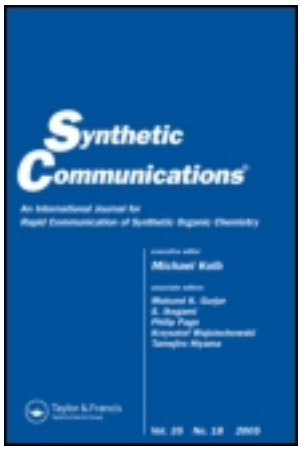

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A Convenient Synthesis of 5-Oxo-5,6,7,8-tetrahydro-4 H -benzo-[b]-pyran Derivatives Catalyzed by KF-Alumina

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A Convenient Synthesis of 5-Oxo-5,6,7,8-tetrahydro-4*H*-benzo-[b]-pyran Derivatives Catalyzed by KF-Alumina

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ABSTRACT

A series of 5-oxo-5,6,7,8-tetrahydro-4*H*-benzo-[b]-pyran derivatives were prepared by the reaction of arylmethylidenemalononitriles or 2-cyano-3-aryl-l-acrylate with 5,5-dimethyl-1,3-cyclohexanedione (dimedone) in DMF at room temperature catalyzed by KF-alumina. The structure of the product was confirmed by X-ray analysis.

Key Words: 4H-benzo-[6]-pyran; Arylmethylidenemalononitriles; 2-cyano-3-aryl-1-acrylate; Synthesis.

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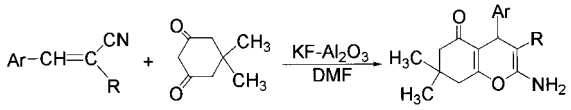

1 2 3

Scheme 1.

The utility of fluoride salts as potential base in variety of synthetic reactions has been recognized in recent years.[1,2] However, low solubility of fluoride salts in ordinary solvents hamper their wide applications in organic synthesis. On the other hand, there has been increasing use of inorganic solid supports as catalyst resulting in higher selectivity, milder reaction conditions and easier work-up, which has been reported as a useful catalyst for many reactions.[3,4] In our previous paper,[5,6] we have reported that alumina coated with potassium fluoride (KF-alumina) is a versatile solid-supported reagent for Knoevenagel reaction and Michael addition condensation. In this paper, we would like to report that preparation of 5-oxo-5,6,7,8-tetrahydro-4*H*-benzo-[b]-pyran derivatives catalyzed by KF-alumina.

When arylmethylidenemalononitriles or 2-cyano-3-aryl-1-acrylate (**1**) and 5,5-dimethyl-1,3-cyclohexanedione (dimedone) (**2**) were treated with KF-alumina in DMF at room temperature (Sch. 1). The desired 5-oxo-5,6,7,8-tetrahydro-4*H*-benzo-[b]-pyran derivatives (**3**) were obtained in good yields (60–89%) (Table 1) within very short reaction time (1–3 h).

The structures of the products (X-ray crystal structures of **3c** and **3n** shown in Figs. 1 and 2) were established on the basis of spectroscopic data and confirmed by X-ray diffraction studies on monocrystal of **3c**[7] and **3n**.[8]

The reactions also can be catalyzed by potassium fluoride (not alumina), only 41% yield of **3a** was obtained, when the same reaction was carried out in DMF at 80°C using potassium fluoride as the catalyst. In conclusion, with good yields and mild conditions, we think that the present work described here in provide a useful method for the preparation of 5-oxo-5,6,7,8-tetrahydro-4*H*-benzo-[b]-pyran derivatives.

EXPERIMENTAL

Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded on a FT IR-8101 spectrometer.

Table 1. The yields of the products.

Entry	Ar	*R*	Isolated yield (%)
3a	C_6H_5	CN	71
3b	4-$CH_3C_6H_4$	CN	80
3c	3,4-$OCH_2OC_6H_3$	CN	79
3d	3,4-$(OCH_3)_2C_6H_3$	CN	70
3e	4-ClC_6H_4	CN	81
3f	4-$CH_3OC_6H_4$	CN	75
3g	2-ClC_6H_4	CN	70
3h	4-$NO_2C_6H_4$	CN	72
3i	2-furyl	CN	72
3j	C_6H_5	CO_2Me	78
3k	C_6H_5	CO_2Et	73
3l	4-$CH_3C_6H_4$	CO_2Me	80
3m	4-$CH_3C_6H_4$	CO_2Et	66
3n	4-ClC_6H_4	CO_2Me	63
3o	4-ClC_6H_4	CO_2Et	89
3p	2-ClC_6H_4	CO_2Me	70
3q	2-ClC_6H_4	CO_2Et	60
3r	3,4-$OCH_2OC_6H_3$	CO_2Et	70

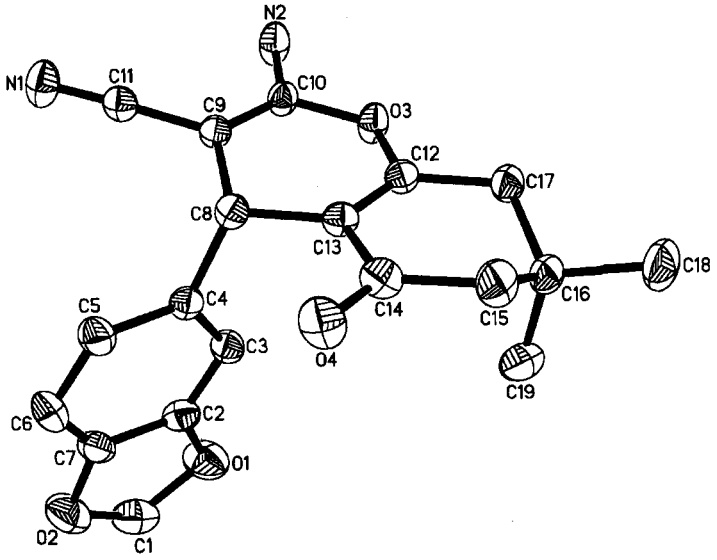

Figure 1. X-ray crystal structure of **3c**.

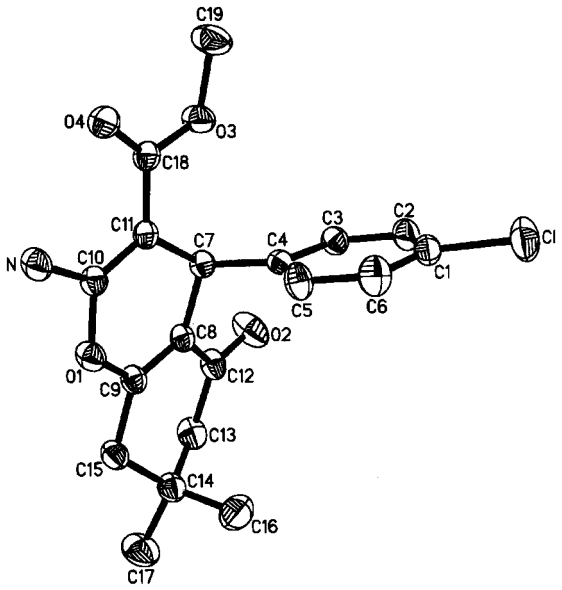

Figure 2. X-ray crystal structure of **3n**.

^{1}H NMR spectra were measured on a R-1500A spectrometer using TMS as internal standard. Mass spectra were determined on Micromass OA-TOFMS instrument. Elemental analyses were carried out using Carlo Erba 1110 analyzer. X-ray diffraction were measured on a Siemens P4 diffractometer.

General Procedure

A dry 50-mL flask was charged with arylmethylidene malononitriles or 2-cyano-3-aryl-1-acrylate (**1**) (2 mmol), 5,5-dimethyl-1,3-cyclohexanedione (dimedone) (2.5 mmol), KF-alumina (250 mg) and DMF (10 mL). The mixture was stirred at room temperature for 1–3 h. Then the solid material was filtered off and washed with a little DMF. The filterate was poured into 200 mL water. The white solid was filtered off, then washed with water. The crude solid was purified by recrystallization from 95% EtOH to give (**3**).

3a: M.p. 226–228°C; IR (KBr, ν, cm^{-1}): 3280, 3250, 3040, 2990, 2980, 2245, 1650, 1600, 1480, 740, 700; ^{1}H NMR (CD_3COCD_3, δ, ppm): 1.01

(3H, s, CH_3), 1.10 (3H, s, CH_3), 2.21 (2H, s, CH_2), 2.56 (2H, s, CH_2), 3.06 (2H, br., s, NH_2), 4.28 (1H, s, CH), 7.27 (5H, s, ArH); MS: *m*/*e* (%) 294 (M^+, 8), 227 (100), 217 (15), 171 (19), 102 (17); Elemental analysis: Found (%): C, 73.60; H, 6.07; N, 9.38. Calcd. for $C_{18}H_{18}N_2O_2$: C, 73.45; H, 6.16; N, 9.52.

3b: M.p. 208–210°C; IR (KBr, ν, cm^{-1}): 3320, 3280, 3040, 2990, 2980, 2240, 1680, 1600, 1510, 850; ^{1}H NMR (CD_3COCD_3, δ, ppm): 1.06 (3H, s, CH_3), 1.11 (3H, s, CH_3), 2.25 (5H, d, CH_2, CH_3), 2.54 (2H, s, CH_2), 3.05 (2H, br., s, NH_2), 4.25 (1H, s, CH), 7.13 (4H, s, ArH); MS: *m*/*e* (%) 308 (M^+, 7), 241 (27), 227 (100), 171 (21), 115 (19); Elemental analysis: Found (%): C, 74.12; H, 6.41; N, 8.97. Calcd. for $C_{19}H_{20}N_2O_2$: C, 74.00; H, 6.54; N, 9.09.

3c: M.p. 212–214°C; IR (KBr, ν, cm^{-1}): 3280, 3200, 3040, 2990, 2970, 2240, 1680, 1600, 1500, 1490, 870, 790; ^{1}H NMR (CD_3COCD_3, δ, ppm): 0.98 (3H, s, CH_3), 1.06 (3H, s, CH_3), 2.19 (2H, s, CH_2), 2.51 (2H, s, CH_2), 3.28 (2H, br., s, NH_2), 4.12 (1H, s, CH), 6.00 (2H, s, OCH_2O), 6.69–6.93 (3H, m, ArH); MS: *m*/*e* (%) 338 (M^+, 8), 271 (100), 242 (9), 215 (9), 188 (15), 173 (17), 160 (16), 145 (12); Elemental analysis: Found (%): C, 67.61; H, 5.24; N, 8.16. Calcd. for $C_{19}H_{18}N_2O_4$: C, 67.44; H, 5.36; N, 8.28.

3d: M.p. 173–174°C; IR (KBr, ν, cm^{-1}): 3300, 3250, 3040, 2990, 2240, 1650, 1600, 1520, 860, 820; ^{1}H NMR (CD_3COCD_3, δ, ppm): 1.02 (3H, s, CH_3), 1.08 (3H, s, CH_3), 2.21 (2H, s, CH_2), 2.54 (2H, s, CH_2), 3.07 (2H, br., s, NH_2), 3.75 (6H, s, $2 \times OCH_3$), 4.23 (1H, s, CH), 6.82 (3H, s, ArH); MS: *m*/*e* (%) 354 (M^+, 9), 323 (17), 288 (95), 273 (58), 257 (100), 217 (12), 201 (31), 176 (14); Elemental analysis: Found (%): C, 67.92; H, 6.16; N, 7.83. Calcd. for $C_{20}H_{22}N_2O_4$: C, 67.78; H, 6.26; N, 7.91.

3e: M.p. 207–209°C; IR (KBr, ν, cm^{-1}): 3300, 3200, 3040, 2990, 2970, 2240, 1650, 1610, 1490, 850; ^{1}H NMR (CD_3COCD_3, δ, ppm): 1.01 (3H, s, CH_3), 1.09 (3H, s, CH_3), 2.22 (2H, s, CH_2), 2.59 (2H, s, CH_2), 3.07 (2H, br., s, NH_2), 4.30 (1H, s, CH), 7.30 (4H, s, ArH); MS: *m*/*e* (%) 328 (M^+, 12), 261 (62), 227 (100), 217 (25), 171 (30), 150 (22), 136 (28); Elemental analysis: Found (%): C, 65.84; H, 5.20; N, 8.51. Calcd. for $C_{18}H_{17}ClN_2O_2$: C, 65.75; H, 5.21; N, 8.52.

3f: M.p. 198–200°C; IR (KBr, ν, cm^{-1}): 3400, 3300, 3040, 2990, 2980, 2970, 2240, 1680, 1610, 1510, 840; ^{1}H NMR (CD_3COCD_3, δ, ppm): 0.95 (3H, s, CH_3), 1.02 (3H, s, CH_3), 2.16 (2H, s, CH_2), 2.48 (2H, s, CH_2), 3.28 (2H, br., s, NH_2), 3.71 (3H, s, OCH_3), 4.12 (1H, s, CH), 6.87–6.99 (4H, m, ArH); MS: *m*/*e* (%) 324 (M^+, 9), 257 (100), 243 (20), 227 (50), 201 (12), 146 (17); Elemental analysis: Found (%): C, 70.42; H, 6.13; N, 8.62. Calcd. for $C_{19}H_{20}N_2O_3$: C, 70.35; H, 6.22; N, 8.64.

3g: M.p. 200–202°C; IR (KBr, ν, cm^{-1}): 3300, 3200, 3040, 2990, 2970, 2240, 1680, 1600, 1450, 770; ^{1}H NMR (CD_3COCD_3, δ, ppm): 1.08 (3H, s, CH_3), 1.10 (3H, s, CH_3), 2.20 (2H, s, CH_2), 2.54 (2H, s, CH_2), 3.05 (2H, br., s, NH_2), 4.86 (1H, s, CH), 7.29 (4H, s, ArH); MS: *m*/*e* (%) 328 (M^+, 4), 293 (15), 227 (100), 211 (34), 171 (80), 136 (11), 115 (7); Elemental analysis: Found (%): C, 65.92; H, 5.18; N, 8.43. Calcd. for $C_{18}H_{17}ClN_2O_2$: C, 65.75; H, 5.21; N, 8.52.

3h: M.p. 130–132°C; IR (KBr, ν, cm^{-1}): 3300, 3200, 3040, 2990, 2970, 2240, 1650, 1600, 1510, 830; ^{1}H NMR (CD_3COCD_3, δ, ppm): 1.00 (3H, s, CH_3), 1.10 (3H, s, CH_3), 2.20 (2H, s, CH_2), 2.60 (2H, s, CH_2), 3.06 (2H, br., s, NH_2), 4.49 (1H, s, CH), 7.26–8.29 (4H, m, ArH); MS: *m*/*e* (%) 339 (M^+, 20), 242 (100), 217 (35), 186 (14), 145 (20), 117 (15); Elemental analysis: Found (%): C, 63.95; H, 4.98; N, 12.27. Calcd. for $C_{18}H_{17}N_3O_4$: C, 63.71; H, 5.05; N, 12.38.

3i: M.p. 218–220°C; IR (KBr, ν, cm^{-1}): 3400, 3300, 3050, 2990, 2980, 2240, 1680, 1600, 730; ^{1}H NMR (CD_3COCD_3, δ, ppm): 1.00 (3H, s, CH_3), 1.10 (3H, s, CH_3), 2.28 (2H, s, CH_2), 2.54 (2H, s, CH_2), 3.05 (2H, br., s, NH_2), 4.44 (1H, s, CH), 6.18–7.37 (3H, m, ArH); MS: *m*/*e* (%) 284 (M^+, 4), 256 (11), 218 (100), 203 (30), 190 (35), 162 (69), 134 (48), 120 (30), 106 (35); Elemental analysis: Found (%): C, 67.62; H, 5.54; N, 9.79. Calcd. for $C_{16}H_{16}N_2O_3$: C, 67.59; H, 5.67; N, 9.86.

3j: M.p. 146–148°C, IR (KBr, ν, cm^{-1}) 3410, 3270, 3020, 2980, 1700, 1660, 1610, 1500, 1450, 740, 710; δ_H 0.96 (3H, s, CH_3), 1.09 (3H, s, CH_3), 2.19 (2H, s, CH_2), 2.42 (2H, s, CH_2), 3.60 (3H, s, OCH_3), 4.72 (1H, s, CH), 6.16 (2H, br., s, NH_2), 7.22 (5H, s, ArH); Elemental analysis: Found (%): C, 69.52; H, 6.57; N, 4.20. Calcd. for $C_{19}H_{21}NO_4$: C, 69.72; H, 6.42; N, 4.28.

3k: M.p. 158–160°C, IR (KBr, ν, cm^{-1}) 3400, 3260, 3020, 2980, 1700, 1660, 1610, 1520, 1460, 730, 700; δ_H 0.93–1.23 (9H, m, $3 \times CH_3$), 2.15 (2H, s, CH_2), 2.38 (2H, s, CH_2), 3.82–4.18 (2H, q, $J = 7.2$ Hz, OCH_2), 4.67 (1H, s, CH), 6.04 (2H, br., s, NH_2), 7.17 (5H, s, ArH); Elemental analysis: Found (%): C, 70.27; H, 6.84; N, 4.08. Calcd. for $C_{20}H_{23}NO_4$: C, 70.38; H, 6.74; N, 4.11.

3l: M.p. 172–174°C, IR (KBr, ν, cm^{-1}) 3310, 3260, 3020, 2980, 1730, 1700, 1610, 1510, 1460, 840; δ_H 0.97 (3H, s, CH_3), 1.09 (3H, s, CH_3), 2.18 (2H, s, CH_2), 2.26 (3H, s, CH_3), 2.41 (2H, s, CH_2), 3.60 (3H, s, OCH_3), 4.68 (1H, s, CH), 6.10 (2H, br., s, NH_2), 7.06–7.10 (4H, m, ArH); Elemental analysis: Found (%): C, 70.33; H, 6.90; N, 4.05. Calcd. for $C_{20}H_{23}NO_4$: C, 70.38; H, 6.74; N, 4.11.

3m: M.p. 156–157°C, IR (KBr, ν, cm^{-1}) 3300, 3250, 3020, 2980, 1720, 1690, 1610, 1500, 1470, 830; δ_H 0.98–1.29 (9H, m, $3 \times CH_3$), 2.19

(2H, s, CH_2), 2.26 (3H, s, CH_3), 2.42 (2H, s, CH_2), 3.87–4.22 (2H, q, $J = 7.2$ Hz, OCH_2), 4.67 (1H, s, CH), 6.10 (2H, br., s, NH_2), 7.06–7.10 (4H, m, ArH); Elemental analysis: Found (%): C, 70.84; H, 7.20; N, 3.89. Calcd. for $C_{21}H_{25}NO_4$: C, 70.98; H, 7.04; N, 3.94.

3n: M.p. 167–168°C, IR (KBr, ν, cm^{-1}) 3500, 3300, 3020, 2980, 1680, 1670, 1600, 1520, 1450, 840; δ_H 0.96 (3H, s, CH_3), 1.09 (3H, s, CH_3), 2.19 (2H, s, CH_2), 2.41 (2H, s, CH_2), 3.59 (3H, s, OCH_3), 4.68 (1H, s, CH), 6.19 (2H, br., s, NH_2), 7.19 (4H, s, ArH); Elemental analysis: Found (%): C, 63.04; H, 5.68; N, 3.79. Calcd. for $C_{19}H_{20}NClO_4$: C, 63.07; H, 5.53; N, 3.87.

3o: M.p. 150–152°C, IR (KBr, ν, cm^{-1}) 3400, 3260, 3020, 2990, 1700, 1660, 1620, 1520, 1480, 840; δ_H 0.97–1.26 (9H, m, $3 \times CH_3$), 2.19 (2H, s, CH_2), 2.42 (2H, s, CH_2), 3.86–4.22 (2H, q, $J = 7.2$ Hz, OCH_2), 4.68 (1H, s, CH), 6.20 (2H, br., s, NH_2), 7.19 (4H, s, ArH); Elemental analysis: Found (%): C, 63.97; H, 5.98; N, 3.69. Calcd. for $C_{20}H_{22}NClO_4$: C, 63.91; H, 5.86; N, 3.73.

3p: M.p. 198–200°C, IR (KBr, ν, cm^{-1}) 3450, 3270, 3020, 2980, 1690, 1650, 1610, 1500, 1460, 750; δ_H 0.99 (3H, s, CH_3), 1.09 (3H, s, CH_3), 2.17 (2H, s, CH_2), 2.42 (2H, s, CH_2), 3.57 (3H, s, OCH_3), 5.02 (1H, s, CH), 6.15 (2H, br., s, NH_2), 7.15–1.19 (4H, m, ArH); Elemental analysis: Found (%): C, 63.31; H, 5.68; N, 3.85. Calcd. for $C_{19}H_{20}NClO_4$: C, 63.07; H, 5.53; N, 3.87.

3q: M.p. 181–183°C, IR (KBr, ν, cm^{-1}) 3450, 3250, 3020, 2990, 1680, 1660, 1610, 1510, 1470, 740; δ_H 0.99–1.24 (9H, m, $3 \times CH_3$), 2.17 (2H, s, CH_2), 2.41 (2H, s, CH_2), 3.84–4.20 (2H, q, $J = 7.2$ Hz, OCH_2), 5.02 (1H, s, CH), 6.22 (2H, br., s, NH_2), 7.06–7.16 (4H, m, ArH); Elemental analysis; Found (%): C, 63.68; H, 5.99; N, 3.63. Calcd. for $C_{20}H_{22}NClO_4$: C, 63.91; H, 5.86; N, 3.73.

3r: M.p. 156–158°C, IR (KBr, ν, cm^{-1}) 3480, 3300, 1730, 1680; δ_H 0.99–1.29 (9H, m, $3 \times CH_3$), 2.20 (2H, s, CH_2), 2.41 (2H, s, CH_2), 3.88–4.24 (2H, q, $J = 7.2$ Hz, OCH_2), 4.63 (1H, s, CH), 5.87 (2H, s, OCH_2O), 6.21 (2H, br., s, NH_2), 6.68–6.84 (3H, m, ArH); Elemental analysis: Found (%): C, 65.47; H, 6.11; N, 3.58. Calcd. for $C_{21}H_{23}NO_6$: C, 65.45; H, 5.97; N, 3.64.

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7. X-ray crystallography for **3c**: Empirical formula $C_{19}H_{18}N_2O_4$, $F_w = 338.35$, $T = 297(2)$ K, monoclinic, space group $C2/c$, $a = 26.753(5)$ Å, $b = 9.409(2)$ Å, $c = 16.036(2)$ Å, $\alpha = 90^\circ$, $\beta = 121.000(10)^\circ$, $\gamma = 90^\circ$, $V = 3460.0(12)$ Å^3, $Z = 8$, $Dc = 1.299$ Mg/m^3, λ ($MoK\alpha$) = 0.71073 Å, $\mu = 0.092$ mm^{-1}, $F(000) = 1424$. $1.78^\circ < \theta < 25.25^\circ$, $R = 0.0410$, $wR = 0.0926$. $S = 0.905$, largest diff. peak and hole: 0.161 and -0.159 e·Å^{-3}.
8. X-ray crystallography for **3n**: Empirical formula $C_{19}H_{20}ClNO_4$, $F_w = 361.81$, $T = 297(2)$K, triclinic, space group P-1, $a = 8.519(2)$ Å, $b = 10.346(2)$ Å, $c = 11.481(2)$ Å, $\alpha = 108.16(1)^\circ$, $\beta = 107.78(2)^\circ$, $\gamma = 91.83(2)^\circ$, $V = 906.5(3)$ Å^3, $Z = 2$, $Dc = 1.326$ Mg/m^3, $\lambda(MoK\alpha) = 0.71073$ Å, $\mu = 0.234$ mm^{-1}, $F(000) = 380$. $1.98^\circ < \theta < 25.00^\circ$, $R = 0.0467$, $wR = 0.1270$. $S = 1.050$, largest diff. peak and hole: 0.487 and -0.423 e.Å^{-3}.

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