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Arylhydrazonals as the aldehyde component in Baylis–Hillman reactions

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ABSTRACT

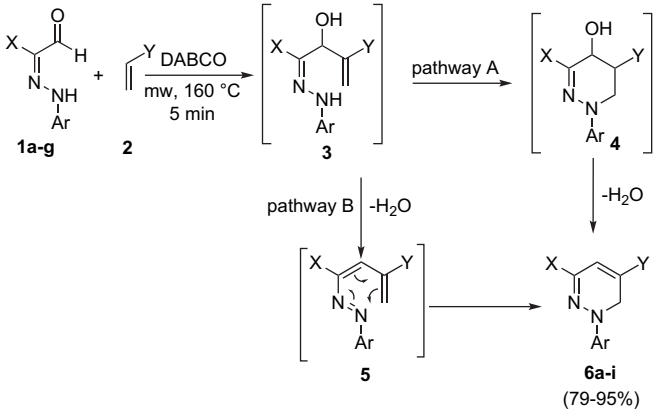
Arylhydrazonals were added to acrylonitrile or methyl vinyl ketone in the presence of DABCO or benzotriazole to yield the intermediate Baylis–Hillman adduct that cyclized under the reaction conditions with water elimination to yield dihydropyridazines. A pyridazine reacted with DMAD to yield a pyridine via a [4+2] Diels–Alder addition followed by retro Diels–Alder elimination of methylene aniline. Two pyridazines were condensed with DMFDMA to yield the corresponding enaminones that reacted with NH_2NH_2 to afford the pyrazolylpyridazines.

1. Introduction

Arylhydrazonals **1** are readily obtained versatile reagents[1–8] with an electrophilic carbonyl carbon and a nucleophilic hydrazone nitrogen suitably located to enable their utility as a four-atom component for the synthesis of five- and six-membered ring systems. We have already shown that they are valuable precursors to pyrazoles, pyridazines, and cinolines.[4–8] We now report on the reactivity of **1** as aldehyde components in Baylis–Hillman reactions[9–11] that lead to the synthesis of 1,6-dihydropyridazines, new azadienes with a unique substitution pattern.

2. Results and discussion

Heating the arylhydrazonals **1a–g** with acrylonitrile or methyl vinyl ketone in the presence of 1,4-diazabicyclo[2.2.2]octane (DABCO) utilizing microwaves as the energy source for 5 min in the absence of solvent resulted in the formation of condensation products via water elimination (Scheme 1). ^{13}C NMR spectroscopy indicated the presence, in each case, of a sp^3 carbon at δ 44 ppm in addition to a cyano or carbonyl carbon as expected for structure **6**. Compounds **6a–i** were assumed to result from cyclization and dehydration of the initially formed Baylis–Hillman adduct **3**. One would assume ready conversion of **3** to **4**, which then undergo either E1 or E2 water elimination to yield the final isolable pyridazines (pathway A). Alternatively, dehydration of the adduct via a six-membered transition state, similar to those commonly encountered in our pyrolytic reactions,[12,13] to yield the azadiene **5** that then would undergo 6π electrocyclization to yield the pyridazine **6** (pathway **B**) cannot, however, be overlooked. A third



Compd.		X	Ar	Y	6 (%yield)
1,6	a	COC_6H_5	C_6H_5	CN	85
	b	$COC_6H_4Cl(p)$	C_6H_5	CN	90
	c	CO_2Et	$C_6H_4Cl(p)$	CN	79
	d	thiophene-2-yl-methanone	C_6H_5	CN	88
	e	furane-2-yl-methanone	C_6H_5	CN	86
	f	COC_6H_5	$C_6H_4CH_3(p)$	CN	83
	g	COC_6H_5	$C_6H_4Cl(p)$	$COCH_3$	88
	h	COC_6H_5	C_6H_5	$COCH_3$	92
	i	furane-2-yl-methanone	C_6H_5	$COCH_3$	95

Scheme 1.

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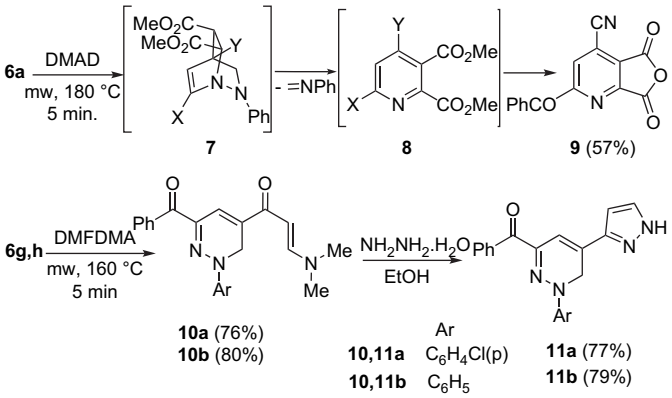
possibility is initial cyanoethylation of the arylhydrazone nitrogen and subsequent cyclization. To decide upon the most feasible mechanism, the arylhydrazonal **1a** was reacted with acrylonitrile in THF, $NaHCO_3$, and benzotriazole at room temperature. After two days, a 1:1 adduct was isolated, although contaminated with some condensation product. ^1H NMR spectroscopy as well as ^{13}C NMR spectroscopy of this adduct indicated that it is **4a** formed via addition of the arylhydrazone NH to the methylene moiety in **3**. Attempts to isolate **4** in pure form failed, which suggests that the conversion of **3** into **4** proceeds either by pathway A or by cyanoethylation. Moreover, the cyanoethylation possibility was excluded as arylhydrazones did not undergo cyanoethylation under the reaction condition. We thus believe that the reaction proceeds via pathway A. In a similar way arylhydrazonals **1a**,**e**,**g** reacted with methyl vinyl ketone to yield the corresponding dihydropyridazine derivatives **6h**,**i**,**g**.

Compound **6a** reacted with dimethyl acetylenedicarboxylate (DMAD) under microwave conditions at 180 °C for 5 min to yield the pyridine **9** formed most likely via intermediate cycloadduct **7**. This then undergoes retroaddition via loss of methylene aniline to yield **8** that is converted under the reaction conditions to **9**. Also, compounds **6g**,**h** reacted with dimethylformamide dimethylacetal (DMFDMA) in the microwave at 160 °C for 5 min to yield the enaminones **10a**,**b** that can be readily used for the synthesis of azoles and azines.[14,15] For example, reacting pyridazine derivatives **10a**,**b** with hydrazine hydrate afforded the corresponding pyrazolopyridazines **11a**,**b** (Scheme 2).



Scheme 2.

3. Conclusion

The present study offers an interesting new simple and efficient route to dihydropyridazines via the first reported Baylis–Hillman reaction of arylhydrazonals with electron-poor olefins. Moreover, the formed pyridazines proved active azadienes.

4. Experimental

4.1. General

IR spectra were recorded in KBr disks on a Perkin–Elmer System 2000 FT-IR spectrophotometer. ^1H and ^{13}C NMR spectra were recorded on a Bruker DPX 400, 400 MHz super-conducting NMR spectrometer. Mass spectra were measured on VG Autospec-Q (high resolution, high performance, tri-sector GC/MS/MS). Microanalyses were performed on LECO CH NS-932 Elemental Analyzer. Separation of reaction products was performed using silica gel column chromatography using ethyl acetate/pet. ether (60–80) as an eluent. The starting arylhydrazonals **1a–g** were prepared and characterized by mp and ^1H NMR spectroscopy as reported.[4]

4.2. Preparation of starting compounds 1a–g

General procedure. A cooled solution (0–5 °C) of the diazonium salt (10 mmol) [prepared by adding a cooled solution of sodium nitrite (0.7 g) in water (5 mL) to a solution of the appropriate arylamine (10 mmol) in concd HCl (5 mL)] was added to a cooled solution (0–5 °C) of the appropriate enaminones in ethanol (50 mL) containing NaOH (1.6 g). The mixture was then stirred at room temperature for 1 h, and the solid precipitated was collected and crystallized from ethanol to give **1a–g**.

*4.2.1. 3-Oxo-3-phenyl-2-phenylhydrazonopropanal **1a***
Red crystals from ethanol, mp 82–83 °C (lit.[4] mp 82–84 °C).

*4.2.2. 3-Oxo-3-(p-chlorophenyl)-2-phenylhydrazonopropanal **1b***
Red crystals from ethanol, mp 135–36 °C (lit.[4] mp 135–37 °C).

*4.2.3. 3-Ethoxy-3-oxo-2-p-chlorophenylhydrazonopropanal **1c***
Red crystals from ethanol, mp 82–83 °C (lit.[16] mp 86–88 °C).

*4.2.4. 3-Oxo-2-phenylhydrazono-3-(2-thienyl)propanal **1d***
Yellow crystals from ethanol, mp 113–114 °C (lit.[4] mp 114–115 °C).

*4.2.5. 3-(2-Furyl)-3-oxo-2-phenylhydrazonopropanal **1e***
Red crystals from ethanol, mp 114–15 °C (lit.[4] mp 114–16 °C).

*4.2.6. 3-Oxo-3-phenyl-2-p-tolylhydrazonopropanal **1f***
Red crystals from ethanol, mp 116–118 °C (lit.[17] mp 115–17 °C).

*4.2.7. 2-p-Chlorophenylhydrazono-3-oxo-3-phenylpropinaldehyde **1g***
Red crystals from ethanol, mp 143–145 °C. MS: m/z=286 (M^+, 35%), 250 (15%), 132 (75%), 105 (100%). IR: 3166, 3084, 1653, 1643, 1489, 1312, 1293, 1267, 1091, 957, 890, 822, 712. ^1H NMR ($CDCl_3$) δ 14.85 (s, 1H, NH), 10.25 (s, 1H), 7.97 (d, 2H, J=7.8 Hz), 7.58 (t, 1H, J=7.6 Hz), 7.54 (t, 2H, J=7.6 Hz), 7.38–7.26 (m, 4H). ^{13}C NMR ($CDCl_3$): δ 191.2 (CO), 189.8 (CO), 139.8 (C), 136.9 (C), 132.5 (C), 132.4 (CH), 131.7 (C), 130.4 (2CH), 129.9 (2CH), 128.0 (2CH), 117.7 (2CH). Anal. Calcd for $C_{15}H_{11}ClN_2O_2$ (286.7): C, 62.84; H, 3.87; N, 9.77. Found: C, 62.79; H, 3.69; N, 9.75.

4.3. Preparation of 6-aroylpyridazine 6a–i

Method A. A mixture of the corresponding arylhydrazonal derivatives **1a–g** (1 mmol), acrylonitrile or methyl vinyl ketone (2 mmol) and DABCO (0.112 g, 1 mmol) was mixed and placed in a single mode cavity Explorer Microwave Synthesizer (CEM Corporation, NC, USA) and irradiated at temperature 160 °C for 5 min. The reaction product was extracted with ethyl acetate (50 mL), the solvent was removed in vacuo, and purified with silica gel flash column chromatography using ethyl acetate/pet. ether (60–80) as an eluent to give **6a-i**, which was recrystallized from ethanol.

Method B. To a stirred mixture of arylhydrazonal **1a** (0.5 mmol) and benzotriazole (0.5 mmol) in 1 M $NaHCO_3$ (2 mL) and THF (0.5 mL) was added acrylonitrile (0.75 mmol). The mixture was stirred at ambient temperature and monitored by TLC. Upon completion or after the indicated reaction time, the mixture was quenched with 1 N HCl (3 mL) and extracted with ethyl acetate (50 mL). The organic layer was dried over anhydrous Na_2SO_4 and the solvent was removed in vacuo. The residue was purified with column chromatography using EtOAc/ pet. ether as an eluent.

4.3.1. 6-Benzoyl-2-phenyl-2,3-dihydropyridazin-4-carbonitrile ***6a***

Yellow crystals from ethanol, yield (0.25 g) 85%, mp 142–43 °C. MS: *m*/*z*=287 (M^+, 80%), 149 (70%), 105 (100%). IR: 3433, 3081, 2221, 1619, 1595, 1514, 1498, 1380, 1319, 1219, 1178, 921, 723. ^{1}H NMR ($CDCl_3$): δ 7.98 (d, 2H, *J*=7.6 Hz), 7.59 (t, 1H, *J*=7.2 Hz), 7.51 (t, 2H, *J*=7.8 Hz), 7.44 (t, 2H, *J*=7.8 Hz), 7.32 (s, 1H), 7.28 (m, 3H), 4.71 (s, 2H). ^{13}C NMR ($CDCl_3$): δ 188.0 (CO), 144.0 (C), 136.8 (C), 136.5 (C), 132.3 (CH), 130.4 (2CH), 129.5 (2CH), 128.4 (CH), 128.0 (2CH), 125.4 (CH), 116.4 (2CH), 116.3 (C), 101.2 (CN), 44.3 (CH_2). Anal. Calcd for $C_{18}H_{13}N_3O$ (287.3): C, 75.25; H, 4.56; N, 14.62. Found: C, 75.15; H, 4.67; N, 14.70.

4.3.2. 6-p-Chlorobenzoyl-2-phenyl-2,3-dihydropyridazine-4-carbonitrile ***6b***

Yellow crystals from ethanol, yield (0.29 g) 90%, mp 214–216 °C. MS: *m*/*z*=321 (M^+, 90%), 139 (100%), 111 (50%). IR: 3432, 3084, 2215, 1642, 1630, 1589, 1518, 1379, 1262, 959, 922, 828, 748, 683. ^{1}H NMR (DMSO-d_6): δ 7.91 (d, 2H, *J*=8.4 Hz), 7.60 (d, 2H, *J*=8.4 Hz), 7.44 (t, 2H, *J*=7.8 Hz), 7.42 (s, 1H), 7.39 (d, 2H, *J*=7.8 Hz), 7.28 (t, 1H, *J*=7.6 Hz), 4.84 (s, 2H). ^{13}C NMR (DMSO-d_6): δ 191.7 (CO), 149.0 (C), 142.2 (C), 141.4 (C), 140.6 (C), 137.0 (2CH), 134.6 (2CH), 133.4 (2CH), 132.6 (CH), 130.3 (CH), 122.0 (2CH), 121.9 (C), 107.5 (CN), 49.1 (CH_2). Anal. Calcd for $C_{18}H_{12}ClN_3O$ (321.8): C, 67.19; H, 3.72; N, 13.06. Found: C, 67.10; H, 3.55; N, 13.10.

4.3.3. 1-p-Chlorophenyl-5-cyano-1,6-dihydropyridazin-3-carboxylic acid ethyl ester ***6c***

Orange crystals from ethanol, yield (0.23 g) 79%, mp 155–56 °C. MS: *m*/*z*=289 (M^+, 90%), 260 (20%), 111 (100%). IR: 3428, 3080, 2981, 2215, 1701, 1516, 1493, 1416, 1325, 1210, 1176, 1092, 921, 820. ^{1}H NMR (DMSO-d_6): δ 7.52 (d, 2H, *J*=8.8 Hz), 7.45 (d, 2H, *J*=8.8 Hz), 7.25 (s, 1H), 4.72 (s, 2H), 4.25 (q, 2H, *J*=7.2 Hz), 1.28 (t, 3H, *J*=7.2 Hz). ^{13}C NMR (DMSO-d_6): δ 161.9 (CO), 142.7 (C), 130.5 (C), 129.1 (2CH), 128.8 (C), 128.0 (CH), 118.2 (2CH), 116.6 (C), 101.3 (CN), 60.8 (CH_2), 43.3 (CH_2), 14.1 (CH_3). Anal. Calcd for $C_{14}H_{12}ClN_3O_2$ (289.7): C, 58.04; H, 4.17; N, 14.50. Found: C, 57.90; H, 4.20; N, 14.30.

4.3.4. 2-Phenyl-6-(thiophene-2-carbonyl)-2,3-dihydropyridazine-4-carbonitrile ***6d***

Yellow crystals from ethanol, yield (0.26 g) 88%, mp 156–58 °C. MS: *m*/*z*=293 (M^+, 80%), 174 (10%), 111 (100%). IR: 3421, 3079, 2217, 1614, 1512, 1499, 1413, 1387, 1345, 1262, 1160, 1045, 921, 744. ^{1}H NMR (DMSO-d_6): δ 8.08 (m, 2H), 7.57–7.52 (m, 4H), 7.43 (s, 1H), 7.27 (m, 2H), 4.86 (s, 2H). ^{13}C NMR (DMSO-d_6): δ 178.0 (CO), 144.3 (C), 138.7 (C), 137.2 (C), 136.5 (CH), 135.3 (CH), 129.9 (2CH), 128.3 (CH), 127.5 (CH), 125.7 (CH), 117.9 (2CH), 117.2 (C), 102.6 (CN), 44.6 (CH_2). Anal. Calcd for $C_{16}H_{11}N_3OS$ (293.4): C, 65.51; H, 3.78; N, 14.32; S, 10.95. Found: C, 65.40; H, 3.89; N, 14.25; S, 10.79.

4.3.5. 6-(Furan-2-carbonyl)-2-phenyl-2,3-dihydropyridazine-4-carbonitrile ***6e***

Orange crystals from ethanol, yield (0.24 g) 86%, mp 145–46 °C. MS: *m*/*z*=277 (M^+, 90%), 158 (10%), 95 (100%). IR: 3430, 3130, 3110, 2213, 1626, 1498, 1459, 1394, 1279, 1196, 1112, 1015, 925, 820, 750. ^{1}H NMR ($CDCl_3$): δ 7.74 (d, 1H, *J*=3.8 Hz), 7.56 (d, 1H, *J*=3.6 Hz), 7.52 (m, 3H), 7.40 (d, 2H, *J*=7.8 Hz), 7.32 (t, 1H, *J*=7.4 Hz), 6.59 (dd, 1H, *J*=3.2, 1.6 Hz), 4.70 (s, 2H). ^{13}C NMR ($CDCl_3$): δ 174.0 (CO), 150.1 (C), 147.2 (CH), 144.1 (C), 137.4 (C), 129.7 (2CH), 127.7 (CH), 125.7 (CH), 121.6 (CH), 117.0 (2CH), 116.3 (C), 112.3 (CH), 100.3 (CN), 44.5 (CH_2). Anal. Calcd for $C_{16}H_{11}N_3O_2$ (277.3): C, 69.31; H, 4.00; N, 15.15. Found: C, 69.19; H, 3.99; N, 15.11.

4.3.6. 6-Benzoyl-2-p-tolyl-2,3-dihydropyridazine-4-carbonitrile ***6f***

Yellow crystals from ethanol, yield (0.25 g) 83%, mp 173–75 °C. MS: *m*/*z*=301 (M^+, 40%), 215 (30%), 185 (35%), 85 (100%). IR: 3426, 3090, 2217, 1620, 1505, 1378, 1352, 1263, 1220, 1177, 1040, 922, 810, 722. ^{1}H NMR ($CDCl_3$): δ 7.98 (d, 2H, *J*=7.6 Hz), 7.58 (t, 1H, *J*=7.6 Hz), 7.52 (s, 1H), 7.48 (t, 2H, *J*=7.8 Hz), 7.28–7.18 (m, 4H), 4.69 (s, 2H), 2.38 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 187.9 (CO), 141.8 (C), 136.7 (C), 136.5 (C), 135.5 (C), 132.2 (CH), 130.4 (2CH), 130.1 (2CH), 128.4 (CH), 127.9 (2CH), 116.5 (C), 116.4 (2CH), 100.3 (CN), 44.5 (CH_2), 21.0 (CH_3). Anal. Calcd for $C_{19}H_{15}N_3O$ (301.3): C, 75.73; H, 5.02; N, 13.94. Found: C, 75.66; H, 5.06; N, 14.00.

4.3.7. 1-[6-Benzoyl-2-p-chlorophenyl-2,3-dihydropyridazin-4-yl]ethanone ***6g***

Orange crystals from ethanol, yield (0.3 g) 88%, mp 185–87 °C. MS: *m*/*z*=338 (M^+, 75%), 296 (25%), 105 (100%). IR: 3435, 3068, 2919, 1657, 1626, 1490, 1337, 1253, 1211, 1095, 919, 823, 721. ^{1}H NMR ($CDCl_3$): δ 7.98 (dd, 2H, *J*=8.0, 1.4 Hz), 7.68 (s, 1H), 7.60 (dt, 1H, *J*=8.0, 1.2 Hz), 7.50 (t, 2H, *J*=7.8 Hz), 7.37 (dd, 2H, *J*=7.8, 1.2 Hz), 7.30 (dd, 2H, *J*=8.0, 1.2 Hz), 4.68 (s, 2H), 2.54 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 196.7 (CO), 189.1 (CO), 143.2 (C), 137.1 (C), 136.8 (C), 132.2 (CH), 130.3 (2CH), 130.2 (C), 129.4 (2CH), 128.0 (2CH), 123.1 (CH), 117.4 (2CH), 117.3 (C), 43.6 (CH_2), 25.1 (CH_3). Anal. Calcd for $C_{19}H_{15}ClN_2O_2$ (338.8): C, 67.36; H, 4.46; N, 8.27. Found: C, 67.32; H, 4.39; N, 8.25.

4.3.8. 1-[6-Benzoyl-2-phenyl-2,3-dihydropyridazine-4-yl]-ethanone ***6h***

Orange crystals from ethanol, yield (0.28 g) 92%, mp 160–62 °C. MS: *m*/*z*=304 (M^+ 50%), 262 (15%), 105 (100%). IR: 3435, 3059, 1654, 1627, 1503, 1487, 1373, 1243, 1213, 1031, 921, 715. ^{1}H NMR ($CDCl_3$): δ 8.01 (d, 2H, *J*=8.0 Hz), 7.70 (s, 1H), 7.59 (t, 1H, *J*=7.8 Hz), 7.50 (t, 2H, *J*=7.6 Hz), 7.42 (m, 4H), 7.22 (m, 1H), 4.73 (s, 2H), 2.54 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 196.7 (CO), 189.1 (CO), 144.6 (C), 137.2 (C), 136.6 (C), 132.0 (CH), 130.4 (2CH), 129.4 (2CH), 127.8 (2CH), 127.5 (C), 124.9 (CH), 123.3 (CH), 116.4 (2CH), 43.6 (CH_2), 25.2 (CH_3). Anal. Calcd for $C_{19}H_{16}N_2O_2$ (304.3): C, 74.98; H, 5.30; N, 9.20. Found: C, 74.97; H, 5.29; N, 9.33.

4.3.9. 1-[6-(Furan-2-carbonyl)-2-phenyl-2,3-dihydropyridazin-4-yl]ethanone ***6i***

Orange crystals from ethanol, yield (0.28 g) 95%, mp 190–92 °C. MS: *m*/*z*=294 (M^+, 70%), 252 (15%), 95 (100%). IR: 3433, 2918, 1653, 1627, 1503, 1488, 1373, 1243, 1213, 1031, 921, 715. ^{1}H NMR ($CDCl_3$): δ 7.74 (d, 1H, *J*=8.0 Hz), 7.66 (s, 1H), 7.60 (dd, 1H, *J*=7.6, 1.2 Hz), 7.50 (m, 4H), 7.27 (t, 1H, *J*=7.8 Hz), 6.60 (dd, 1H, *J*=3.2, 1.2 Hz), 4.73 (s, 2H), 2.52 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 196.6 (CO), 175.0 (CO), 150.5 (C), 146.9 (CH), 144.8 (C), 137.3 (C), 129.5 (2CH), 126.8 (C), 125.2 (CH), 122.6 (CH), 121.4 (CH), 117.0 (2CH), 112.2 (CH), 43.6 (CH_2), 25.2 (CH_3). Anal. Calcd for $C_{17}H_{14}N_2O_3$ (294.3): C, 69.38; H, 4.79; N, 9.52. Found: C, 69.32; H, 4.79; N, 9.55.

4.4. Reaction of compound 6a with dimethyl acetylenedicarboxylate (DMAD)

A mixture of compounds **6a** (1 mmol) and DMAD (2 mmol) was mixed and placed in a microwave oven and irradiated at temperature 180 °C for 5 min. The reaction product were extracted with ethyl acetate and purified with column chromatography using ethyl acetate/pet. ether as an eluent to give **9**.

4.4.1. 2-Benzoyl-4-cyano-furo[3,4-b]pyridine-5,7-dione ***9***

Yellow crystals from ethanol, yield (0.16 g) 57%, mp 188–90 °C. MS: *m*/*z*=278 (M^+, 100%), 167 (60%), 149 (100%). IR: 3423, 3111, 2959, 2213, 1728, 1626, 1499, 1459, 1394, 1279, 1197, 1114, 1015, 925, 821, 749. ^{1}H NMR ($CDCl_3$): δ 8.92 (s, 1H), 7.72 (d, 2H, *J*=7.8 Hz), 7.66 (t, 1H, *J*=7.6 Hz), 7.52 (t, 2H, *J*=7.6 Hz). ^{13}C NMR ($CDCl_3$): δ 189.7 (CO), 165.5 (CO), 164.4 (CO), 153.7 (C), 145.9 (C), 137.7 (C), 137.5 (C), 131.6 (CH), 130.4 (CH), 129.2 (2CH), 127.8 (2CH), 124.1 (C), 116.2 (CN). Anal. Calcd for $C_{15}H_6N_2O_4$ (278.2): C, 64.76; H, 2.17; N, 10.07. Found: C, 64.65; H, 2.09; N, 10.05.

4.5. Reaction of compounds 6g,h with *N,N*-dimethylformamide dimethylacetal (DMFDMA)

A mixture of each of compounds **6g**,**h** (1 mmol) and DMFDMA (2 mmol) was mixed and placed in a microwave oven and irradiated at temperature 160 °C for 5 min. The reaction product were extracted with ethyl acetate and purified with column chromatography using ethyl acetate/pet. ether as an eluent to give **10a**,**b**.

4.5.1. 1-(6-Benzoyl-2-p-chlorophenyl-2,3-dihydropyridazin-4-yl)-3-dimethylamino-propenone ***10a***

Orange crystals from ethanol, yield (0.30 g) 76%, mp 208–210 °C. MS: m/z=393 (M^+, 60%), 254 (20%), 98 (100%). IR: 3432, 3054, 1630, 1526, 1491, 1325, 1266, 1208, 1153, 1094, 915, 725. ^{1}H NMR ($CDCl_3$): δ 7.98 (d, 2H, J=8.0 Hz), 7.76 (d, 1H, J=12.0 Hz), 7.58 (t, 1H, J=7.8 Hz), 7.49 (m, 3H), 7.40 (m, 4H), 5.73 (d, 1H, J=12.0 Hz), 4.77 (s, 2H), 3.19, 2.98 (2s, $2CH_3$). ^{13}C NMR ($CDCl_3$): δ 189.7 (CO), 185.3 (CO), 153.8 (C), 143.7 (C), 137.9 (C), 137.6 (C), 131.8 (CH), 130.4 (C), 130.3 (2CH), 129.4 (CH), 129.2 (2CH), 127.8 (2CH), 117.2 (2CH), 117.1 (CH), 90.6 (CH), 44.5 (CH_2), 37.3 ($2CH_3$). Anal. Calcd for $C_{22}H_{20}ClN_3O_2$ (393.8): C, 67.09; H, 5.12; N, 10.67. Found: C, 67.00; H, 5.08; N, 10.69.

4.5.2. 1-(6-Benzoyl-2-phenyl-2,3-dihydropyridazin-4-yl)-3-dimethylamino-propenone ***10b***

Orange crystals from ethanol, yield (0.29 g) 80%, mp 192–94 °C. MS: m/z=359 (M^+, 30%), 254 (20%), 98 (100%). IR: 3431, 3059, 1632, 1554, 1439, 1371, 1320, 1234, 1180, 1115, 925, 754. ^{1}H NMR ($CDCl_3$): δ 8.0 (dd, 2H, J=8.0, 1.6 Hz), 7.77 (d, 1H, J=12.0 Hz), 7.57 (t, 1H, J=7.8 Hz), 7.49 (m, 3H), 7.40 (m, 4H), 7.18 (m, 1H), 5.73 (d, 1H, J=12.0 Hz), 4.82 (s, 2H), 3.19, 2.97 (2s, $2CH_3$). ^{13}C NMR ($CDCl_3$): δ 189.7 (CO), 185.5 (CO), 153.7 (C), 145.0 (C), 137.7 (C), 137.5 (C), 131.6 (CH), 131.1 (CH), 130.4 (2CH), 129.2 (2CH), 127.8 (2CH), 124.1 (CH), 117.4 (CH), 116.2 (2CH), 90.6 (CH), 44.5 (CH_2), 37.5 ($2CH_3$). Anal. Calcd for $C_{22}H_{21}N_3O_2$ (359.4): C, 73.52; H, 5.89; N, 11.69. Found: C, 73.49; H, 5.83; N, 11.67.

4.6. Reaction of compounds 10a,b with NH_2NH_2

A mixture of each of compounds **10a**,**b** (1 mmol) and hydrazine hydrate (2 mmol) in ethanol (50 mL) was refluxed for 4 h. The solvent was then removed in vacuo, cooled water (10 mL) was added to the reaction mixture, filtered and crystallized from ethanol to give **11a**,**b**.

4.6.1. 1-[p-Chlorophenyl-5-(1H-pyrazol-3-yl)-1,6-dihydropyridazin-3-yl]phenylmethanone ***11a***

Yellow crystals from ethanol, yield (0.28 g) 77%, mp 186–188 °C. MS: m/z=362 (M^+, 70%), 257 (40%), 105 (100%). IR: 3434, 3260, 3054, 1630, 1595, 1526, 1491, 1325, 1267, 1208, 1177, 1155, 914, 725. ^{1}H NMR ($CDCl_3$): δ 8.03 (dd, 2H, J=7.8, 1.4 Hz), 7.67 (dd, 1H, J=7.4, 1.2 Hz), 7.58 (t, 1H, J=7.6 Hz), 7.47 (t, 2H, J=7.6 Hz), 7.42–7.38 (m, 6H), 6.82 (dd, 1H, J=7.4, 1.2 Hz), 4.94 (s, 2H). ^{13}C NMR ($CDCl_3$): δ 190.0 (CO), 156.9 (C), 149.6 (C), 144.3 (C), 137.9 (C), 137.6 (C), 131.5 (CH), 130.5 (2CH), 129.2 (2CH), 128.6 (CH), 127.8 (2CH), 125.9 (C), 116.6 (2CH), 110.3 (CH), 103.1 (CH), 45.1 (CH_2). Anal. Calcd for $C_{20}H_{15}ClN_4O$ (362.8): C, 66.21; H, 4.17; N, 15.44. Found: C, 66.13; H, 4.08; N, 15.39.

4.6.2. Phenyl-[1-phenyl-5-(1H-pyrazol-3-yl)-1,6-dihydropyridazin-3-yl]methanone ***11b***

Yellow crystals from ethanol, yield (0.26 g) 79%, mp 216–218 °C. MS: m/z=328 (M^+, 100%), 223 (90%), 105 (100%). IR: 3440, 3294, 3056, 1620, 1596, 1524, 1498, 1329, 1266, 1214, 1175, 1150, 924, 762. ^{1}H NMR ($CDCl_3$): δ 8.05 (dd, 2H, J=7.8, 1.4 Hz), 7.67 (d, 1H, J=7.4 Hz), 7.58 (t, 1H, J=7.6 Hz), 7.47 (t, 2H, J=7.6 Hz), 7.42–7.38 (m, 5H), 7.30 (m, 1H), 7.14 (t, 1H, J=7.6 Hz), 6.82 (d, 1H, J=7.6 Hz), 4.99 (s, 2H). ^{13}C NMR ($CDCl_3$): δ 189.9 (CO), 156.9 (C), 149.4 (C), 145.4 (C), 137.8 (CH), 134.4 (C), 131.5 (CH), 130.5 (2CH), 129.2 (2CH), 127.7 (2CH), 125.4 (C), 123.4 (CH), 115.6 (2CH), 110.5 (CH), 103.0 (CH), 45.0 (CH_2). Anal. Calcd for $C_{20}H_{16}N_4O$ (328.4): C, 73.15; H, 4.91; N, 17.06. Found: C, 73.05; H, 4.88; N, 17.09.

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