-lithiated-4-fluoro-1*H*-pyrazole generated from **2a** with a wide range of electrophiles allowed a facile introduction of different substituents at position 5 in good yields. The adduct **3d** was efficiently converted to *N*-methyl-chromeno[2,3-*d*]pyrazol-9-one **9** in 3 steps.

The pyrazole skeleton is found widely not only in agrochemical compounds but also in pharmaceutically active compounds.[1] On the other hand, it has been documented that the introduction of fluorine in azaheterocycles may play an important role in their biological activity.[2] For example, Celecoxib having a trifluoromethyl group on the pyrazole ring shows anti-inflammatory and analgetic activity.[3] Accordingly, exploration of fluorinated pyrazoles bearing potential functional groups would be promising for introducing more complex compounds in the field of fine chemicals. As a part of our ongoing research on incorporating fluorine into pyrazoles, we have recently reported the synthesis and some cross-coupling reactions of 5-tributylstannyl-4-fluoro-1*H*-pyrazole (**1**).[4] Our next objective was to synthesize and develop *N*-methylpyrazoles since these units are widely encountered in agrochemicals and pharmaceuticals.[5] We herein report the facile preparation and reactions of *N*-methylpyrazole derivatives including an application to the synthesis of *N*-methylchromeno[2,3-*d*]pyrazol-9-one (**9**).

SCHEME 1. *N*-Methylation of 1



According to our previous procedure for the preparation of *N*-methyl-5-tributylstannyl- 4-trifluoromethyl-1*H*-pyrazole, the preliminary reaction of **1** with iodomethane was carried out by using LDA under similar conditions.[6] The reaction proceeded smoothly providing the corresponding *N*-methylpyrazole derivative in 91% yield as a single regioisomer (Scheme 1). To confirm the regiochemistry of **2a** we attempted NOE experiments; however, we could obtain no useful information. Although the correct regioselectivity was not determined at this point, we tentatively assigned this *N*-methylpyrazole to *N*-methyl-5-tributylstannyl-4-fluoro-1*H*-pyrazole (**2a**) on the basis of our previous results.[6]

It is well-accepted that transmetalation of tributylstannyl compound with BuLi at low temperatures gives the corresponding lithiated species in high yield.[7] The transmetalation of **2a** was performed by addition of BuLi at −78 °C in THF to yield the corresponding 5-lithiated-4-fluoro-1*H*-pyrazole. Then benzaldehyde was added, and the mixture was gradually warmed to room temperature while being stirred to yield the desired product in 91% yield (Table 1, entry 1). Under similar

* Author to whom correspondence should be addressed. Fax: 81-952-28-8548.
† Saga University.
‡ Kyushu University.

(1) Elguero, J. *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., Eds.; Pergamon: Oxford, UK, 1996; Vol. 5.

(2) (a) Müller, K.; Faeh, C.; Diederich, F. *Science* **2007**, *317*, 1881. (b) Bégué, J.-P.; Bonnet-Delpon, D. *J. Fluorine Chem.* **2006**, *127*, 992. (c) Uneyama, K. *Organofluorine Chemistry*; Blackwell Publishing: Oxforf, UK, 2006. (d) Chambers, R. D. *Fluorine in Organic Chemistry*; Blackwell Publishing: Oxford, UK, 2004. (e) Lemal, D. M. *J. Org. Chem.* **2004**, *69*, 1. (f) Hiyama, T. *Organofluorine Compounds*; Springer: Berlin, Germany, 2000. (g) Hudlicky, M.; Pavlath, A. E. *Chemistry of Organic Fluorine Compounds II*; ACS Monogragh No. 187; American Chemical Society: Washington, DC, 1995.

(3) (a) Liu, H.; Huang, X.; Shen, J.; Luo, X.; Li, M.; Xiong, B.; Chen, G.; Shen, J.; Yang, Y.; Jiang, H.; Chen, K. *J. Med. Chem.* **2002**, *45*, 4816. (b) Price, M. L. P.; Jørgensen, W. L. *J. Am. Chem. Soc.* **2000**, *122*, 9455. (c) Penning, T. D.; Talley, J. J.; Bertenshaw, S. R.; Carter, J. S.; Collins, P. W.; Doctor, S.; Graneto, M. J.; Lee, L. F.; Malecha, J. W.; Miyashiro, J. M.; Rogers, R. S.; Rogier, D. J.; Yu, S. S.; Anderson, G. D.; Burton, E. G.; Cogburn, J. N.; Gregory, S. A.; Koboldt, C. M.; Perkins, W. E.; Seibert, K.; Veenhuizen, A. W.; Zhang, Y. Y.; Isakson, P. C. *J. Med. Chem.* **1997**, *40*, 1347.

(4) (a) Hanamoto, T.; Koga, Y.; Kido, E.; Kawanami, T.; Furuno, H.; Inanaga, J. *Chem. Commun.* **2005**, 2041. (b) Hanamoto, T.; Suetake, T.; Koga, Y.; Kawanami, T.; Furuno, H.; Inanaga, J. *Tetrahedron* **2007**, *63*, 5062.

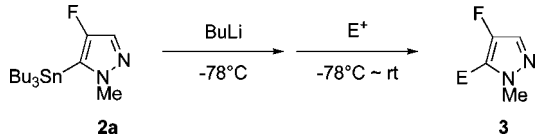
(5) (a) Calle, M.; Calvo, M.; González-Ortega, A.; González-Nogal, A. *Tetrahedron* **2006**, *62*, 611. (b) Cottineau, B.; Chenault, J.; Guillaumet, G. *Tetrahedron Lett.* **2006**, *47*, 817. (c) Ivachtchenko, A. V.; Kravchenko, D. V.; Zheludeva, V. I.; Pershin, D. G. *J. Heterocycl. Chem.* **2004**, *41*, 931. (d) Cottineau, B.; Chenault, J. *Synlett* **2002**, 769. (e) Smith, T. E.; Mourad, M. S.; Velander, A. J. *Heterocycles* **2002**, *57*, 1211. (f) Katritzky, A. R.; Wang, M.; Zhang, S.; Voronkov, M. V.; Steel, P. J. *J. Org. Chem.* **2001**, *66*, 6787. (g) Azami, H.; Barrett, D.; Tanaka, A.; Sasaki, H.; Matsuda, K.; Sakurai, M.; Terasawa, T.; Shirai, F.; Chiba, T.; Matsumoto, Y.; Tawara, S. *Bioorg. Med. Chem.* **2001**, *9*, 961. (h) Calle, M.; Cuadrado, P.; González-Nogal, A. M.; Valero, R. *Synthesis* **2001**, 1949. (i) Okada, I.; Fukuchi, T. *J. Pestic. Sci.* **2000**, *25*, 310. *Chem. Abstr.* **2000**, *133*, 218748. (j) Chatani, N.; Fukuyama, T.; Tatamidani, H.; Kakiuchi, F.; Murai, S. *J. Org. Chem.* **2000**, *65*, 4039. (k) Torrens, A.; Castrillo, J. A.; Redondo, J. *Synlett* **1999**, 765. (l) Hueso-Rodríguez, J. A.; Berrocal, J.; Gutiérrez, B.; Farré, A. J.; Frigola, J. *Bioorg. Med. Chem. Lett.* **1993**, *3*, 269. (m) Yamamoto, S.; Sato, T.; Morimoto, K.; Makino, K. *J. Heterocycl. Chem.* **1991**, *28*, 1849. (n) Effenberger, F.; Krebs, A. *J. Org. Chem.* **1984**, *49*, 4687.

(6) Hanamoto, T.; Egashira, M.; Ishizuka, K.; Furuno, H.; Inanaga, J. *Tetrahedron* **2006**, *62*, 6332.

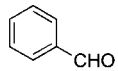
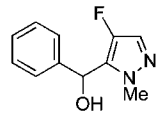
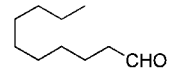
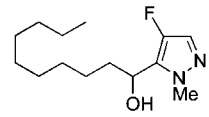
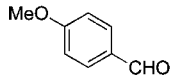
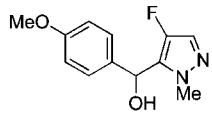
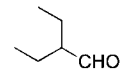
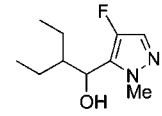
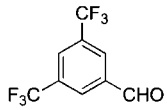
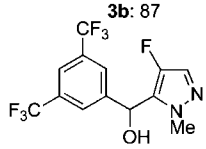
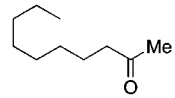
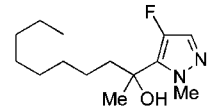
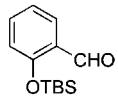
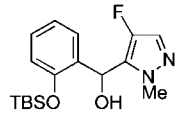
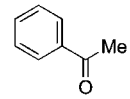
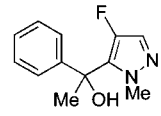
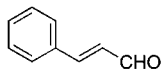
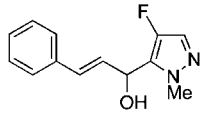
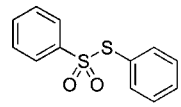
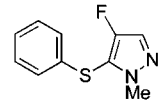
(7) Harrison, P. G. *Chemistry of Tin*; Blackie & Son Limited: Glasgow, UK, 1989.

10.1021/jo800431t CCC: $40.75
Published on Web 05/24/2008

TABLE 1. Reaction of 2a with Various Electrophiles[a]



2a **3**

entry	E^+	product yield[b] (%)	entry	E^+	product yield[b] (%)
1		 **3a**: 91	6		 **3f**: 72
2		 **3b**: 87	7		 **3g**: 71
3		 **3c**: 84	8		 **3h**: 72
4[c]		 **3d**: 94	9		 **3i**: 74
5		 **3e**: 76	10[c]		 **3j**: 80

[a] Aldehyde or ketone, 1.5 equiv. [b] Isolated yield. [c] The reaction was quenched at −78 °C.

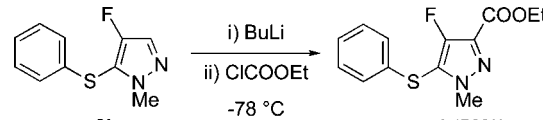
conditions, the reaction of **2a** with other aromatic aldehydes bearing either an electron-donating or an electron-withdrawing substituent on the aromatic ring proceeded to give the corresponding adducts in high yields (entries 2−4). Cinnamaldehyde, as an α,β-unsaturated aldehyde, proved to be a good electrophile and delivered the 1,2-addition adduct. No conjugated addition product was observed (entry 5). Linear and branched aliphatic aldehydes successfully underwent addition reaction to give the corresponding adducts in good yields (entries 6 and 7). Not only 2-undecanone as an aliphatic ketone but also acetophenone as an aromatic ketone reacted satisfactorily (entries 8 and 9). In addition to the above carbonyl compounds, *S*-phenyl benzenethiosulfate gave the corresponding *N*-methyl-5-phenylthio-1*H*-pyrazole in 80% yield (entry 10). These results are summarized in Table 1.

Interestingly, the product **3g** gave single crystals suitable for X-ray crystallographic analysis. A crystal drawing of **3g** is shown in the Supporting Information. This X-ray analysis revealed unambiguous proof of the regiochemistry of *N*-methyl-5-alkylated-4-fluoro-1*H*-pyrazoles and definitely assigned the structure of **2a** as *N*-methyl-5-tributylstannyl-4-fluoro-1*H*-pyrazole. Consequently, our findings and synthetic procedures proved to be useful for the complete *C*-5-lithiation of *N*-methyl-1*H*-pyrazole.[5c,e,h,k–lm,8]

On the basis of the successful syntheses of various *N*-methyl-5-substituted-1*H*-pyrazoles shown in Table 1, we designed procedures for further incorporation of substituents at position 3 of the *N*-methyl-4,5-disubstituted-1*H*-pyrazole ring. For this purpose, we selected the product **3j**, bearing no hydroxy group, and examined the reaction conditions. The 3-lithiated species was generated from **3j** by treatment of BuLi at −78 °C in THF followed by reaction with ethyl chloroformate to give the corresponding 3,4,5-trisubstituted pyrazole in 52% yield (Scheme 2).[9]

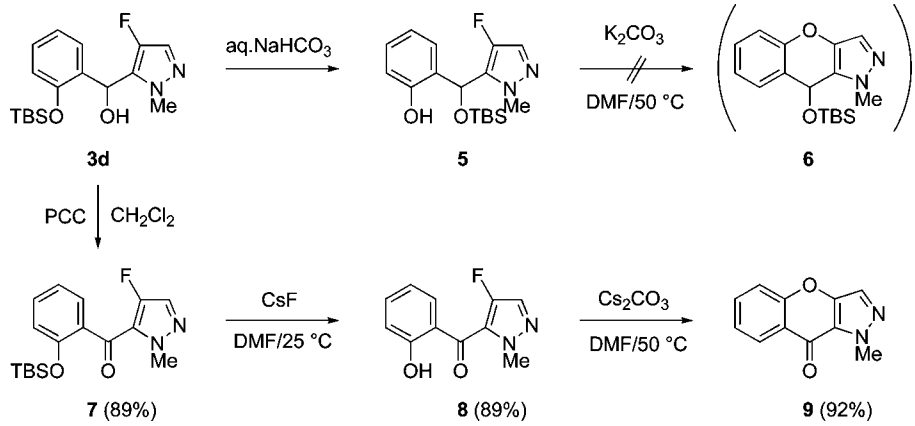
Finally, application of the product **3d** (Table 1) to the preparation of novel azaxanthones was planned.[10] We hoped that the corresponding tricyclic structure should be built up via an intramolecular nucleophilic aromatic substitution using

SCHEME 2. Reaction of 3j



3j **4** (52%)

SCHEME 3. Preparation of *N*-Methyl-chromeno[2,3-*d*]pyrazol-9-one 9



fluorine as a scaffold on the pyrazole ring. According to the literature procedure, treatment of compound **5** with K_2CO_3 in DMF at 50 °C resulted in decomposition.[10c] However, the vital ring closure via the addition−elimination process of the 4-fluoro-1*H*-pyrazole **8** bearing the keto-structure effectively took place to produce the desired *N*-methyl-chromeno[2,3-*d*]pyrazol-9-one (**9**) in 73% overall yield from **3d** under similar reaction conditions with Cs_2CO_3 (Scheme 3).[11] To the best of our knowledge, this is the first selective and high-yielding preparation of such compounds.[10f,i]

In summary, we have developed a facile method for the preparation of various *N*-methyl-4-fluoro-5-substituted-1*H*-pyrazoles in high yield, and have illustrated the possibility of construction of 3,4,5-trisubstituted pyrazoles. Furthermore, we achieved the first selective and high-yielding preparation of chromeno[2,3-*d*]pyrazol-9-one compound as a new class of azaxanthones.

Experimental Section

***N*-Methyl-5-tributylstannyl-4-fluoro-1*H*-pyrazole (2a).** To a solution containing 971.0 mg (2.59 mmol) of pyrazole **1**[4a] in THF (10 mL) was added LDA-THF solution (3.11 mmol) by a double-ended needle at −78 °C. At this temperature 0.21 mL (3.37 mmol) of MeI was added to the mixture, and the reaction was allowed to warm to room temperature with stirring overnight. The reaction was quenched with water and hexane and extracted with hexane/ether = 3/1. The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/ethyl acetate/triethylamine = 150/50/1) to give the desired compound **2a** as a colorless oil (934.7 mg, 91%, >99:1): IR (neat) 2958, 2927, 2872, 2854, 1522, 1464, 1388, 1348, 1077, 977, 816 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.90 (9H, t, J = 7.2 Hz), 1.05−1.70 (18H, m), 3.82 (3H, s), 7.29 (1H, d, J = 4.8 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 10.1, 13.6, 27.1, 28.8, 41.6, 124.6 (d, J = 17.4 Hz), 127.1 (d, J = 43.1 Hz), 158.1 (q, J = 238.8 Hz); ^{19}F NMR ($CDCl_3$, 283 MHz) δ −172.3 [dm, J = 4.2 Hz, $J_{F\text{-}^{117}Sn}$ = 25.3 Hz (7.6%), $J_{F\text{-}^{119}Sn}$ = 25.3 Hz (8.6%)]; GC-MS *m*/*z* 332 (2, M^+ − Bu), 276 (21), 221 (51), 218 (100), 138 (37), 137 (31), 121 (44), 120 (62), 101 (36), 57 (25). Anal. Calcd for $C_{16}H_{31}FN_2Sn$: C, 49.38; H, 8.03; N, 7.20. Found: C, 49.41; H, 7.97; N, 7.05.

***N*-Methyl-5-[(phenyl)hydroxymethyl]-4-fluoro-1*H*-pyrazole (3a).** To a solution containing 351.7 mg (0.903 mmol) of pyrazole **2a** in THF (2 mL) was added BuLi (2.71 M in hexane solution, 0.37 mL, 1.00 mmol) by means of a syringe at −78 °C. At this temperature 110 μL (1.08 mmol) of benzaldehyde was added to the mixture, and the reaction was allowed to warm to room temperature with stirring for 2 h. The reaction was quenched with a saturated aqueous $NaHCO_3$ solution and extracted with hexane/ether = 3/1. The extraction was repeated twice. The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/ethyl acetate/triethylamine = 150/50/1) to give the desired compound **3a** as a white solid (170.2 mg, 91%): mp 34.2−35.1 °C; IR (KBr) 3296, 1585, 1444, 1402, 1357, 1319, 1044, 835, 764, 720 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.34 (1H, d, J = 4.4 Hz), 3.65 (3H, d, J = 0.6 Hz), 6.11 (1H, d, J = 4.4 Hz), 7.30−7.40 (5H, m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 38.5, 65.0, 124.6 (d, J = 12.5 Hz), 125.7, 127.8, 128.5, 139.7, 147.0 (d, J = 246.6 Hz); ^{19}F NMR ($CDCl_3$, 283 MHz) δ −177.0 (d, J = 4.9 Hz); GC-MS *m*/*z* 206 (16, M^+), 205 (20), 127 (67), 115 (21), 109 (30), 105 (37), 99 (34), 77 (100), 51 (38). Anal. Calcd for $C_{11}H_{11}FN_2O$: C, 64.07; H, 5.38; N, 13.58. Found: C, 64.05; H, 5.40; N, 13.50.

***N*-Methyl-5-[2′-(*tert*-butyldimethylsilyloxy)benzoyl]-4-fluoro-1*H*-pyrazole (7).** To a solution containing 211.0 mg (0.63 mmol) of **3d** in CH_2Cl_2 (3 mL) was added PCC (265.7 mg, 1.25 mmol) at room temperature. The reaction mixture was stirred for 90 min and diluted with ether. After the mixture was filtered through a short Celite pad (ether as an eluent), the combined filtrate was concentrated in vacuo. The residue was purified by silica gel column chromatography (hexane/ethyl acetate/triethylamine = 200/20/1)

(8) For the regiospecific *C*-5 lithiation of *N*-1 substituted pyrazoles, see:(a) Hoffmann, M. G. *Tetrahedron* **1995**, *51*, 9511. (b) Subramanyam, C. *Synth. Commun.* **1995**, *25*, 761. (c) Booker-Milburn, K. I. *Synlett* **1992**, 327. (d) Effenberger, F.; Roos, M.; Ahmad, R.; Krebs, A. *Chem. Ber.* **1991**, *124*, 1639. (e) Heinisch, G.; Holzer, W.; Pock, S. *J. Chem. Soc. Perkin. Trans. 1* **1990**, 1829.

(9) For some reports on 4-fluoro-3,5-disubstituted-pyrazole derivatives, see: (a) Chanteau, F.; Plantier-Royon, R.; Portella, C. *Synlett* **2004**, 512. (b) Katoch-Rouse, T.; Pavlova, O. A.; Caulder, T.; Hoffman, A. F.; Mukhin, A. G.; Horti, A. G. *J. Med. Chem.* **2003**, *46*, 642. (c) Sloop, J. C.; Bumgardner, C. L.; Loehle, W. D. *J. Fluorine Chem.* **2002**, *118*, 135. (d) Bouillon, J.-P.; Didier, B.; Dondy, B.; Doussot, P.; Plantier-Royon, R.; Portella, C. *Eur. J. Org. Chem.* **2001**, 187. (e) Dondy, B.; Doussot, P.; Portella, C. *Tetrahedron Lett.* **1994**, *35*, 409. (f) Bumgardner, C.; Sloop, J. C. *J. Fluorine Chem.* **1992**, *56*, 141. (g) Ishihara, T.; Okada, Y.; Kuroboshi, M.; Shinozaki, T.; Ando, T. *Chem. Lett.* **1988**, 819.

(10) (a) Ghosh, T.; Bandyopadhyay, C. *J. Heterocycl. Chem.* **2006**, *43*, 1431. (b) Atkinson, P.; Findlay, K. S.; Kielar, F.; Pal, R.; Parker, D.; Poole, R. A.; Puschmann, H.; Richardson, S. L.; Stenson, P. A.; Thompson, A. L.; Yu, J. *Org. Biomol. Chem.* **2006**, *4*, 1707. (c) Kristensen, J. L.; Vedsø, P.; Begtrup, M. *Tetrahedron* **2002**, *58*, 2397. (d) Trécourt, F.; Breton, G.; Bonnet, V.; Mongin, F.; Marsais, F.; Quéguiner, G. *Tetrahedron* **2000**, *56*, 1349. (e) Rampa, A.; Bisi, A.; Valenti, P.; Recanatini, M.; Cavalli, A.; Andrisano, V.; Cavrini, V.; Fin, L.; Buriani, A.; Giusti, P. *J. Med. Chem.* **1998**, *41*, 3976. (f) Ghosh, C. K.; Sahana, S.; Ghosh, C. *Indian J. Chem. Sect. B.* **1996**, *35*, 669. (g) Mongin, O.; Rocca, P.; Thomas-dit-Dumont, L.; Trécourt, F.; Marsais, F.; Godard, A.; Quéguiner, G. *J. Chem. Soc., Perkin Trans. 1* **1995**, 2503. (h) Ghosh, C. K.; Bhattacharya, K.; Ghosh, C. *Tetrahedron* **1994**, *50*, 4905. (i) Ghosh, C. K.; Bhattacharyya, A.; Ghosh-Dastidar, P. P. *Indian J. Chem. Sect. B.* **1987**, *26*, 128. (j) Beelitz, K.; Praefcke, K. *Justus Liebigs Ann. Chem.* **1979**, 1081. (k) Sliwa, H.; Cordonnier, G. *J. Heterocycl. Chem.* **1977**, *14*, 169. (l) Villani, F. J.; Magatti, C. V. *J. Heterocycl. Chem.* **1975**, *12*, 1239. (m) Villani, F. J.; Hannon, J.; Wefer, E. A.; Mann, T. A.; Morton, J. B. *J. Org. Chem.* **1975**, *40*, 1734.

(11) The product yield was comparable when **8** was treated with K_2CO_3 under similar conditions.

to give the desired compound **7** as a white solid (186.4 mg, 89%); mp 48.7−50.6 °C; IR (KBr) 3120, 2858, 1651, 1600, 1557, 1487, 1301, 1106, 1011, 898, 841, 673 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.12 (6H, s), 0.77 (9H, s), 4.14 (3H, s), 6.86 (1H, dd, J = 6.1, 2.6 Hz), 7.04 (1H, t, J = 7.5 Hz), 7.27 (1H, d, J = 4.4 Hz), 7.36 (1H, d, J = 1.7 Hz), 7.40 (1H, dt, J = 7.7, 1.8 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −4.6, 17.9, 25.2, 40.9, 119.5, 121.2, 124.8 (d, J = 13.8 Hz), 126.8 (d, J = 18.7 Hz), 129.5, 131.2 (d, J = 1.2 Hz), 132.8, 150.8 (d, J = 261.6 Hz), 153.8 (d, J = 1.2 Hz), 184.1 (d, J = 3.7 Hz); ^{19}F NMR ($CDCl_3$, 283 MHz) δ −162.3 (d, J = 3.7 Hz); GC-MS *m*/*z* 278 (23), 277 (100), 276 (18), 135 (4), 127 (4), 95 (5), 91 (5), 77 (23), 76 (5), 73 (13). Anal. Calcd for $C_{17}H_{23}FN_2O_2Si$: C, 61.05; H, 6.93; N, 8.38. Found: C, 60.99; H, 6.92; N, 8.31.

***N*-Methyl-5-(2′-hydroxybenzoyl)-4-fluoro-1*H*-pyrazole (8).** To a solution containing 94.2 mg (0.28 mmol) of **7** in DMF (2 mL) was added CsF (78.1 mg, 0.74 mmol) at room temperature. After stirring for 15 min, the reaction mixture was quenched with aqueous NH_4Cl solution, then extracted with hexane/ether = 3/1. Additional extraction was repeated twice. The combined organic solution was dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel column chromatography (hexane/ethyl acetate/triethylamine = 150/30/1) to give the desired compound **8** as a white solid (55.0 mg, 89%): mp 86.1−87.2 °C; IR (KBr) 3003, 2882, 1651, 1574, 1557, 1417, 1394, 1010, 818, 777 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 4.04 (3H, d, J = 0.7 Hz), 6.90−7.00 (1H, m), 7.06 (1H, dd, J = 8.4, 0.9 Hz), 7.41 (1H, d, J = 4.6 Hz), 7.56 (1H, ddd, J = 8.6, 7.2, 1.5 Hz), 7.67 (1H, ddd, J = 7.8, 6.0, 1.7 Hz), 11.61 (1H, s); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 40.1, 118.2, 119.4, 125.1 (d, J = 14.3 Hz), 132.3, 132.4, 137.4, 148.4 (d, J = 259.1 Hz), 163.0, 188.2 (d, J = 3.7 Hz); ^{19}F NMR ($CDCl_3$, 283 MHz) δ −162.5 (t, J = 5.2 Hz); GC-MS *m*/*z* 221 (M^+ + 1, 1), 220 (M^+, 17), 219 (2), 127 (3), 121 (33), 120 (100), 99 (3), 92 (35), 76 (2), 65 (27). Anal. Calcd for $C_{11}H_9FN_2O_2$: C, 60.00; H, 4.12; N, 12.72. Found: C, 60.09; H, 4.16; N, 12.71.

***N*-Methylchromeno[2,3-*d*]pyrazol-9-one (9).** To a solution containing 15.1 mg (0.07 mmol) of **8** in DMF (0.5 mL) was added Cs_2CO_3 (31.2 mg, 0.09 mmol) at 25 °C. The mixture was heated to 50 °C, then stirred for 2 h. The reaction was quenched with aq NH_4Cl solution and extracted with hexane/ether = 3/1. Additional extraction was repeated twice. The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/ethyl acetate/triethylamine = 150/30/1) to give the desired compound **9** as a white solid (12.6 mg, 92%): mp 166.4−168.2 °C; IR (KBr) 3107, 2923, 1668, 1524, 1435, 1333, 1092, 913, 793, 660 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 4.36 (3H, s), 7.41 (1H, t, J = 7.5 Hz), 7.53 (1H, dd, J = 8.5, 0.5 Hz), 7.69 (1H, s), 7.72 (1H, ddd, J = 8.6, 7.0, 1.6 Hz), 8.37 (1H, dd, J = 8.0, 1.7 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 39.2, 112.9, 118.3, 123.9, 124.8, 126.5, 134.1, 146.5, 156.3, 169.1; GC-MS *m*/*z* 200 (M^+, 70), 199 (100), 171 (4), 146 (6), 121 (5), 116 (3), 104 (37), 89 (15), 76 (61), 68 (4), 63 (10), 50 (24). Anal. Calcd for $C_{11}H_8N_2O_2$: C, 66.00; H, 4.03; N, 13.99. Found: C, 65.98; H, 4.09; N, 13.94.

Acknowledgement.. We greatly thank F-Tech Co. Ltd for a gift of 1,1-difluoroethylene and Professor M. Jelokhani-Niaraki at Wilfrid Laurier University for his crucial reading of this manuscript.

Supporting Information Available: Characterization of new compounds **3b**−**j**, preparation of compound **4**, NMR spectra for all new compounds, ORTEP drawing of **3g**, and crystal data for **3g**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO800431T