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Saba Farooq & Zainab Ngaini

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Efficient and Selective Hydrazinolysis of Pyranopyrazole Derivatives Using Phenylhydrazine

Saba Farooq*[a,b], Zainab Ngaini*[a]

[a] Faculty of Resource Science and Technology, Universiti Malaysia Sarawak, 94300 Kota Samarahan, Sarawak, Malaysia.

[b] Department of Basic & Applied Chemistry, Faculty of Science and Technology, University of Central Punjab, 54000 Lahore, Pakistan.

Corresponding Address: sabafarooq61@yahoo.com and nzainab@unimas.my

Abstract

This study explores the efficient and selective hydrazinolysis of pyranopyrazole derivatives through phenylhydrazine under mild conditions. The reaction provides a facile approach to ring cleavage *via* a new mild protocol and a catalyst-free environment, yielding hydrazone products. Structural characterization was performed using FTIR, ^{1}H and ^{13}C NMR analyses, confirming the transformation. The findings elaborated mechanistic insights into pyranopyrazole transformations in the presence of phenylhydrazine, to contribute to heterocyclic chemistry.

Keywords: Aldehyde, Hydrazine, Pyrazolone, Synthesis, Cleavage

Introduction

Pyranopyrazole is a heterocyclic compound featuring a pyrazole ring fused to a pyran ring [1],[2]. It occurs in two isomeric forms: 1,4-dihydropyrano[2,3-c]pyrazole and 2,4-dihydropyrano[2,3-c]pyrazole [3].

Among these isomers, 1,4-dihydropyrano[2,3-c]pyrazole exhibits greater stability than its counterpart [4]. It is frequently referred to in the literature by alternative names, such as 4H-pyrano[2,3-c]pyrazoles, pyrano[2,3-c]pyrazoles, and 1,4-dihydropyrano[2,3-c]pyrazol-5-yl cyanides [5]. Pyranopyrazole is a bioactive scaffold that has versatile applications in agrochemicals, fungicides, insecticides [6], herbicides [7], molluscicidal[8], larvicidal[9], and biological activities *i.e.*, antimicrobial[10], antibacterial[11], antitubercular[12], anticancer[13], antioxidant[14], antiallergenic[15], antineoplastic[16] and anti-inflammatory [17], antimalarial and cardiovascular applications (**Figure 1**) [2].

Pyranopyrazole derivatives are generally synthesized by different approaches, such as two-component approach *via* the reaction of pyrazolone with arylidenemalononitriles [6] or epoxychalcone [11], three-component approach *via* the reaction of pyrazolone, malononitrile and aldehyde derivative [18], and four-component approach *via* the reaction of benzyl alcohols, ethyl acetoacetate, phenylhydrazine and malononitrile [3],[19]. Interestingly, the four-component approach modified by several researchers, including Koohshari *et al.* (2014), was used by using aldehydes, ethyl acetoacetate, phenylhydrazine, and malononitrile *via* Knoevenagel-Michael mechanism. The reaction was conducted in ethanol: water (8:2), for 12 h stirring at 60 ^{o}C under catalyst-free conditions to achieve 60-78 % yield of the desired product [20]. Recent studies contributed to improve the yield of pyranopyrazoles by using $Fe_3O_4@gC_3N_4$ as a catalyst under 1 h reflux, to produce 97 % product [21].

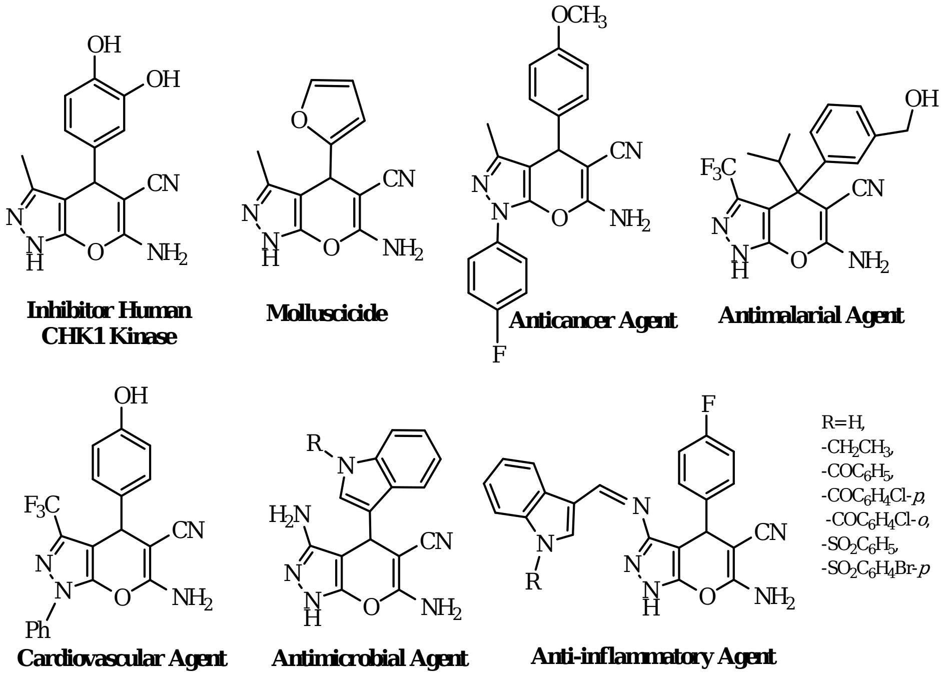


Figure 1: Pyranopyrazole derivatives applications

A wide range of catalysts has been used for the four-component reaction of pyrazolone namely, isonicotinic acid [22], thiourea dioxide [23], lemon juice [24], $NiWO_4$[25], NaOH [26], sodium lactate [27], piperidine [28], PBCMO-amine [29], baker's yeast [30], Zn(L-proline)$_2$ [31], solar radiation [32], $H_4[SiW_{12}O_{40}]$ [33], lactic acid:urea: NH_4Cl [34], agave leaf ash extract [35], HMS/Pr-Rh-Zr [36], PVC–EDA–Ce^{III} [37], $NiFe_2O_4$@SiO_2–$H_3PW_{12}O_{40}$ [38], $Na_2CaP_2O_7$ [39], Fe_3O_4/MIP-202-H_4WO_5 [40], Zn-CA-MOFs [41], PdO/Al-SBA-15[42], Fe_3O_4@SiO_2@CoSB [43], nano-[Fe-PSMP]Cl_2 [44], nano-ZrO_2 [45], nano-CaO [46], nano-FSiPSS [47], Fe_3O_4@chitosan-tannic acid [48], PAN@melamine/Fe_3O_4 [49], Cu-DABP@Fe_3O_4/ MCM-41 [50], ($MnCoFe_2O_4$@Niacin-SO_3H)$^+$$Cl^-$ [51], [DBU][Ac] [52], P_2O_5/SiO_2, H_3PO_4/Al_2O_3, starch sulfuric acid and cellulose sulfuric acid [53].

Many studies have been reported on pyranopyrazole due to its facile synthesis and various applications in biological activities and electronic properties [2]. The available NH_2 and CN modification in the pyranopyrazole network is prone to further modification, such as pyranopyrazole-Schiff base and pyran-bispyrazoles for COX-2 Inhibitors and cytotoxicity activities, respectively [54],[55],[56].

In this study, we report the synthesis of pyranopyrazoles featuring (CN & NH_2 substituents) at the C_2-$C_{3,}$ which were subsequently reacted with aldehyde derivatives and phenylhydrazine *via* suitable protocols to achieve Schiff bases and cyclized products, respectively. Heterocyclic pyranopyrazoles featuring CN & NH_2 substituents are envisaged to be effectively transformed into new biologically active materials. This study is significant in the development of heterocyclic chemistry-based drugs.

Experimental

General synthesis of pyranopyrazoles (1a-f)

The synthesis of compounds **1a-f** was conducted following Vasuki *et al.* (2008), with some modifications [57]. Ethyl acetoacetate (0.1275 ml, 1 mmol), aldehyde (0.1019 ml, 1 mmol), phenylhydrazine (0.1179 ml, 1.2 mmol) and malononitrile (0.792 ml, 1.2 mmol) were added to 20 ml ethanol: distilled water (8:2) mixture in the presence of the catalyst piperidine (15% mmol). The resultant mixture was heated at 60 ^{o}C and stirred well for about 40 min. The reaction was monitored using TLC, and after the reaction completion, the solid residue was filtered and dried to obtain and recrystallize the pure product. The compounds were confirmed by FTIR, ^{1}H and ^{13}C NMR spectroscopy.

6-Amino-3-methyl-1,4-diphenyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile **(1a)**

White solid (0.3182 g, 96.98 % yield), m.p. 184–185 °C (lit. m.p. 182-185 °C [58]), (Found: C, 73.05; H, 4.80; N, 16.63 %. $C_{20}H_{16}N_4O$ Requires C, 73.15; H, 4.91; N, 17.06). FTIR: 3471, 3321, 3260, 3186, 3067, 2196, 1655, 1594, 1515, 1493, 1441, 1383, 1258, 1185, 1127, 1062, 1026, 904, 827, 754, 702, 702, 687, 647, 613. ^{1}HNMR δ_H (500 MHz, DMSO *d₆*): 7.80 (dd, *J* = 8.9, 1.2 Hz, 2H), 7.49 (t, *J* = 8.7, 2H), 7.39 – 7.15 (m, 8H), 4.68 (s, 1H), 1.78 (s, 3H). ^{13}C NMR δ_C (125 MHz, DMSO *d₆*): 159.4 (C-NH_2), 145.2, 143.8, 143.6, 137.5, 129.3, 128.5, 127.7, 127.0, 126.1, 119.9 (C-Ar), 98.6 (CN), 58.2 (C-CN), 36.7 (CH), 12.5 (CH_3).

4-(6-Amino-5-cyano-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)benzoic acid **(1b)**

White solid (0.3351 g, 90.00 % yield), m.p. 205-206 °C, (Found: C, 66.95; H, 4.13; N, 14.98 %. $C_{21}H_{16}N_4O_3$ Requires C, 67.73; H, 4.33; N, 15.05). FTIR: 3403, 3318, 3199, 2175, 1713, 1661, 1634, 1579, 1518, 1454, 1399, 1273, 1218, 1130, 1105, 1069, 1032, 907, 836, 790, 754, 687, 650. ^{1}HNMR δ_H (500 MHz, DMSO *d₆*): 7.94 (d, *J* = 7.9 Hz, 2H), 7.81 – 7.77 (d, *J* = 7.3, 2H), 7.49 (t, *J* = 8.8, 2H), 7.40 (d, *J* = 8.3 Hz, 2H), 7.32 (t, *J* = 8.3, 1H), 7.29 (s, 2H), 4.79 (s, 1H), 1.78 (s, 3H). ^{13}C NMR δ_C (125 MHz, DMSO *d₆*):

167.1, 159.6, 148.5, 145.2, 143.9, 137.5, 129.7, 129.6, 129.3, 128.0, 126.2, 120.0, 98.1, 57.6, 36.6, 12.5.

6-Amino-4-(4-cyanophenyl)-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile **(1c)**

Light yellow solid (0.3396 g, 96.12 % yield), m.p. 193-194 °C decomposed, (Found: C, 71.15; H, 4.10; N, 19.53 %. $C_{21}H_{15}N_5O$ Requires C, 71.38; H, 4.28; N, 19.82). FTIR: 3380, 3306, 3198, 2234, 2188, 1648, 1589, 1512, 1446, 1384, 1262, 1120, 1066, 1026, 827, 755, 675, 545. ^{1}HNMR δ_H (500 MHz, DMSO *d₆*): 7.81 (dd, *J* = 16.8, 6.2 Hz, 4H), 7.49 (dd, *J* = 9.2, 3.7 Hz, 4H), 7.38 – 7.24 (m, 3H), 4.83 (s, 1H), 1.77 (s, 3H). ^{13}C NMR δ_C (125 MHz, DMSO d_6): 159.7, 149.1, 145.1, 144.0, 137.4, 132.6, 129.3, 128.9, 126.2, 120.1, 119.7, 118.7, 109.9, 97.6, 57.0, 36.6, 12.5.

6-Amino-4-(4-fluorophenyl)-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile **(1d)**

White solid (0.3151 g, 90.99 % yield), m.p. 169–171 °C (lit. m.p. 170-172 °C [58]), (Found: C, 68.95; H, 4.22; N, 16.03 %. $C_{20}H_{15}FN_4O$ Requires C, 69.35; H, 4.37; N, 16.18). FTIR: 3449, 3320, 3214, 3046, 2199, 1660, 1592, 1507, 1444, 1387, 1222, 1124, 1066, 1021, 813, 751, 674. ^{1}HNMR δ_H (500 MHz, DMSO d_6): 7.78 (d, *J* = 7.6 Hz, 2H), 7.52 – 7.46 (m, 2H), 7.35 – 7.28 (m, 3H), 7.23 (s, 2H), 7.17 (t, *J* = 8.8 Hz, 2H), 4.72 (s, 1H), 1.78 (s, 3H). ^{13}C NMR δ_C (125 MHz, DMSO d_6): 162.1, 160.1, 159.3, 145.2, 143.8, 139.8, 139.8, 137.5, 129.7, 129.6, 129.3, 126.2, 120.0, 119.9, 115.3, 115.1, 98.4, 58.0, 35.9, 12.5.

***6-Amino-4-(4-bromophenyl)-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile* (1e)**

White solid (0.3787 g, 93.00 % yield), m.p. 170–172 ºC (lit. m.p. 171.5-173 ºC [58]), (Found: C, 57.65; H, 3.60; N, 13.33 %. $C_{20}H_{15}BrN_4O$ Requires C, 58.98; H, 3.71; N, 13.76). FTIR: 3448, 3322, 3203, 3053, 2196, 1658, 1588, 1506, 1388, 1258, 1123, 1065, 1018, 805, 748, 680. ^{1}HNMR δ_H (500 MHz, DMSO d_6): 7.78 (d, *J* = 7.6 Hz, 2H), 7.53 (d, *J* = 8.4 Hz, 2H), 7.50 – 7.45 (m, 2H), 7.31 (t, *J* = 7.4 Hz, 1H), 7.24 (d, *J* = 5.8 Hz, 3H), 7.22 (s, 1H), 4.70 (s, 1H), 1.79 (s, 3H). ^{13}C NMR δ_C (125 MHz, DMSO d_6): 159.5, 145.2, 143.9, 143.0, 137.5, 131.4, 130.1, 129.3, 126.2, 120.1, 120.0, 119.9, 98.1, 57.7, 12.6.

***6-Amino-3-methyl-1-phenyl-4-(thiophen-2-yl)-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile* (1f)**

Orange solid (0.2976 g, 88.02 % yield), m.p. 224–225 ºC (lit. m.p. 220-225 ºC [58]), (Found: C, 64.45; H, 4.40; N, 16.53 %. $C_{18}H_{14}N_4OS$ Requires C, 64.65; H, 4.22; N, 16.75). FTIR: 3452, 3306, 3194, 3059, 2191, 1652, 1585, 1502, 1441, 1379, 1118, 1056, 747, 690. ^{1}HNMR δ_H (500 MHz, DMSO d_6): 7.78 (d, *J* = 8.7 Hz, 2H), 7.49 (t, *J* = 7.2 Hz, 1H), 7.43 (d, *J* = 5.1 Hz, 2H), 7.32 (t, *J* = 6.9 Hz, 1H), 7.27 (s, 2H), 7.07 (d, *J* = 3.4 Hz, 1H), 7.00 – 6.96 (m, 1H), 5.09 (s, 1H), 1.92 (s, 3H). ^{13}C NMR δ_C (125 MHz, DMSO d_6): 159.2, 148.7, 145.4, 143.4, 137.4, 137.3, 129.3, 126.6, 126.2, 125.4, 124.9, 119.9, 119.7, 98.6, 58.5, 31.9, 12.4.

General Synthesis of Compounds (2a-f)

The synthesis of compounds **2a-f** was conducted following the procedure described by Murahari *et al.* (2019) [54] with some modifications. An equimolar amount of suitable pyranopyrazole derivative **1a-f** (1 mmol) and benzaldehyde derivatives (1 mmol) were reacted in the presence of 0.5-1 ml of different catalysts (*i.e.,* glacial acetic acid, piperidine, TEA) and 25 ml solvents (*i.e.,* THF, absolute ethanol, EtOH, MeOH under altered reflux for 3 h, 6 h, 12 h, and overnight. After reaction completion, the mixture was cooled and poured into crushed ice to achieve a crude product, which was purified with a neutral alumina column. Unfortunately, the final target compound **2a-f** was not achieved.

General Synthesis of Compounds (3a-f)

The synthesis of compounds **3a-f** was conducted following the procedure described by El-Arab *et al.* (2015) and Aziz *et al.* (1982) using different hydrazine derivatives. An equimolar amount of suitable pyranopyrazole derivative **1a-f** (1 mmol) and phenylhydrazine (0.0983 ml, 1 mmol) was refluxed for 2-4 h in the absence of acid or base in either 1,4-dioxane [55] or ethanol [56].

The resultant mixture was then cooled and poured onto a mixture of hydrochloric acid and ice/water. The formed solid product was not the desired product.

General Synthesis of Compounds (4a-f)

Pyranopyrazole derivative **1a-f** (1 mmol) was treated with phenylhydrazine (0.0983 ml, 1 mmol) in the absence of acid and base in ethanol. The resultant mixture was heated at 80 ^{o}C for 5-6 h under reflux. The reaction was monitored using TLC. After completion, the solid residue was filtered and dried to obtain the product, which was subsequently recrystallized to achieve a pure product. The compounds were analyzed using CHN elemental analysis, and confirmed by FTIR, ^{1}H and ^{13}C NMR spectroscopy.

(E)-1-benzylidene-2-phenylhydrazine **(4a)**

Light yellow crystal (0.1628 g, 82.95 % yield), m.p. 155-156 ^{o}C (lit. m.p. 156-157 ^{o}C [59]), (Found: C, 78.95; H, 5.96; N, 14.03 %. $C_{13}H_{12}N_2$ Requires C, 79.56; H, 6.16; N, 14.27). FTIR: 3305, 3030, 2885, 1586, 1491, 1252, 1128, 1062, 748, 685. ^{1}HNMR ▯$_{H}$ (500 MHz, DMSO *d₆*): 10.31 (s, 1H), 7.87 (s, 1H), 7.64 (d, *J* = 7.8 Hz, 2H), 7.38 (t, *J* = 7.6 Hz, 2H), 7.28 (t, *J* = 7.3 Hz, 1H), 7.22 (t, *J* = 7.9 Hz, 2H), 7.08 (d, *J* = 8.5 Hz, 2H), 6.75 (t, *J* = 7.2 Hz, 1H). ^{13}C NMR ▯$_{C}$ (125 MHz, DMSO d_6): 145.3, 136.4, 135.8, 129.1, 128.6, 127.9, 125.6, 118.8, 112.0 [60].

(E)-4-((2-phenylhydrazono)methyl)benzoic acid **(4b)**

White solid (0.1922 g, 80.01 % yield), m.p. 209-210 ^{o}C, (Found: C, 69.65; H, 4.60; N, 11.33 %. $C_{14}H_{12}N_2O_2$ Requires C, 69.99; H, 5.03; N, 11.66). FTIR: 3309, 2992, 2822, 2657, 2530, 1679, 1585, 1499, 1414, 1260, 1129, 916, 754, 688. ^{1}HNMR ▯$_{H}$ (500 MHz, DMSO d_6): 10.59 (s, 1H), 7.97 (d, *J* = 8.4 Hz, 2H), 7.91 (s, 1H), 7.74 (d, *J* = 8.4 Hz, 2H), 7.27 – 7.21 (m, 2H), 7.12 (d, *J* = 7.6 Hz, 2H), 6.78 (t, *J* = 7.3 Hz, 1H). ^{13}C NMR ▯$_{C}$ (125 MHz, DMSO d_6): 167.3, 144.9, 140.2, 135.2, 129.8, 129.6, 129.2, 125.5, 119.4, 112.3.

***(E)-4-((2-phenylhydrazono)methyl)benzonitrile* (4c)**

Yellow solid (0.1924 g, 86.98 % yield), m.p. 149-151 ^{o}C, (Found: C, 75.75; H, 4.88; N, 18.63 %. $C_{14}H_{11}N_3$ Requires C, 76.00; H, 5.01; N, 18.99). FTIR: 3286, 3044, 2212, 1575, 1494, 1256, 897, 832, 750, 688. ^{1}HNMR δ_H (500 MHz, DMSO d_6): 10.72 (s, 1H), 7.88 (s, 1H), 7.82 – 7.76 (m, 4H), 7.28 – 7.21 (m, 2H), 7.13 (d, *J* = 7.6 Hz, 2H), 6.81 (t, *J* = 7.3 Hz, 1H). ^{13}C NMR δ_C (125 MHz, DMSO d_6): 144.5, 140.4, 134.0, 132.4, 129.1, 125.9, 119.6, 119.0, 112.4, 109.2.

***(E)-1-(4-fluorobenzylidene)-2-phenylhydrazine* (4d)**

Brown solid (0.1671 g, 78.01 % yield), m.p. 129-130 ^{o}C, (Found: C, 72.75; H, 4.86; N, 12.93 %. $C_{13}H_{11}FN_2$ Requires C, 72.88; H, 5.18; N, 13.08). FTIR: 3307, 3048, 1588, 1489, 1228, 911, 830, 752, 691. ^{1}HNMR δ_H (500 MHz, DMSO d_6): 10.31 (s, 1H), 7.87 (s, 1H), 7.69 (dd, *J* = 8.8, 5.7 Hz, 2H), 7.25 – 7.18 (m, *J* = 8.6, 5.1 Hz, 4H), 7.08 (d, *J* = 7.5 Hz, 2H), 6.75 (t, *J* = 7.3 Hz, 1H). ^{13}C NMR δ_C (125 MHz, DMSO d_6): 162.8, 160.8, 145.2, 135.3, 132.4, 129.0, 127.4, 127.4, 118.7, 115.6, 115.4, 111.9.

***(E)-1-(4-bromobenzylidene)-2-phenylhydrazine* (4e)**

Brown solid (0.2228 g, 80.98 % yield), m.p. 119-120 ^{o}C, (Found: C, 56.25; H, 3.99; N, 10.03 %. $C_{13}H_{11}BrN_2$ Requires C, 56.75; H, 4.03; N, 10.18). FTIR: 3303, 3044, 1587, 1488, 1248, 1129, 999, 901, 745, 687. ^{1}HNMR δ_H (500 MHz, DMSO d_6): 10.43 (s, 1H), 7.83 (s, 1H), 7.57 (dd, *J* = 19.7, 8.6 Hz, 4H), 7.25 – 7.19 (m, 2H), 7.09 (d, *J* = 7.5 Hz, 2H), 6.76 (t, *J* = 7.3 Hz, 1H). ^{13}C NMR δ_C (125 MHz, DMSO d_6): 145.0, 135.1, 135.0, 131.5, 129.0, 127.3, 120.6, 118.9, 112.0.

***(E)-1-phenyl-2-(thiophen-2-ylmethylene)hydrazine* (4f)**

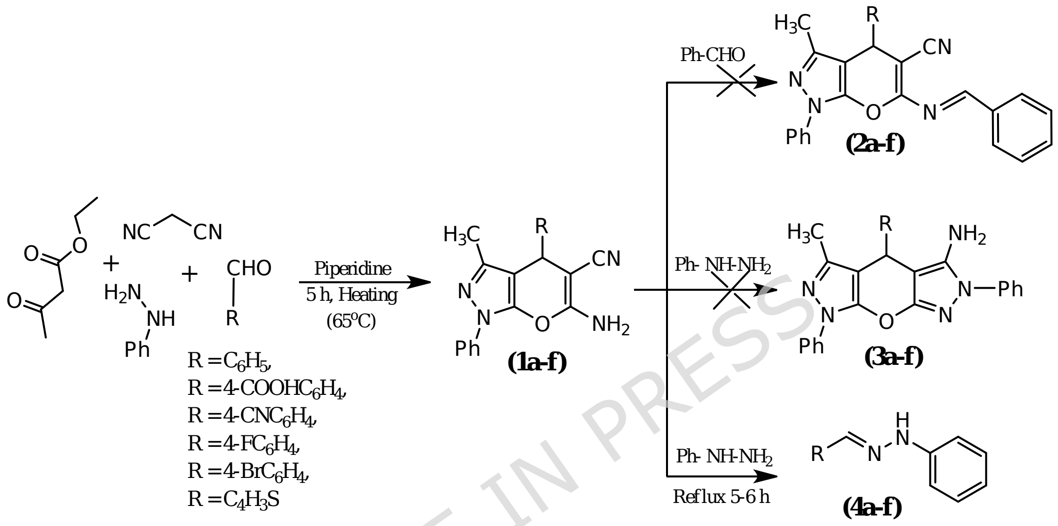
Yellow solid (0.1557 g, 77.00 % yield), m.p. 108-109 °C, (Found: C, 64.95; H, 4.86; N, 13.63 %. $C_{11}H_{10}N_2S$ Requires C, 65.32; H, 4.98; N, 13.85). FTIR: 3308, 3086, 1589, 1493, 1248, 1130, 896, 836, 745, 694. ^{1}HNMR δ_H (500 MHz, DMSO d_6): 10.29 (s, 1H), 8.08 (s, 1H), 7.44 (d, *J* = 5.1 Hz, 1H), 7.26 – 7.17 (m, 3H), 7.09 – 6.98 (m, 3H), 6.75 (t, *J* = 7.3 Hz, 1H). ^{13}C NMR δ_C (125 MHz, DMSO d_6): 145.0, 140.9, 131.9, 129.1, 127.5, 126.4, 125.6, 118.7, 111.8.

Results and Discussions

The cleavage of pyranopyrazole derivatives under phenylhydrazine, as described in **Scheme 1**, and the spectroscopic elucidation of these compounds were reported in the **Supplementary Information, Figures S1-3**. In this study, ethyl acetoacetate, aldehyde, phenylhydrazine, and malononitrile were reacted *via* condensation in a one-pot reaction at 60 °C for 40 min to achieve pyranopyrazole derivatives **(1a-f)** in 88.02-96.98 % yields. In the preparation of pyrazole-Schiff bases **(2a-f)**, further modification of the available NH_2 active group was attempted by reaction with a series of aldehydes following the protocol [54]. However, the route to the synthesis of the pyrazole-Schiff base was not as anticipated for heterocyclic moieties. Treatment of **(1a-f)** with halogenated aldehydes in a series of acidic (acetic acid, sulfuric acid) and basic media (piperidine, sodium hydroxide, potassium hydroxide) in organic solvents (EtOH, MeOH, THF) under various reaction conditions (reflux, room temperature) produced unstable intermediates as monitored by TLC. Thus, under both acidic and basic conditions, the pyran framework proved unstable, consistently undergoing ring cleavage and yielding transient intermediates [61]. Given these limitations, this pathway was discontinued in favor of alternative strategies.

To overcome the instability, cyclization reactions were focused on to afford *bis*-pyrazole pyran derivatives. In these reactions, pyranopyrazole cyclized to form pyrazole, with the amino group departing as ammonium. Primarily, the hydrazine moiety acts as a nucleophile attacking the electrophilic carbon of the pyran ring and destabilising the pyran framework, which causes ring opening. The resulting intermediate *via* intramolecular rearrangement is not favourable to form the targeted product. The substituted hydrazines (NH_2–NH–R) contributed a significant role in modulating the reaction due to the two nitrogen atoms. In ongoing studies, the R=Ph group increased the nucleophilicity of the terminal -NH_2, which also promoted ring closure by positing the phenyl moiety at the second nitrogen atom [63]. Attempts for compounds **3a–f** synthesis were unsuccessful under the applied conditions (*i.e.,* under catalyst-free conditions for 2-4 h reflux) due to the sensitive pyran and the delicate balance between ring stability and nucleophilic reactivity [64],[65]. The FTIR spectra for compound (**3a-f**) exhibited the disappearance of cyanide (CN) signal [56] while ^{1}HNMR displayed N-NH signal at 10.31-10.72 ppm, attributed to the formation of benzylidenes **4a-f** [66]. Additionally, ^{13}C

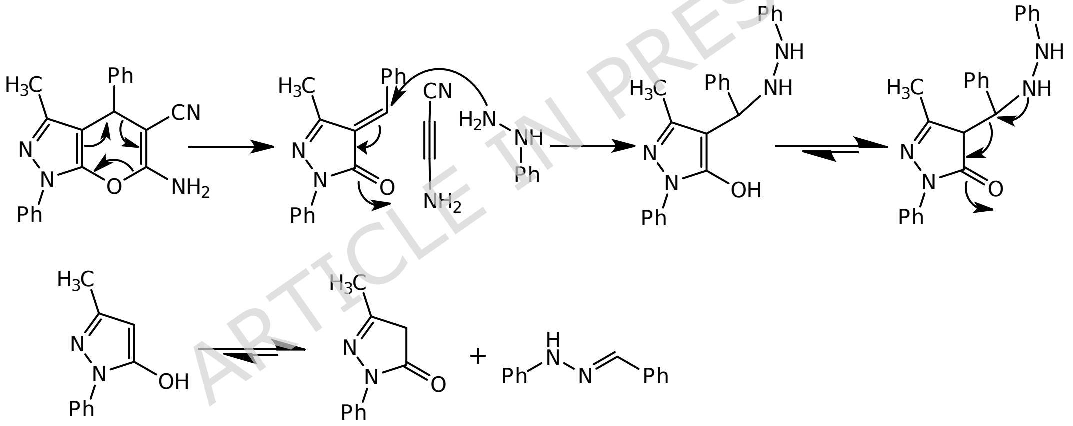
NMR showed fewer carbon atoms, while the characteristic -C=N-NH signal at 131.9-135.8 ppm further supported the formation of benzylidenes **(4a-f)**. The phenyl group position was difficult to identify [67] and required further resolution. Based on the pKa values of phenylhydrazine, the NH_2 group (pKa=27.8) is more nucleophilic compared to the NH group (pKa=21.7).



Scheme 1: Synthesis of pyranopyrazole-Schiff bases **(2a-f)**; *bis*-pyrazole pyran derivatives **(3a-f)** and pyranopyrazole cleavage to benzylidenes **(4a-f)**

The C-C bond cleavage and ring-opening phenomena of heterocyclic compounds are commonly reported, as observed in Biginelli pyrimidines *via* hydrazinolysis [65]. Several studies have highlighted the exclusive behavior of phenylhydrazine as a cleaving agent [62],[63] of different heterocyclic compounds. Under moderate reaction conditions, the reaction of pyranopyrazole with phenylhydrazine produced hydrazone instead of the pyrano-*bis*-pyrazole product. Consequently, hydrazone (**4a-f**) was confirmed and obtained in 77-87 % yield.

The basic nature of phenylhydrazine enables it to cleave pyranopyrazoles into the stable hydrazone compound, as supported by NMR and elemental analysis. A plausible mechanism is proposed in **Scheme 2**. Pyranopyrazole exhibits pronounced sensitivity to both acidic and basic conditions [68], which predisposes the pyran ring to cleavage upon treatment with phenylhydrazine. Phenylydrazine acts as a strong nucleophile, attacking the electrophilic carbon of the heterocyclic pyran ring to facilitate ring-opening and the subsequent formation of a stable hydrazone derivative.



Scheme 2: Plausible pyranopyrazole cleavage mechanism *via* phenylhydrazine

Conclusion

This study presents a facile and selective hydrazinolysis of pyranopyrazole derivatives using phenylhydrazine under mild conditions. The pyranopyrazole derivatives are highly sensitive under the applied reaction conditions, often leading to ring cleavage and instability during interactions with phenylhydrazines to yield hydrazones. The findings contribute to heterocyclic chemistry by highlighting the role of pyranopyrazole derivatives towards phenylhydrazines, thereby offering valuable insights into eco-friendly synthetic methodologies that support the efficient preparation of hydrazone frameworks with potential biological relevance.

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Authors Contribution Statement

Conceptualization, S.F and Z.N; Methodology, Formal Analysis, Investigation, Writing–Original Draft Preparation, S.F; Writing – Review & Editing, S.F and Z.N; Supervision, Z.N.

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Data availability

The data generated during this study are available from the corresponding author upon reasonable request.

Declarations

Ethical approval and consent to participate Not applicable

Consent for publication Not applicable

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Competing interests

The authors declare no competing interest

ORCID

Saba Farooq http://orcid.org/0000-0002-0159-9540

Zainab Ngaini http://orcid.org/0000-0001-7243-6856

References

1. Faisal M, Saeed A, Hussain S, Dar P, Larik FA (2019) Recent developments in synthetic chemistry and biological activities of pyrazole derivatives. J Chem Sci 131:70. https://doi.org/10.1007/s12039-019-1646-1

2. Farooq S, Ngaini Z (2024) Recent Synthesis of Mono- & Bis-Pyranopyrazole Derivatives. ChemistrySelect 9:e202400028. https://doi.org/10.1002/slct.202400028

3. Chakraborty S, Paul B, De UC, Natarajan R, Majumdar S (2023) Water–SDS–[BMIm]Br composite system for one-pot multicomponent

synthesis of pyrano[2,3- *c*]pyrazole derivatives and their structural assessment by NMR, X-ray, and DFT studies. RSC Adv 13:6747–6759. https://doi.org/10.1039/D3RA00137G

4. D’Souza A, D’Souza AS, Ceyana M, Hani IU, Nikhil CP, Rabiya B (2023) A Novel Synthesis of Some Pyranopyrazoles Derivatives. Journal of Applicable Chemistry 12:138–143

5. Balaskar RS, Gavade SN, Mane MS, Shingate BB, Shingare MS, Mane DV (2010) Greener approach towards the facile synthesis of 1,4-dihydropyrano[2,3-c]pyrazol-5-yl cyanide derivatives at room temperature. Chinese Chemical Letters 21:1175–1179. https://doi.org/10.1016/j.cclet.2010.06.013

6. Tacconi G, Gatti G, Desimoni G, Messori V (1980) A New Route to 4H-Pyrano[2,3-c]pyrazoles. J Prakt Chem 322:831–834. https://doi.org/10.1002/prac.19803220519

7. Dandia A, Bansal S, Sharma R, Parewa V (2018) Water-Triggered Metal-Free Synthesis of Pyranopyrazoles *via* One-Pot Oxidation/Michael Addition/Cyclization/Dehydration Sequence. ChemistrySelect 3:9785–9789. https://doi.org/10.1002/slct.201801691

8. Nawwar GAM, Abdelrazek FM, Swellam RH (1991) Cinnamoylnitrile-, pyran-, and pyranopyrazole-derivatives containing the salicylanilide moiety with anticipated molluscicidal activity. Archiv der Pharmazie 324:875–877. https://doi.org/10.1002/ardp.2503241110

9. El-Sayed MKF, El-Shahawi MM, Ali YM, Abdel-Haleem DR, Abu El-Azm FSM (2023) Synthesis, larvicidal efficiency and molecular docking studies of novel annulated pyrano[2,3-c]pyrazoles against Culex pipiens L. and Musca domestica L. larvae. Bioorganic Chemistry 130:106258. https://doi.org/10.1016/j.bioorg.2022.106258

10. Mhiri C, Boubakri L, Ternane R, Mansour L, Harrath AH, Al-Tamimi J, Baklouti L, Hamdi N (2020) Three-component, one-pot synthesis of pyrano[3,2-c]chromene derivatives catalyzed by ammonium acetate: Synthesis, characterization, cation binding, and biological determination. Journal of Heterocyclic Chem 57:291–298. https://doi.org/10.1002/jhet.3776

11. Bakthadoss M, Surendar M (2020) Cascade annulation reaction (CAR): highly diastereoselective synthesis of pyranopyrazole scaffolds. RSC Adv 10:19003–19007. https://doi.org/10.1039/D0RA03400B

12. Amiri Z, Bayat M (2021) A catalyst-free approach to synthesis of spiroacenaphthylene-pyranopyrazole derivatives in water media. Mol Divers 25:121–129. https://doi.org/10.1007/s11030-019-10030-z

13. Asif M, Aqil F, Alasmary FA, almalki A salem, Khan AR, Nasibullah M (2023) Lewis base-catalyzed synthesis of highly functionalized spirooxindole-pyranopyrazoles and their in vitro anticancer studies. Med Chem Res 32:1001–1015. https://doi.org/10.1007/s00044-023-03053-7

14. Ardiansah B (2019) Current Progress on the Synthesis Methods of Pyranopyrazoles. International Journal of ChemTech Research 12:273–280

15. Sharanina LG, Promonenkov VK, Marshtupa VP, Pashchenko AV, Puzanova VV, Sharanin YuA, Klyuev NA, Gusev LF, Gnatusina AP (1982) 6-Amino-5-cyano-1H,4H-pyrazolo[3,4-b]pyrans. Chem Heterocycl Compd 18:607–611. https://doi.org/10.1007/BF00506154

16. Wang M, Li B, Gong B, Yao H, Lin A (2022) Synthesis of pyranopyrazoles with a chiral quaternary carbon stereocenter *via* copper-catalyzed enantioselective [3 + 3] cycloaddition. Chem Commun 58:2850–2853. https://doi.org/10.1039/D1CC07058D

17. A. Fadda A, A.-H. Abdel-Rahman A, A. Hamed E, H. Khalil E (2012) Utility of Enaminonitriles in Heterocyclic Synthesis: Synthesis and Antimicrobial Activity of Some New Azole and Azine Derivatives. AJOC 2:7–13. https://doi.org/10.5923/j.ajoc.20120202.02

18. Amer MMK, Abdellattif MH, Mouneir SM, Zordok WA, Shehab WS (2021) Synthesis, DFT calculation, pharmacological evaluation, and catalytic application in the synthesis of diverse pyrano[2,3-c]pyrazole derivatives. Bioorganic Chemistry 114:105136. https://doi.org/10.1016/j.bioorg.2021.105136

19. Vala RM, Tandon V, Nicely LG, Guo L, Gu Y, Banerjee S, Patel HM (2022) Synthesis of *N* -(4-chlorophenyl) substituted pyrano[2,3-c]pyrazoles enabling PKBβ/AKT2 inhibitory and *in vitro* anti-glioma

activity. Annals of Medicine 54:2548–2560. https://doi.org/10.1080/07853890.2022.2123559

20. Koohshari M, Dabiri M, Salehi P (2014) Catalyst-free domino reaction in water/ethanol: an efficient, regio- and chemoselective one-pot multi-component synthesis of pyranopyrazole derivatives. RSC Adv 4:10669. https://doi.org/10.1039/c3ra47639a

21. Sajjadi A (2023) A New Simple Methodology for the Synthesis of dihydropyrano[23-c]pyrazoles with Fe3O4@gC3N4 as a Green Catalyst. J Synth Chem 2:. https://doi.org/10.22034/jsc.2023.174302

22. Moosavi-Zare AR, Goudarziafshar H, Ghaffari L (2017) Nano-Mn-[4-nitrophenyl-salicylaldimine-methyl pyranopyrazole]Cl $_2$ as a new nanostructured Schiff base complex and catalyst for the synthesis of hexahydroquinolines. Appl Organometal Chem 31:e3845. https://doi.org/10.1002/aoc.3845

23. Vekariya RH, Patel KD, Patel HD (2016) A green and one-pot synthesis of a library of 1,4-dihydropyrano[2,3-c]-pyrazole-5-carbonitrile derivatives using thiourea dioxide (TUD) as an efficient and reusable organocatalyst. Res Chem Intermed 42:4683–4696. https://doi.org/10.1007/s11164-015-2308-7

24. Vekariya RH, Patel KD, Patel HD (2016) Fruit juice of Citrus limon as a biodegradable and reusable catalyst for facile, eco-friendly and green synthesis of 3,4-disubstituted isoxazol-5(4H)-ones and

dihydropyrano[2,3-c]-pyrazole derivatives. Res Chem Intermed 42:7559–7579. https://doi.org/10.1007/s11164-016-2553-4

25. Godinho M, Salgaonkar LN, Anvekar TS, Vaz T, Kadam HK (2023) NiWO4 catalyzed expeditious synthesis of pyranopyrazoles. IJC 62:196–201. https://doi.org/10.56042/ijc.v62i3.72066

26. Kathrotiya H, Patel R, Patel M (2012) Microwave-assisted multi-component synthesis of 3’-indolyl substituted pyrano[2,3-c]pyrazoles and their antimicrobial activity. J Serb Chem Soc 77:983–991. https://doi.org/10.2298/JSC110805199K

27. Sonar JP, Pardeshi SD, Dokhe SA, Bhavar GM, Tekale SU, Zine M, Thore SN (2019) one pot synthesis of pyranopyrazoles using sodium lactate as an efficient catalyst. Eur Chem Bull 8:207–211

28. Yadav DK, Quraishi MA (2012) Electrochemical investigation of Substituted Pyranopyrazoles Adsorption on Mild Steel in Acid Solution. Ind Eng Chem Res 51:8194–8210. https://doi.org/10.1021/ie3002155

29. Avudaiappan G, Unnimaya T. J, Asha P, Unnikrishnan V, Sreekumar K (2020) Green synthesis of pyrazolopyranopyrimidinone and pyranopyrazole derivatives using porphyrin-initiated amine-functionalized PolyBCMO dendritic polymer as sonocatalyst. Journal of Heterocyclic Chem 57:197–209. https://doi.org/10.1002/jhet.3765

30. Shrivas P, Pandey R, Zodape S, Wankhade A, Pratap U (2020) Green synthesis of pyranopyrazoles via biocatalytic one-pot Knoevenagel condensation–Michael-type addition–heterocyclization cascade in non-aqueous media. Res Chem Intermed 46:2805–2816. https://doi.org/10.1007/s11164-020-04122-x

31. Tahmassebi D, Blevins JE, Gerardot SS (2019) Zn(L-proline) $_2$ as an efficient and reusable catalyst for the multi-component synthesis of pyran-annulated heterocyclic compounds. Applied Organom Chemis 33:e4807. https://doi.org/10.1002/aoc.4807

32. Gadkari YU, Hatvate NT, Telvekar VN (2021) Concentrated solar radiation-assisted one-pot/multicomponent synthesis of pyranopyrazole derivatives under neat condition. Res Chem Intermed 47:4245–4255. https://doi.org/10.1007/s11164-021-04530-7

33. Chavan HV, Babar SB, Hoval RU, Bandgar BP (2011) Rapid One-pot, Four Component Synthesis of Pyranopyrazoles Using Heteropolyacid Under Solvent-free Condition. Bulletin of the Korean Chemical Society 32:3963–3966. https://doi.org/10.5012/BKCS.2011.32.11.3963

34. Theresa LV, Pradeep SD, Sebastian D, Sreekumar K (2021) Sustainable multicomponent one pot synthesis of pyranopyrazole derivatives in the presence of Lactic acid: Urea: NH4Cl. Current Research in Green and Sustainable Chemistry 4:100194. https://doi.org/10.1016/j.crgsc.2021.100194

35. Patil UP, Patil RC, Patil SS (2019) An Eco-friendly Catalytic System for One-pot Multicomponent Synthesis of Diverse and Densely Functionalized Pyranopyrazole and Benzochromene Derivatives. Journal of Heterocyclic Chem 56:1898–1913. https://doi.org/10.1002/jhet.3564

36. Abdolahi S, Hajjami M, Gholamian F (2021) An approach to the synthesis and characterization of HMS/Pr-Rh-Zr as efficient catalyst for synthesis of tetrahydrobenzo[b]pyran and 1,4-dihydropyrano[2,3-c]pyrazole derivatives. Res Chem Intermed 47:1883–1904. https://doi.org/10.1007/s11164-021-04411-z

37. Zhang T, Zhou J, Chen Y, Li Y (2018) Ce(III) immobilized on aminated poly(vinyl chloride): high-performance synergistic bifunctional acid–base catalyst for one-pot synthesis of 1,4-dihydropyrano[2,3-c]pyrazoles. Res Chem Intermed 44:5329–5344. https://doi.org/10.1007/s11164-018-3425-x

38. Maleki B, Eshghi H, Barghamadi M, Nasiri N, Khojastehnezhad A, Sedigh Ashrafi S, Pourshiani O (2016) Silica-coated magnetic NiFe2O4 nanoparticles-supported H3PW12O40; synthesis, preparation, and application as an efficient, magnetic, green catalyst for one-pot synthesis of tetrahydrobenzo[b]pyran and pyrano[2,3-c]pyrazole derivatives. Res Chem Intermed 42:3071–3093. https://doi.org/10.1007/s11164-015-2198-8

39. Maleki B, Nasiri N, Tayebee R, Khojastehnezhad A, Akhlaghi HA (2016) Green synthesis of tetrahydrobenzo[b]pyrans, pyrano[2,3-c]pyrazoles and spiro[indoline-3,4′-pyrano[2,3-c]pyrazoles catalyzed by nano-structured diphosphate in water. RSC Adv 6:79128–79134. https://doi.org/10.1039/C6RA15800E

40. Khademi S, Zahmatkesh S, Aghili A, Badri R (2021) Tungstic acid ($H_4 WO_5$) immobilized on magnetic-based zirconium amino acid metal–organic framework: An efficient heterogeneous Brønsted acid catalyst for l-(4-phenyl)-2,4-dihydropyrano[2,3c]pyrazole derivatives preparation. Applied Organom Chemis 35:e6192. https://doi.org/10.1002/aoc.6192

41. Koolivand M, Nikoorazm M, Ghorbani-Choghamarani A, Mohammadi M (2022) A novel cubic Zn-citric acid-based MOF as a highly efficient and reusable catalyst for the synthesis of pyranopyrazoles and 5-substituted 1H-tetrazoles. Applied Organom Chemis 36:e6656. https://doi.org/10.1002/aoc.6656

42. Heravi MM, Malakooti R, Kafshdarzadeh K, Amiri Z, Zadsirjan V, Atashin H (2022) Supported palladium oxide nanoparticles in Al-SBA-15 as an efficient and reusable catalyst for the synthesis of pyranopyrazole and benzylpyrazolyl coumarin derivatives via multicomponent reactions. Res Chem Intermed 48:203–234. https://doi.org/10.1007/s11164-021-04619-z

43. Shaabani B, Maleki H, Rakhtshah J (2019) Environmentally benign synthesis of pyranopyrazole derivatives by cobalt Schiff-base complexes immobilized on magnetic iron oxide nanoparticles. Journal of Organometallic Chemistry 897:139–147. https://doi.org/10.1016/j.jorganchem.2019.06.030

44. Moosavi-Zare AR, Goudarziafshar H, Saki K (2018) Synthesis of pyranopyrazoles using nano-Fe-[phenylsalicylaldiminemethylpyranopyrazole]Cl_2 as a new Schiff base complex and catalyst. Appl Organometal Chem 32:e3968. https://doi.org/10.1002/aoc.3968

45. Basappa B, Poonacha LK, Xi Z, Vishwanath D, Yang J-R, Nagaraja O, Swamynayaka A, Madegowda M, Chinnathambi A, Alharbi SA, Gurudatt DM, Pandey V, Shivananju N, Ahn KS, Sethi G, Lobie PE, Shubha PB (2023) Nano-Zirconium Dioxide Catalyzed Multicomponent Synthesis of Bioactive Pyranopyrazoles That Target Cyclin Dependent Kinase 1 in Human Breast Cancer Cells. Biomedicines 11:172. https://doi.org/10.3390/biomedicines11010172

46. Sangeeta, Singh HL, Chahar M, Sahal S, Khaturia S (2022) greener synthesis of pyranopyrazole derivatives catalyzed by CaO nanoparticles. RJC 15:326–333. https://doi.org/10.31788/RJC.2022.1516823

47. Beiranvand M, Habibi D (2022) Design, preparation and application of the semicarbazide-pyridoyl-sulfonic acid-based nanocatalyst for the

synthesis of pyranopyrazoles. Sci Rep 12:14347. https://doi.org/10.1038/s41598-022-18651-5

48. Kamalzare M, Ahghari MR, Bayat M, Maleki A (2021) Fe3O4@chitosan-tannic acid bionanocomposite as a novel nanocatalyst for the synthesis of pyranopyrazoles. Sci Rep 11:20021. https://doi.org/10.1038/s41598-021-99121-2

49. Hassanzadeh-Afruzi F, Dogari H, Esmailzadeh F, Maleki A (2021) Magnetized melamine-modified polyacrylonitrile (PAN@melamine/Fe $_3$ O $_4$) organometallic nanomaterial: Preparation, characterization, and application as a multifunctional catalyst in the synthesis of bioactive dihydropyrano [2,3-c]pyrazole and 2-amino-3-cyano 4H-pyran derivatives. Applied Organom Chemis 35:e6363. https://doi.org/10.1002/aoc.6363

50. Kikhavani T, Moradi P, Mashari-Karir M, Naji J (2022) A new copper Schiff-base complex of 3,4-diaminobenzophenone stabilized on magnetic MCM-41 as a homoselective and reusable catalyst in the synthesis of tetrazoles and pyranopyrazoles. Applied Organom Chemis 36:e6895. https://doi.org/10.1002/aoc.6895

51. Omidi M, Mobinikhaledi A (2022) Sulfonic acid pyridinium chloride-functionalized nanoparticles (MnCoFe2O4@Niacin-SO3H)+Cl− as a novel and reusable catalyst for synthesis of tetrahydrodipyrazolopyridines and pyranopyrazoles. Res Chem Intermed 48:4347–4371. https://doi.org/10.1007/s11164-022-04800-y

52. Shaterian HR, Sedghipour M, Mollashahi E (2014) [DBU][Ac]-catalyzed mild preparation of 6-amino-4-aryl-5-cyano-3-methyl-1,4-dihydropyrano[2,3-c]pyrazole derivatives. Res Chem Intermed 40:2721–2728. https://doi.org/10.1007/s11164-013-1124-1

53. Shaterian HR, Kangani M (2014) Synthesis of 6-amino-4-aryl-3-methyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitriles by heterogeneous reusable catalysts. Res Chem Intermed 40:1997–2005. https://doi.org/10.1007/s11164-013-1097-0

54. Murahari M, Mahajan V, Neeladri S, Kumar MS, Mayur YC (2019) Ligand based design and synthesis of pyrazole based derivatives as selective COX-2 inhibitors. Bioorganic Chemistry 86:583–597. https://doi.org/10.1016/j.bioorg.2019.02.031

55. El-Arab EE (2015) Synthesis and Cytotoxicity of Novel Pyrazole Derivatives Derived from 3-Methyl-1-phenyl-1Hpyrazol-5(4H)-one. Egypt J Chem 58:741–753. https://doi.org/10.21608/ejchem.2015.1017

56. Aziz SI, Riad BY, Elfabham HA, Elnagdi MH (1982) Activated nitriles in herocyclic synthesis: a novel synthesis of fyrazolo [5,6: 3,4] pyrano[5,4-b]isoxazoles. Heterocycles 19:2251–2254

57. Vasuki G, Kumaravel K (2008) Rapid four-component reactions in water: synthesis of pyranopyrazoles. Tetrahedron Letters 49:5636–5638. https://doi.org/10.1016/j.tetlet.2008.07.055

58. Akbarpour T, Yousefi Seyf J, Khazaei A, Sarmasti N (2022) Synthesis of Pyrano [2,3-c] Pyrazole Derivatives Using a Novel Ionic-Liquid Based Nano-Magnetic Catalyst (Fe_3O_4 @SiO_2@$(CH_2)_3$ NH@CC@Imidazole@$SO_3H^+Cl^-$). Polycyclic Aromatic Compounds 42:3844–3864. https://doi.org/10.1080/10406638.2021.1873152

59. Liu P, Pan Y-M, Xu Y-L, Wang H-S (2012) PTSA-catalyzed Mannich-type–cyclization–oxidation tandem reactions: one-pot synthesis of 1,3,5-substituted pyrazoles from aldehydes, hydrazines and alkynes. Org Biomol Chem 10:4696–4698. https://doi.org/10.1039/C2OB25487E

60. Ding Y, Li H, Meng Y, Zhang T, Li J, Chen Q-Y, Zhu C (2017) Direct synthesis of hydrazones by visible light mediated aerobic oxidative cleavage of the CC bond. Org Chem Front 4:1611–1614. https://doi.org/10.1039/C7QO00276A

61. Wang Q, Liu L, Lin C, Sun H, Zhang W-X, Xi Z (2009) Hydride-induced cleavage of C–O bond in pyran ring of 2-pyranylidene carbene complexes: mechanism and synthetic application. Dalton Trans 10433–10435. https://doi.org/10.1039/B918679B

62. Elnagdi MH, Moustafa MS, Al-Mousawi SM, Mekheimer RA, Sadek KU (2015) Recent developments in utility of green multi-component reactions for the efficient synthesis of polysubstituted pyrans, thiopyrans, pyridines, and pyrazoles. Mol Divers 19:625–651. https://doi.org/10.1007/s11030-015-9594-2

63. Bou-Petit E, Picas E, Puigjaner C, Font-Bardia M, Ferrer N, Sempere J, Puig de la Bellacasa R, Batllori X, Teixidó J, Estrada-Tejedor R, Ramon y Cajal S, Borrell JI (2017) An Unequivocal Synthesis of 2-Aryl Substituted 3-Amino-2,4,5,7-tetrahydro-6 *H* -pyrazolo[3,4- *b*]pyridin-6-ones. ChemistrySelect 2:3668–3672. https://doi.org/10.1002/slct.201700732

64. Phukan K, Borphukan P, Tripathy PK (2023) A Facile Synthesis of 4-Anilinomethylene-2- Phenyl-2-Oxazolin-5-one and its 1, 5-Bond Cleavage Products. INTERNATIONAL ADVANCED RESEARCH JOURNAL IN SCIENCE, ENGINEERING AND TECHNOLOGY 10:. https://doi.org/10.17148/IARJSET.2023.10562

65. Said MA, Eldehna WM, Ghabbour HA, Kabil MM, Al-shakliah NS, Abdel-Aziz HA (2018) Solvent-Free Ring Cleavage Hydrazinolysis of Certain Biginelli Pyrimidines. Journal of Chemistry 2018:1–6. https://doi.org/10.1155/2018/6354742

66. Salem M, Ayyad R, Sakr H, Gaafer A (2022) Design and Synthesis of New Compounds Derived from Phenyl Hydrazine and Different Aldehydes as Anticancer Agents. austinjanalpharmchem 9:1141

67. Rodrigues-Santos CE, Echevarria A (2011) Convenient syntheses of pyrazolo[3,4-b]pyridin-6-ones using either microwave or ultrasound irradiation. Tetrahedron Letters 52:336–340. https://doi.org/10.1016/j.tetlet.2010.11.054

68. Troudt BK, Vue JW, Bühlmann P (2022) Comparison of the kinetics of aldehyde sensing by covalent bond formation with hydrazines and hydroxylamines. Tetrahedron 119:132852. https://doi.org/10.1016/j.tet.2022.132852