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Solvent-Less Synthesis of Hybrid Molecules of 3-Formylchromones Catalyzed by Boric Acid

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Abstract: In our effort to develop hybrid molecules, we conceived the synthesis of hydrazones from 3-formylchromone and carboxylic acid hydrazides in presence of boric acid as a green catalyst.

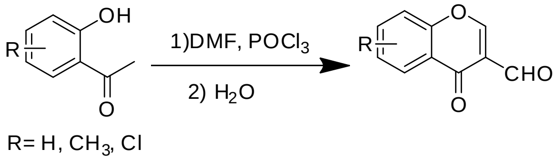
Keywords: 3-formylchromone, carboxylic acid hydrazides, hydrazones, boric acid

I. INTRODUCTION

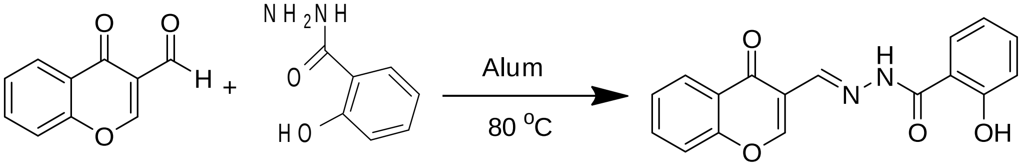
Hybrid molecules[1] are defined as chemical entities with two (or more than two) structural domains having different biological functions. The dual activity indicates that a hybrid molecule acts as two distinct pharmacophores. Both entities of the hybrid molecule are not necessarily acting on the same biological target.[2] 3-Formylchromone also reacts with carboxylic acid hydrazides producing respective acyl hydrazones.[3] Hydrazones are known to possess antidepressant properties[4] and possess kinase inhibitor properties, in particular for SGK. These also act as M1/M3 selective muscarinic agonists.[5] These also possess antimicrobial activity[6] and anticonvulsant activity,[7] antifungal properties,[8] proinflammatory activity.[9] 3-Formylchromone[10] derivatives have been extensively used as versatile building blocks for the synthesis of variety of heterocyclic systems.[11] In our effort to develop hybrid molecules, we conceived the synthesis of hydrazones from 3-formylchromone[12] and carboxylic acid hydrazides in presence of pulverized boric acid (0.154 g)[13] as a green catalyst in extension to our work.[14]

II. RESULTS AND DISCUSSION

3-Formylchromones[15] can be synthesized by Vilsmeier reaction. The desired compounds carrying various substituents were prepared by the similar method in one step.



When a mixture of 3-formylchromone (1 mmol), 2-hydroxybenzoic acid hydrazide (1 mmol) and pulverized boric acid (0.154 g) was heated, under solvent free conditions in a round bottom flask at 80°C for about 40 - 60 minutes, the formation of a newer compound was noticed on TLC and was isolated in 80 - 85% yield by recrystallization from ethanol. This compound was found to be 3-(2-hydroxybenzoylhydrazonomethyl)-4-oxo-4*H*-chromene as revealed by the comparison of its spectral and physical data with the authentic sample.[16] ^{1}H NMR spectrum (in DMSO) of compounds showed a singlet signal of the C=N-NH group at δ 11.6, two singlets at δ 8.8 and 8.7 corresponding to two C-H and at δ 8.0 – 7.3 corresponding to eight aromatic protons showing multiplet. ^{13}C NMR spectrum showed peaks at δ 187, 165, 158, 157, 156, 153, 135, 133, 130, 128, 126, 125, 124, 122, 120, 118 and 106. The IR spectrum showed peaks at 3400 cm^{-1}, 3100cm^{-1} (N-H, O-H), 1645cm^{-1} (CN) and 1620 cm^{-1} (C=O).



III. GENERAL PROCEDURE

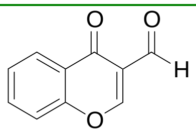
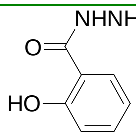
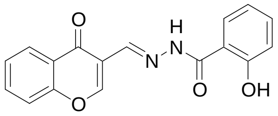
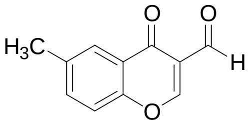
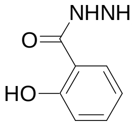
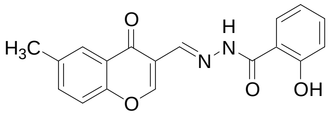
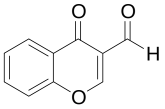
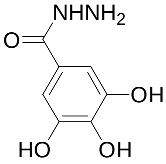
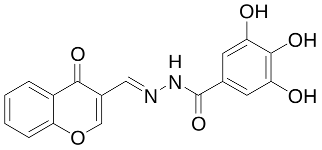
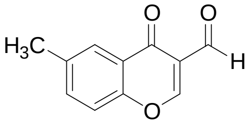
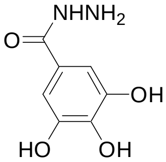
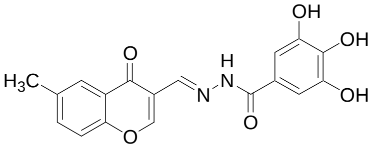
A. Synthesis of 3-formylchromone

The Vilsmeir reagent was prepared by the drop wise addition of freshly distilled phosphorous oxychloride to dry DMF (dimethylformamide) with stirring and cooling in ice. The reagent was allowed to stand at room temperature and was then added to a stirred solution of the substituted *o*-hydroxyacetophenone in dry DMF. The reaction mixture was kept at room temperature for 13 hour. The mixture was then poured into ice cold water. The solution was made basic by the addition of Na_2CO_3 solution and exhaustively extracted with ethyl acetate; combined extracts were washed successively with dil. HCl, H_2O and saturated brine, and finally dried over Na_2SO_4. The different compounds were obtained in varied yields. The compound was isolated in 75% yield and was found to be 3-formylchromone as revealed by the comparison of its spectral and physical data with that of the authentic sample.[17] The ^{1}H NMR of some compounds was not measured due to their extremely low solubility inorganic solvents (DMSO, DMF, etc.).

B. Synthesis of hydrazones of 3-formylchromone and aromatic carboxylic acid hydrazide

A mixture of 3-formylchromone (1 mmol), carboxylic acid hydrazide (1 mmol) and pulverized boric acid (0.154 g) was heated, without any solvent in a round bottom flask at 80 ^{o}C for about 40-60 minutes, the formation of a newer compound was noticed as revealed by TLC. The reaction mixture was diluted with ethyl acetate (30 mL) and filtered. The filterate was washed with brine (2 × 15 mL), dried over anhydrous Na_2SO_4, ethyl acetate was distilled off under reduced pressure and the residue was recrystallized from ethanol mixture in 80 - 85% yield**.**

Table 1: Synthesis of hydrazones of 3-formylchromones

S.No	3-formyl chromone	Carboxylic acid hydrazide	Product	Time (min.)	Yield %^{a}
1				40	85
2				40	83
3				60	82
4				60	80

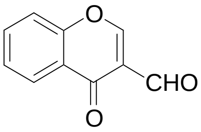
[a] Isolated yields.

IV. EXPERIMENTAL

All experiments were performed in an oven dried glass apparatus. Melting points were measured in open capillaries on Buchi melting point apparatus and are uncorrected. Elemental analysis was performed on Leco CHNS-932. IR spectra on KBr were recorded on Perkin-Elmer FTIR spectrophotometer. NMR (^{1}H broadband decoupled and ^{13}CNMR) spectra were recorded on Brucker Ac-200 (400 MHz and 100 MHz respectively) spectrometer. ^{1}H NMR and ^{13}C NMR of the compounds 3b, 3c, 3e, 3f were not measured due to low solubility in organic solvents. ESI-MS spectra were recorded on Micro-Mass VG- 7070 H mass spectrometer. The recrystallization of imines was carried from DMSO/ethanol mixture. The column chromatography was performed over silica gel (60-120 mesh) with graded solvent systems of ethyl acetate – *n*-hexane. The solvents were dried before use as per the established procedures.

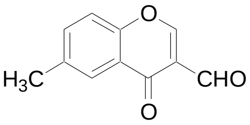
V. PHYSICAL AND SPECTRAL DATA

4-Oxo-4*H*-chromene-3-carbaldehyde



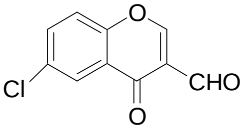
White solid, M.pt. 151 - 153 ^{o}C.^{1}H NMR ($CDCl_3$, 400 MHz) δ: 10.1 (1H, s), 7.8 (1H, s), 8.0 - 7.6 (4H, m). IR(KBr)ν_{max}/cm^{-1}: 3315, 2890, 1685, 1650.*Anal Calcd.*for $C_{10}H_6O_3$:C, 68.97, H, 3.47. Found: C, 69.33, H, 3.82.

6-Methyl-4-oxo-4*H*-chromene-3-carbaldehyde



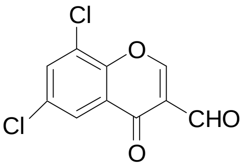
White solid, M.pt. 174 - 175 ^{o}C.^{1}H NMR ($CDCl_3$, 400 MHz) δ: 9.8 (1H, s), 7.8 (1H, s), 8.0 – 7.7 (3H, m), 2.1 (3H, s).IR(KBr)ν_{max}/cm^{-1}: 3310, 2890, 1695, 1655.*Anal Calcd.*for $C_{11}H_8O_3$:C, 70.21, H, 4.29. Found: C, 70.52, H, 4.62.

6-Chloro-4-oxo-4*H*-chromene-3-carbaldehyde



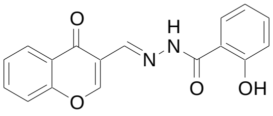
White solid, M.pt. 166 - 168^{o}C.^{1}H NMR ($CDCl_3$, 400 MHz) δ: 10.2 (1H, s), 8.0 (1H, s), 8.1 – 7.7 (3H, s). IR (KBr)ν_{max}/cm^{-1}: 3315, 2892, 1695, 1660.*Anal Calcd.*for $C_{10}H_5ClO_3$:C, 57.58, H, 2.42. Found: C, 57.92, H, 2.76.

6,8-Dichloro-4-oxo-4*H*-chromene-3-carbaldehyde



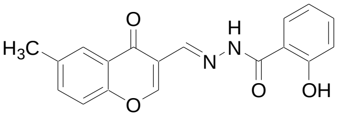
White solid, M.pt. 171 - 173 ^{o}C.^{1}H NMR ($CDCl_3$, 400 MHz) δ: 10.3 (1H, s), 8.1 (1H, s) 8.0 - 7.7 (2H, s).IR(KBr)ν_{max}/cm^{-1}: 3310, 2895, 1695, 1655.*Anal Calcd.*for $C_{10}H_4Cl_2O_3$:C, 49.42, H, 2.10. Found: C, 57.78, H,2.53.

3-(2-Hydroxybenzoylhydrazonomethyl)-4-oxo-4*H*-chromene



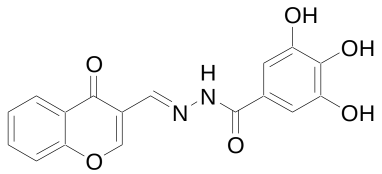
Obs. M.pt. 221 – 223 ^{o}C; Lit.M.pt.^{33}222 - 224 ^{o}C.
^{1}H NMR (DMSO-d_6, 400MHz) δ: 11.6 (1H, brs), 8.4 (1H, s), 8.2 (1H, s), 8.0 - 7.3 (8H, m).
^{13}C NMR (DMSO-d_6, 100MHz) δ: 187, 165, 158, 157, 156, 153, 135, 133, 130, 128, 126, 125, 124, 122, 120, 118, 106.
ESI-MS m/z = 331 (M+Na)$^{+}$.
IR(KBr)ν_{max}/cm^{-1}:3400, 3100, 2980, 1645, 1620.
*Anal Calcd.*for$C_{17}H_{12}N_2O_4$: C, 66.23, H, 3.92, N, 9.09.Found: C, 66.57, H, 4.28, N, 9.32.

3-(2-Hydroxybenzoylhydrazonomethyl)-6-methyl-4-oxo-4*H*-chromene



Obs. M.pt. 218 – 220 ^{o}C; Lit.M.pt.^{33}220 - 222 ^{o}C.
^{1}H NMR (DMSO-d_6, 400MHz) δ: 11.6 (1H, brs), 8.3 (1H, s), 8.1 (1H, s), 8.0 –7.3 (7H, m), 2.1 (3H, s).
^{13}C NMR (DMSO-d_6, 100MHz) δ: 185, 164, 157, 156, 154, 152, 136, 134, 132, 127, 126, 125, 124, 122, 120, 116, 106, 22.
IR(KBr)ν_{max}/cm^{-1}:3500, 3240, 1645, 1630.
*Anal Calcd.*for$C_{18}H_{14}N_2O_4$: C, 67.07, H, 4.38, N, 8.69. Found: C, 67.41, H, 4.72, N, 9.12.

3-(3,4,5-Trihydroxybenzoylhydrazonomethyl)-4-oxo-4*H*-chromene



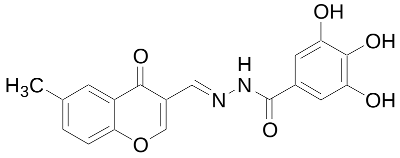
Obs. M.pt. 252 – 254 °C; Lit.M.pt.[33] 255 - 257 °C.

^{1}H NMR (DMSO-d_6, 400MHz) δ: 11.5 (1H, brs), 9.1 (3H, brs), 8.4 (1H, s), 8.2 (1H, s), 8.0 - 7.4 (4H, m), 7.1 (2H, s).

IR (KBr)ν_{max}/cm^{-1}: 3280, 2985, 1645, 1620.

*Anal Calcd.*for $C_{17}H_{12}N_2O_6$: C, 60.00, H, 3.55, N, 8.23. Found: C, 60.38, H, 3.89, N, 8.57.

3-(3,4,5-Trihydroxybenzoylhydrazonomethyl)-6-methyl-4-oxo-4*H*-chromene



Obs. M.pt. 214 – 216 °C; Lit.M.pt.[33]215 - 217 °C.

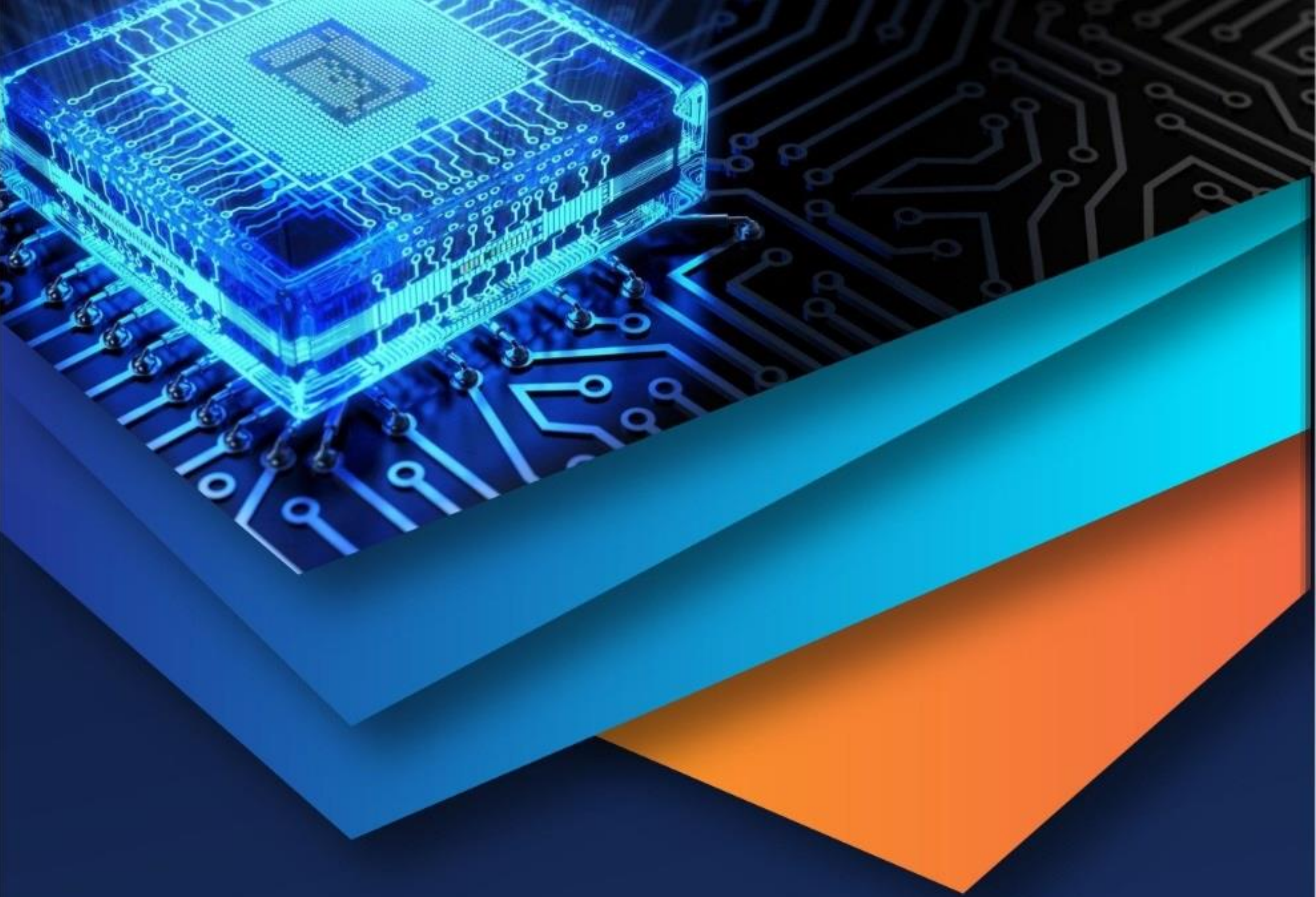
^{1}H NMR (DMSO-d_6, 400MHz) δ: 11.6 (1H, brs), 9.1 (3H, brs), 8.6 (1H, s), 8.4 (1H, s), 8.1 – 7.5 (3H, m), 7.1 (2H, s), 2.1 (3H, s).

IR (KBr)ν_{max}/cm^{-1}: 3300, 2985, 1660, 1622.

*Anal Calcd.*for $C_{18}H_{14}N_2O_6$: C, 61.02, H, 3.98, N, 7.91. Found: C, 61.34, H, 4.32, N, 8.24.

REFERENCES

[1] B. Meunier, Acc. Chem. res.,**2008**, 41, 1, 69.
[2] P. Ettmayer, G. L. Amidon, B. Clement, B. Testa, J. Med. Chem., **2004**, 47, 2393.
[3] H. M. El- Shaaer, P. Foltinova, M. Lacova, J. Chovancova, H. Stankovicova, Il Farmaco, **1998,** 53, 224.
[4] T. A. Smirnova, M. Y. Gavrilov, F. Y. Nazmetdinov, V. E. Kolla, M. E. Konshin, Pharmaceut. Chem. J., **2006**, 33, 370.
[5] E. S. C. Wu, A. Kover, J. T. Loch, L. P. Rosenberg, S. F. Semus, P. R. Verhoest, J. C. Gordon, A. C. Machulskis, S. A. McCreedy, J. Zongrone, J. C. Blosser,Biooig. Med. Chem. Lett., **1996**, 6, 21, 2525.
[6] G. I. Dmitrienko, S. Siemann, D. P. Evanoff, L. Marrone, A. J. Clarke, T. Viswanatha, Antimicrob. Agents Chemother.,**2008,** 46**,** 8, 2450.
[7] S. K. Sridhar, S. N. Pandeya, J. P. Stables, A. Ramesh, Eur. J. Pharmaceut. Sci.,**2002**, 16, 3, 129.
[8] P. Vicini, F. Zani, P. Cozzini, I. Doytchinova, Eur. J. Med. Chem.,**2002,** 37, 7, 553.
[9] D. Darrin R, C. K. Fan, A. Bayan, M. Edmund J, P. Valentin A, A. Yousef, J. Med. Chem., **2007,** 50, 8, 1993.
[10] J. D. Hepworth, A. R. Katritzky, C. W. Rees, Comprehensive Heterocyclic Chemistry,Vol. 3, Eds. Perganon Press, Oxford,**1984**, 737**.**
[11] (a) W. D. Jones, W. L. Albrecht, J. Org. Chem., **1976**, 41, 706. (b) W. Lowe, Synthesis, **1976**, 274. (c) W. Lowe, Ann. Chem., **1977**, 1050. (d) G. Haas, J. L. Stanton, A. V. Sprecher, P. Wenk, J. Heterocycl. Chem., **1981**, 18, 607. (e) C. Pene, M. Hubert-Habart, J. Heterocycl. Chem., **1980**, 17, 329. (f) I. Sigg, G. Haas, T. Winkler, Helv. Chim. Acta, **1982**, 65, 275. (g) G. Rihs, I. Sigg, G. Haas, T. Winkler, Helv. Chim. Act, **1985**, 68, 1933.
[12] A. Nohara, T. Umetani, Y. Sanno, Tetrahedron, **1974**, 30, 3353.
[13] a) Mahajan, D; Austalian journal of chemistry, **2008,**61, 159. b) Mahajan, D; Journal of chemistry and chemical sciences, **2017**,7, 771. c) D. Mahajan, **2019**, 6,636.
[14] Mahajan, D.: International journal of research and analytical reviews,
[15] S. Klutchko, M. P. Cohen, J. Shavel, M. V. Strandtmann, J. Heterocycl. Chem., **1974**, 11, 183.
[16] A.Pinar, P.Yurdakul, I.Yildiz, O.Temiz - Arpaci, N. Lacan, E.Aki - Sener, I. Yalcin, Biochem.Biophys. Res.Commun., **2004**, 317, 670.
[17] H. M. El- Shaaer, P. Foltinova, M. Lacova, J. Chovancova, H. Stankovicova, Il Farmaco, **1998,** 53, 224.



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