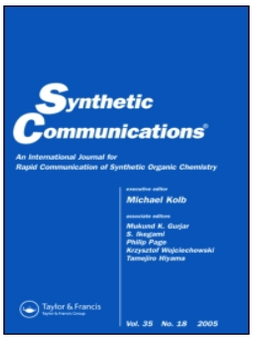

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FACILE ONE-POT SYNTHESIS OF ARYL, HETERYL SUBSTITUTED HYDRAZONO THIAZOLYL-PYRAZOLONE DERIVATIVES VIA THREE-COMPONENT REACTION

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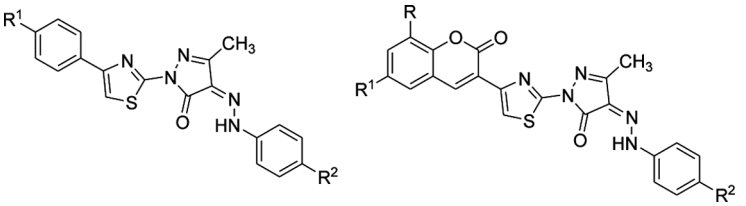
GRAPHICAL ABSTRACT



Abstract *A facile, one-pot, three-component bis heterocyclized reaction for the synthesis of hydrazonothiazolyl-pyrazolones has been described. Reaction of phenacyl bromides or 3-(2-bromoacetyl)coumarins, with thiosemicarbazide and ethyl 2-(2-arylhydrazono)-3-oxobutanoates in AcOH/NaOAc, gave the corresponding products in good yields. All the synthesized compounds were characterized by their analytical and spectral data.*

Keywords 3-(2-Bromoacetyl)coumarin; one-pot synthesis; phenacyl bromide; thiazolyl-pyrazolone; thiosemicarbazide

INTRODUCTION

Nitrogen and sulfur heterocyclic systems are very interesting because of their physicochemical properties, which have relevance to the design of new drugs and new materials. Compounds containing the thiazole ring system are known to possess pharmacological properties of great importance in biological systems. A large number of thiazoles obtained from microbial and marine life exhibit important biological effects[1] such as antitumor, antifungal, antibiotic, and antiviral activities. Synthetically prepared substituted thiazoles are also known to possess a wide range of pharmacological properties,[2–4] including very good novel Src family kinase inhibitory,[5] antitumor,[6] and antimicrobial[7] activities. They have also other applications such as in liquid crystals and cosmetic sunscreens.[8,9]

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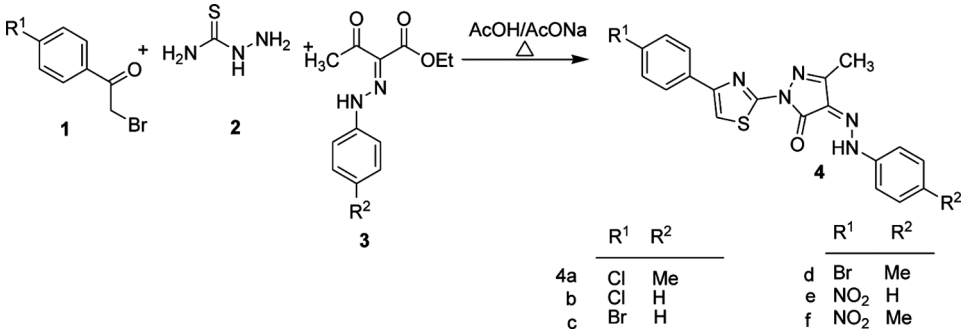
Pyrazoles, key substructures in a large variety of important medicinal compounds, have attracted much attention.[10–12] Various therapeutic activities such as antitumor, antiviral, analgesic, and anti-inflammatory properties have been reported for pyrazoles.[13,14] Coumarin and its derivatives are also biologically active compounds, occur widely in nature, and have a remarkably broad spectrum of pharmacological and physiological activities.[15–17] Also, in recent times there are references to derivatives with anti-HIV activity.[18,19]

In view of the various physiological activities of coumarins, thiazoles, and pyrazoles, our current studies are focused on the development of new routes for the synthesis of thiazole incorporating pyrazole and coumarin moieties. We have developed a one-pot, multicomponent reaction for the synthesis of aryl and heteryl substituted hydrazono thiazolyl-pyrazolone derivatives because these compounds possess anthelmintic, analgesic, anti-inflammatory, antibacterial, and antifungal activities.[20]

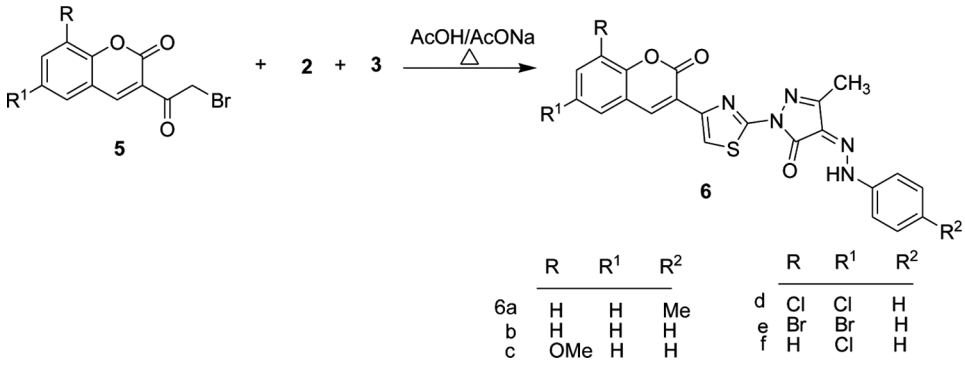
RESULTS AND DISCUSSION

Hydrazonothiazolyl-pyrazolone derivatives were synthesized by Kalluraya et al.[20] in a stepwise manner. In this method, diazotization of ethyl acetoacetate with aryldiazonium salts gave the corresponding oxobutyrates, which on reaction with thiosemicarbazide gave the respective thioamides. Reaction of these thioamides with 3-(2-bromoacetyl)coumarin in a dimethylformamide (DMF)–ethanol mixture gave the title products. However, this method has some limitations, such as multistep synthesis and lower reaction yields. Hence, there is a need for a versatile, simple, and friendly process for the synthesis of target compounds, which would enhance the scope of their applications.

As a part of our continuing work on the synthesis of novel heterocyclic systems,[21–23] a facile and convenient root was developed for the synthesis of aryl, heteryl substituted hydrazonothiazolyl-pyrazolone derivatives via a one-pot, three-component reaction with excellent yields. In this method, thiazole and pyrazolone rings can be synthesized chemoselectively in one pot. Reaction of an equimolar mixture of phenacyl bromide, thiosemicarbazide, and ethyl 2-(2-arylhydrazono)-3-oxobutanoate in AcOH/NaOAc gave the final products 4-(2-arylhydrazono)-3-methyl-1-(4-arylthiazol-2-yl)-1*H*-pyrazol-5(4*H*)-ones **4** (Scheme 1). Reaction of



Scheme 1. One-pot synthesis of hydrazono phenyl thiazolyl-pyrazolones.



Scheme 2. One-pot synthesis of hydrazono-2-oxo-chromenyl thiazolyl-pyrazolones.

an equimolar mixture of 3-(2-bromoacetyl)coumarin, thiosemicarbazide, and ethyl 2-(2-arylhydrazono)-3-oxobutanoate in AcOH/NaOAc gave the target product 4-(2-arylhydrazono)-3-methyl-1-(4-(2-oxo-2*H*-chromen-3-yl)thiazol-2-yl)-1*H*-pyrazol-5(4*H*)-one **6** in excellent yields (Scheme 2). In this reaction a sulfur atom of thiosemicarbazide undergoes nucleophilic substitution with **1** or **5** by eliminating HBr, followed by dehydration to give the Hantzsch thiazole product. The hydrazine part of thiosemicarbazide reacts with **3** to yield the hydrazonopyrazolone moiety.

The infrared (IR) spectrum of compound **4a** showed prominent peaks at $1678\,cm^{-1}$ for $-C{=}O$ of pyrazolone and $3178\,cm^{-1}$ for $-NH$, whereas the ^1H NMR spectrum of compound **4a** showed characteristic singlets for Ar-CH_3 and $-CH_3$ of pyrazolone $-NH$ at δ 2.38, 2.46, and 13.30. Similarly, the IR spectrum of compound **6a** showed prominent peaks at 1670 and $1722\,cm^{-1}$ for $-C{=}O$ of pyrazolone and coumarin lactone. A characteristic absorption peak for –NH appeared at $3122\,cm^{-1}$. The ^1H NMR of compound **6a** showed singlets for Ar-CH_3 and $-CH_3$ of pyrazolone at δ 2.39 and 2.49. The $-NH$ proton appeared as a broad singlet at 13.32. All the spectral data clearly show the formation of products **4a–f** and **6a–f**.

In conclusion, a novel, facile, one-pot, multicomponent reaction for the synthesis of 4-(2-arylhydrazono)-3-methyl-1-(4-arylthiazol-2-yl)-1*H*-pyrazol-5(4*H*)-ones and 4-(2-arylhydrazono)-3-methyl-1-(4-(2-oxo-2*H*-chromen-3-yl)thiazol-2-yl)-1*H*-pyrazol-5(4*H*)-one has been developed via a one-pot reaction. The advantages of this methodology are mild reaction conditions, easy workup, clean reaction profile, short reaction time, and wide range of substrate applicability.

EXPERIMENTAL

All the reagents and solvents were purchased from commercial sources and were used without further purification unless otherwise stated. 3-(2-Bromoacetyl)coumarins[24] and ethyl 2-(2-arylhydrazono)-3-oxobutanoates were prepared by literature procedure.[25] Melting points were determined in open capillaries with a "Cintex" melting-point apparatus (Mumbai, India) and were uncorrected. CHNS analysis was done on a Carlo Erba EA 1108 automatic elemental analyzer. The purity of the compounds was checked by thin-layer

chromatogaphic (TLC) plates (E. Merck, Mumbai, India). IR spectra (KBr) were recorded on a Bruker WM-4(X) spectrometer (577 model). ^{1}H NMR spectra were recorded on a Bruker WM-400 spectrometer in δ ppm using tetramethylsilane (TMS) as standard. Mass spectra (EI-MS) were determined on a Perkin-Elmer (SCIEX API-2000, ESI) instrument at 12.5 eV.

Compounds 4a–f

Compound **1** (1 mmol), thiosemicarbazide (1 mmol), and ethyl 2-(2-arylhydra zono)-3-oxobutanoate (1.2 mmol) were taken in acetic acid (10 mL) and stirred at rt for about 1 h. Sodium acetate (2 mmol) was added to the reaction mixture and heated at 80–85 °C for about 2 h. The product obtained was cooled, filtered, washed with water, and recrystallized from acetic acid.

4-(2-*p*-Tolylhydrazono)-1-(4-(4-chlorophenyl)thiazol-2-yl)-3-methyl-1*H*-pyrazol-5(4*H*)-one (4a). Orange-yellow solid; yield 86%; mp 218–220 °C; IR (KBr, υ_{max}): 1525 (C=C), 1595 (−C=N), 1678 (−C=O, pyrazolone), 3178 (−NH). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.38 (s, 3H, Ar-CH_3), 2.46 (s, 3H, CH_3 of pyrazolone), 7.24–7.26 (m, 3H, 2H-ArH, 1H-thiazole), 7.36–7.38 (m, 4H, ArH), 7.90 (d, 2H, $J = 8.8$ Hz, ArH), 13.30 (s, 1H, −NH, D_2O, exchangeable). EI-MS 410 (100%) $[M + H]^+$, 412 (33%). Anal. calcd. for $C_{20}H_{16}ClN_5OS$: C, 58.60; H, 3.93; N, 17.09. Found: C, 58.55; H, 3.90; N, 16.98.

4-(2-Phenylhydrazono)-1-(4-(4-chlorophenyl)thiazol-2-yl)-3-methyl-1*H*-pyrazol-5(4*H*)-one (4b). Orange-yellow solid; yield 82%; mp 224–226 °C; IR (KBr, υ_{max}): 1523 (C=C), 1600 (−C=N), 1677 (−C=O, pyrazolone), 3140 (−NH). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.47 (s, 3H, CH_3 of pyrazolone), 7.26–7.48 (m, 8H, 7H-ArH, 1H-thiazole ArH), 7.90 (d, 2H, $J = 8.4$ Hz, ArH), 13.26 (s, 1H, −NH, D_2O, exchangeable). EI-MS 396 (100%) $[M + H]^+$, 398 (33%). Anal. calcd. for $C_{19}H_{14}ClN_5OS$: C, 57.65; H, 3.56; N, 17.69. Found: C, 57.61; H, 3.51; N, 17.62.

4-(2-Phenylhydrazono)-1-(4-(4-bromophenyl)thiazol-2-yl)-3-methyl-1*H*-pyrazol-5(4*H*)-one (4c). Yellow solid; yield 78%; mp 216–218 °C; IR (KBr, υ_{max}): 1523 (C=C), 1597 (−C=N), 1668 (−C=O, pyrazolone), 3263 (−NH). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.27 (s, 3H, CH_3 of pyrazolone), 7.24–7.67 (m, 7H, 6H-ArH, 1H-thiazol), 7.92 (d, 1H, $J = 7.6$ Hz, ArH), 8.95 (s, 1H, ArH), 9.49 (s, 1H, ArH), 13.08 (s, 1H, −NH, D_2O, exchangeable). Anal. calcd. for $C_{19}H_{14}BrN_5OS$: C, 51.83; H, 3.20; N, 15.91. Found: C, 51.80; H, 3.16; N, 15.98.

4-(2-*p*-Tolylhydrazono)-1-(4-(4-bromophenyl)thiazol-2-yl)-3-methyl-1*H*-pyrazol-5(4*H*)-one (4d). Yellow solid; yield 80%; mp 208–210 °C; IR (KBr, υ_{max}): 1521 (C=C), 1585 (−C=N), 1689 (−C=O, pyrazolone), 3259 (−NH). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.25 (s, 3H, Ar-CH_3), 2.31 (s, 3H, CH_3 of pyrazolone), 7.27 (m, 3H, ArH), 7.54–7.67 (m, 3H, 2H-ArH, 1H-thiazol), 7.92 (d, 1H, $J = 7.6$ Hz, ArH), 8.97 (s, 1H, ArH), 9.48 (s, 1H, ArH), 13.10 (s, 1H, −NH, D_2O, exchangeable). $C_{20}H_{16}BrN_5OS$: C, 52.87; H, 3.55; N, 15.41. Found: C, 52.82; H, 3.51; N, 15.37.

4-(2-Phenylhydrazono)-3-methyl-1-(4-(4-nitrophenyl)thiazol-2-yl)-1*H*-pyrazol-5(4*H*)-one (4e). Yellow solid; yield 80%; mp >300 °C; IR (KBr, υ_{max}):

1523 (C=C), 1597 (−C=N), 1666 (−C=O, pyrazolone), 3261 (−NH). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.38 (s, 3H, CH_3 of pyrazolone), 7.26 (m, 1H, ArH), 7.47 (m, 2H, ArH), 7.70 (m, 2H, ArH), 8.23–8.35 (m, 5H, 4H-ArH, 1H-thiazole), 13.10 (s, 1H, −NH, D_2O, exchangeable). EI-MS 407 $[M+H]^+$. Anal. calcd. for $C_{19}H_{14}N_6O_3S$: C, 56.15; H, 3.47; N, 20.68. Found: C, 56.12; H, 3.43; N, 20.63.

4-(2-*p*-Tolylhydrazono)-3-methyl-1-(4-(4-nitrophenyl)thiazol-2-yl)-1*H*-pyrazol-5(4*H*)-one (4f). Orange-yellow solid; yield 78%; mp >300 °C; IR (KBr, υ_{max}): 1523 (C=C), 1597 (−C=N), 1668 (−C=O, pyrazolone), 3260 (−NH). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.33 (s, 3H, Ar-CH_3), 2.37 (s, 3H, CH_3 of pyrazolone), 7.28 (m, 2H, ArH), 7.57 (m, 2H, ArH), 8.23–8.34 (m, 5H, 4H-ArH, 1H-thiazole), 13.15 (s, 1H, −NH, D_2O, exchangeable). EI-MS 421 $[M+H]^+$. Anal. calcd. for $C_{20}H_{16}N_6O_3S$: C, 57.13; H, 3.84; N, 19.99. Found: C, 57.20; H, 3.76; N, 19.95.

Compounds 6a–f

Compound **5** (1 mmol), thiosemicarbazide (1 mmol), and ethyl 2-(2-arylhydra zono)-3-oxobutanoate (1.2 mmol) were taken in acetic acid (10 mL) and stirred at rt for about 1 h. Sodium acetate (2 mmol) was added to the reaction mixture heated at 80–85 °C for about 2 h. The product obtained was cooled, filtered, washed with water, and recrystallized from acetic acid.

4-(2-*p*-Tolylhydrazono)-3-methyl-1-(4-(2-oxo-2*H*-chromen-3-yl)thiazol-2-yl)-1*H*-pyrazol-5(4*H*)-one (6a). Orange-yellow solid; yield 85%; mp 274–276 °C; IR (KBr, υ_{max}): 1533 (C=C), 1604 (−C=N), 1670 (−C=O, pyrazolone), 1722 (lactone −C=O), 3122 (−NH). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.39 (s, 3H, Ar-CH_3), 2.49 (s, 3H, CH_3 of pyrazolone), 7.26–7.67 (m, 8H, ArH), 8.33 (s, 1H, thiazole), 8.85 (s, 1H, C-4 of coumarin), 13.32 (s, 1H, −NH, D_2O, exchangeable). EI-MS 444 $[M+H]^+$. Anal. calcd. for $C_{23}H_{17}N_5O_3S$: C, 62.29; H, 3.86; N, 15.79. Found: C, 62.23; H, 3.81; N, 15.72.

4-(2-Phenylhydrazono)-3-methyl-1-(4-(2-oxo-2*H*-chromen-3-yl)thiazol-2-yl)-1*H*-pyrazol-5(4*H*)-one (6b). Orange-yellow solid; yield 84%; mp 268–270 °C; IR (KBr, υ_{max}): 1534 (C=C), 1598 (−C=N), 1657 (−C=O, pyrazolone), 1716 (lactone −C=O), 3144 (−NH). ^{1}H NMR (400 MHz, $CDCl_3$): 2.50 (s, 3H, CH_3 of pyrazolone), 7.28–7.67 (m, 9H, ArH), 8.34 (s, 1H, thiazole), 8.85 (s, 1H, C-4 of coumarin), 13.28 (s, 1H, −NH, D_2O, exchangeable). EI-MS 430 $[M+H]^+$. Anal. calcd. for $C_{22}H_{15}N_5O_3S$: C, 61.53; H, 3.52; N, 16.31, Found: C, 61.50; H, 3.50; N, 16.27.

4-(2-Phenylhydrazono)-1-(4-(8-methoxy-2-oxo-2*H*-chromen-3-yl)thiazol-2-yl)-3-methyl-1*H*-pyrazol-5(4*H*)-one (6c). Yellow solid; yield 81%; mp >300 °C; IR (KBr, υ_{max}): 1521 (C=C), 1599 (−C=N), 1657 (−C=O, pyrazolone), 1724 (lactone −C=O), 3143 (−NH). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.49 (s, 3H, CH_3 of pyrazolone), 3.99 (s, 3H, −OCH_3), 7.08–7.48 (m, 8H, ArH), 7.92 (s, 1H, thiazole), 8.57 (s, 1H, C-4 of coumarin), 12.05 (s, 1H, −NH, D_2O, exchangeable). EI-MS 460 $[M+H]^+$. Anal. calcd. for $C_{23}H_{17}N_5O_4S$: C, 60.12; H, 3.73; N, 15.24. Found: C, 60.16; H, 3.70; N, 15.29.

4-(2-Phenylhydrazono)-1-(4-(6,8-dichloro-2-oxo-2*H*-chromen-3-yl)thiazol-2-yl)-3-methyl-1*H*-pyrazol-5(4*H*)-one (6d). Yellow solid; yield 78%; mp >300 °C; IR (KBr, υ_{max}): 1531 (C=C), 1595 (−C=N), 1666 (−C=O, pyrazolone), 1737 (lactone −C=O), 3140 (−NH). ^{1}HNMR (400 MHz, $CDCl_3$): δ 2.27 (s, 3H, CH_3 of pyrazolone), 7.24–7.63 (m, 7H, ArH), 8.08 (s, 1H, thiazole), 8.54 (s, 1H, C-4 of coumarin), 13.10 (s, 1H, −NH, D_2O, exchangeable). Anal. calcd. for $C_{22}H_{13}Cl_2N_5O_3S$: C, 53.02; H, 2.63; N, 14.05. Found: C, 53.00; H, 2.60; N, 13.98.

4-(2-Phenylhydrazono)-1-(4-(6,8-dibromo-2-oxo-2*H*-chromen-3-yl)thiazol-2-yl)-3-methyl-1*H*-pyrazol-5(4*H*)-one (6e). Yellow solid; yield 85%; mp >300 °C; IR (KBr, υ_{max}): 1525 (C=C), 1602 (−C=N), 1678 (−C=O, pyrazolone), 1735 (lactone −C=O), 3249 (−NH). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.50 (s, 3H, CH_3 of pyrazolone), 7.26–7.62 (m, 7H, ArH), 8.35 (s, 1H, thiazole), 8.76 (s, 1H, C-4 of coumarin), 13.27 (s, 1H, −NH, D_2O, exchangeable). Anal. calcd. for $C_{22}H_{13}Br_2N_5O_3S$: C, 45.00; H, 2.23; N, 11.93. Found: C, 44.92; H, 2.20; N, 11.09.

4-(2-Phenylhydrazono)-1-(4-(6-chloro-2-oxo-2*H*-chromen-3-yl)thiazol-2-yl)-3-methyl-1*H*-pyrazol-5(4*H*)-one (6f). Yellow solid; yield 79%; mp >300 °C; IR (KBr, υ_{max}): 1534 (C=C), 1607 (−C=N), 1657 (−C=O, pyrazolone), 1714 (lactone −C=O), 3151 (−NH). ^{1}H NMR (400 MHz, $CDCl_3$): 2.36 (s, 3H, CH_3 of pyrazolone), 7.39–7.64 (m, 8H, ArH), 7.87 (s, 1H, thiazole), 8.39 (s, 1H, C-4 of coumarin), 12.76 (s, 1H, −NH, D_2O, exchangeable). Anal. calcd. for $C_{22}H_{14}ClN_5O_3S$: C, 56.96; H, 3.04; N, 15.10. Found: C, 58.91; H, 3.00; N, 15.15.

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REFERENCES

1. Lewis, J. R. Muscarine, imidazole, oxazole, thiazole and peptide alkaloids, and other miscellaneous alkaloids. *Nat. Prod. Rep.* **1996**, *13*, 435–467.
2. Kearney, P. C.; Fernandez, M.; Flygare, J. A. Solid-phase synthesis of 2-aminothiazoles. *J. Org. Chem.* **1998**, *63*, 196–200.
3. Geronikaki, A. A.; Dearden, J. C.; Filimonov, D.; Galaeva, I.; Garibova, T. L.; Gloriozova, T.; Krajneva, V.; Lagunin, A.; Macaev, F. Z.; Molodavkin, G.; Poroikov, V. V.; Pogrebnoi, S. I.; Shepeli, F.; Voronina, T. A.; Tsitlakidou, M.; Vlad, L. Design of new cognition enhancers: From computer prediction to synthesis and biological evaluation. *J. Med. Chem.* **2004**, *47*, 2870–2876.
4. Li, G.; Warner, P. M.; Jebaratnam, D. J. Synthesis of a directly connected thiazole-oxazole ring system present in Microcin B17. *J. Org. Chem.* **1996**, *61*, 778–780.
5. Das, J.; Chen, P.; Norris, D.; Padmanabha, R.; Lin, J.; Moquin, R. V.; Shen, Z.; Cook, L. S.; Doweyko, A. M.; Pitt, S.; Pang, S.; Shen, D. R.; Fang, Q.; de Fex, H. F.; McIntyre, K. W.; Shuster, D. J.; Gillooly, K. M.; Behnia, K.; Schieven, G. L.; Wityak, J.; Barrish, J. C. 2-Aminothiazole as a novel kinase inhibitor template: Structure–activity relationship

studies toward the discovery of N-(2-chloro-6-methylphenyl)-2-[[6-[4-(2-hydroxyethyl)-1-piperazinyl)]-2-methyl-4-pyrimidinyl]amino)]-1,3-thiazole-5-carboxamide (Dasatinib, BMS-354825) as a potent pan-Src kinase inhibitor. *J. Med. Chem.* **2006**, *49*, 6819–6832.

6. Lombardo, L. J.; Lee, F. Y.; Chen, P.; Norris, D.; Barrish, J. C.; Behnia, K.; Castaneda, S.; Cornelius, L. A. M.; Das, J.; Doweyko, A. M.; Fairchild, C.; Hunt, J. T.; Inigo, I.; Johnston, K.; Kamath, A.; Kan, D.; Klei, H.; Marathe, P.; Pang, S.; Peterson, R. L.; Pitt, S.; Schieven, G. L.; Schmidt, R. J.; Tokarski, J.; Wen, M.-L.; Wityak, J.; Borzilleri, R. M. Discovery of N-(2-chloro-6-methyl-phenyl)-2-(6-(4-(2-hydroxyethyl)-piperazin-1-yl)-2-methylpyrimidin-4-ylamino)thiazole-5-carboxamide (BMS-354825), a Dual Src/Abl kinase inhibitor with potent antitumor activity in preclinical assays. *J. Med. Chem.* **2004**, *47*, 6658–6661.
7. Argyropoulou, I.; Geronikaki, A.; Vicini, P.; Zanib, F. Synthesis and biological evaluation of sulfonamide thiazole and benzothiazole derivatives as antimicrobial agents. *Arkivoc* **2009**, *6*, 89–102.
8. Kiryanov, A. A.; Sampson, P.; Seed, A. J. Synthesis of 2-alkoxy-substituted thiophenes, 1,3-thiazoles, and related S-heterocycles via Lawesson's reagent-mediated cyclization under microwave irradiation: Applications for liquid crystal synthesis. *J. Org. Chem.* **2001**, *66*, 7925–7929.
9. Bach, T.; Heuser, S. Synthesis of 2-(o-hydroxyaryl)-4-arylthiazoles by regioselective Pd(0)-catalyzed cross-coupling. *Tetrahedron Lett.* **2000**, *41*, 1707–1710.
10. Regan, J.; Capolino, A.; Cirillo, P. F.; Gilmore, T.; Graham, A. G.; Hicky, E.; Kroe, R. R.; Madwed, J.; Torcellini, C.; Tsang, M.; Moss, N. Structure-activity relationships of the p38α MAP kinase inhibitor 1-(5-tert-butyl-2-p-tolyl-2H-pyrazol-3-yl)-3-[4-(2-morpholin-4-yl-ethoxy)naph-thalen-1-yl]urea (BIRB 796). *J. Med. Chem.* **2003**, *46*, 4676–4686.
11. Stauffer, S. R.; Coletta, C. J.; Tedesco, R.; Nishiguchi, G.; Carlson, K.; Sun, J.; Katzenellenbogen, B. S.; Katzenellenbogen, J. A. Pyrazole ligands: Structure-affinity/activity relationships and estrogen receptor-α-selective agonists. *J. Med. Chem.* **2000**, *43*, 4934–4947.
12. Huang, Y. R.; Katzenellenbogen, J. A. Regioselective synthesis of 1,3,5-triaryl-4-alkylpyrazoles: Novel ligands for the estrogen receptor. *Org. Lett.* **2000**, *2*, 2833–2836.
13. Propsavin, M.; Torovic, L.; Spaic, S.; Stankov, S.; Kapor, A.; Tomic, Z.; Popsavin, V. Synthesis and biological evaluation of new pyrazole- and tetrazole-related C-nucleosides with modified sugar moieties. *Tetrahedron* **2002**, *58*, 569–580.
14. Sauzem, P. D.; Machado, P.; Rubin, M. A.; Da, S.; Sant'Anna, G.; Faber, H. B.; De Souza, A. H.; Mello, C. F.; Beck, P.; Burrow, R. A.; Bonacorso, H. G.; Zanatta, N.; Martins, M. A. P.; Patricia, D. Design and microwave-assisted synthesis of 5-trifluoromethyl-4,5-dihydro-1H-pyrazoles: Novel agents with analgesic and anti-inflammatory properties. *Eur. J. Med. Chem.* **2008**, *43*, 1237–1247.
15. O'Kennedy, R.; Thornes, R. D. *Coumarins-Biology, Applications and Mode of Action*; John Wiley and Sons: Chichester, UK, 1997.
16. Melliou, E.; Magiatis, P.; Mitaku, S.; Skaltsounis, A. L.; Chinou, E.; Chinou, I. Natural and synthetic 2,2-dimethylpyranocoumarins with antibacterial activity. *J. Nat. Prod.* **2005**, *68*, 78–82.
17. Valenti, P.; Rampa, A.; Recanatini, M.; Bisi, A.; Belluti, F.; Da Re, P.; Carrara, M.; Cima, L. Synthesis, cytotoxicity, and SAR of simple geiparvarin analogues. *Anticancer Drug Des.* **1997**, *12*, 443–451.
18. Spino, C.; Dodier, M.; Sotheeswaran, S. Anti-HIV coumarins from calophyllum seed oil. *Bioorg. Med. Chem. Lett.* **1998**, *8*, 3475–3478.
19. Thaisrivongs, S.; Watenpaugh, K. D.; Howe, W. J.; Tomich, P. K.; Dolak, L. A.; Chong, K.-T.; Tomich, C.-S. C.; Tomasselli, A. G.; Turner, S. R.; Strohbach, J. W.; Mulichak, A. M.; Janakiraman, M. N.; Moon, J. B.; Lynn, J. C.; Horng, M.-M.; Hinshaw, R. R.;

Curry, K. A.; Rothrock, D. J. Structure-based design of novel HIV protease inhibitors: Carboxamide-containing 4-hydroxycoumarins and 4-hydroxy-2-pyrones as potent nonpeptidic inhibitors. *J. Med. Chem.* **1995**, *38*, 3624–3637.
20. Kalluraya, B. K.; Isloor, A. M.; Frank, P. V.; Jagadeesha, R. L. Synthesis and pharmacological activity of some 4-(substituted)-2-[4-aryhydrazono-3-methyl-5-oxo-2-pyrazolin-1-yl] thiazoles. *Indian J. Het. Chem.* **2004**, *13*, 245.
21. Rajeswar Rao, V.; Vijaya Kumar, P. A facile one-step synthesis of 3-{2-[5-hydroxy-4-(2-hydroxy-ethyl)-3-methyl-pyrazol-1-yl]-thiazol-4-yl}-chromen-2-ones via a three-component reaction. *Synth. Commun.* **2006**, *36*, 2157–2161.
22. Chunduru, V. S. R.; Rajeswar Rao, V. One-pot synthesis of 3-[2-(arylamino)thiazol-4-yl]coumarins in a three-component synthesis and a catalyst and solvent-free synthesis on grinding. *J. Chem. Res.* **2010**, 50–53.
23. Srimanth, K.; Rajeswar Rao, V. A facile one-step synthesis of 3-(2-(3,5-dimethyl-1H-pyrazol-1-yl)-4-thiazolyl)-2H-benzopyran-2-ones under solvent-free condition. *J. Chem. Res.* **2002**, 420–421.
24. Rajeswar Rao, V.; Padmanabha Rao, T. V. Studies of thiazolyl, imidazolyl-2H-1-benzopyran-2-ones. *Indian J. Chem.* **1986**, *25B*, 413.
25. Rajput, A. P.; Rajput, S. S. Synthesis and microbial screening of seven membered heterocyclic ring compounds from 1,2-diaminobenzene. *Int. J. Pharm. Tech. Res.* **2009**, *1*, 900–904.