Reactivity of 
2-Cyano-N-(4-(1-Methyl-1H-benzo[d]imidazol-2-yl)-3-(M ethylthio)-1-Phenyl-1H-Pyrazol-5-yl)Acetamide: A Facile Synthesis of Pyrazole, Thiazole, 1,3,4-Thiadiazole and Polysubstituted Thiophene Derivatives

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Abstract  Treatment of 2-cyano-N-(4-(1-methyl-1H-benzo[d]imidazol-2-yl)-3-(methylthio)-1-phenyl-1H-pyrazol-5-yl) acetamide (4) with phenyl isothiocyanate gave the thiole derivative (6) which on treatment with hydrazonyl chlorides (7a-c) furnished 1,3,4-thiadiazole derivatives (9a-c). Reaction of cyanoacetamide derivative (4) with active methylene reagents such as malononitrile or ethyl cyanoacetate and elemental sulfur afforded the corresponding polysubstituted thiophene derivatives (18a,b). Reaction of cyanoacetamide derivative (4) with benzaldehyde yielded the phenylmethylidene derivative (21). The latter showed interesting reactivity towards cyanomethylene reagent and hydrazine derivatives afforded pyrane (22a,b) and pyrazole (25a,b) derivatives.

Keywords  Cyanoacetamide, Active Methylene, Hydrazonyl Halides, α-halo-carbonyl Compounds

1. Introduction

Several pyrazole derivatives are important pharmaceutical, they have been found to possess diverse biological activities [1-6]. They are also acknowledged for their anticancer[7-11], antipyretic[12], anti-inflammatory[13], antimicrobial activities[14-16], antiviral[17], tranquilizing[18], antihypertensive[19], antidepressant[20], antiarrhythmic[21], psychoanaleptic[22], anticonvulsant[23] and antidiabetic activities[24]. Moreover, the thiazole derivative has received a great deal of attention due to their pharmacological importance. Thiazoles were reported to possess antimicrobial[25-28], analgesic[29], anti-inflammatory[30], anticonvulsant[31], cardio tonic[32], anticancer[33,34], antitubercular[35] and anthelmintic[36] activities. Antimicrobial activities of some substituted thiazoles are well established because it posses (S-C=N) toxophoric unit. Thiazoles have enhanced lipid solubility with hydrophilicity. Also, thiazoles are easily metabolized by routine biochemical reactions and are non-carcinogenic in nature[37]. Many thiophene containing annulated compounds, exhibit biological activities[38,39].

In addition, benzimidazole has been an important pharmacophore and privileged structure in medicinal chemistry[40] encompassing a diverse rank of biological activities including antiarrhythmic, antiulcer, antibacterial, antifungal, antiviral and cytotoxicity[41]. Furthermore, 1,3,4-thiadiazoles were reported as highly anti-inflammatory[42], antimicrobial[43], anticonvulsant[44] and anticancer[45] agents.

Cyanoacetamides are highly reactive compounds. They are extensively utilized as reactants or reaction intermediate since the carbonyl and the cyano functions of these compounds are suitably situated to enable reactions with common bidentate reagents to form a variety of heterocyclic compounds. Moreover function, the active hydrogen on C-2 of these compounds can take part in a variety of condensation and substitution reactions. The synthesis of cyanoacetamides may be carried out in several ways[46, 47]. Cyanoacetyl pyrazole is very handy and cheap cyanoacetylation reagent It was successfully applied for the synthesis of various N-alky and N-aryl cyanoacetamides. The latter are polyfunctional compounds possessing both electrophilic and nucleophilic properties. Cyanoacetamide can be useful for the synthesis of three-six membered rings[48].

In connection with our previous studies[49-58] and in view of utilizing the cyanoacetamide as highly versatile intermediates for the construction of functionalized pyrazole, thiazole, 1,3,4-thiadiazole and polysubstituted thiophene
derivatives of expected potential biological activity and excellent pharmacology encouraged us to synthesis novel entities.

2. Chemistry

Treatment of 2-(1-methyl-1-H-benzo[d]imidazol-2-yl)-3-methylthioacrylonitrile (2) with phenylhydrazine affords the target 4-(1-methyl-1H-benzo[d]imidazol-2-yl)3-(methylthio)-1-phenyl-1H-pyrazol-5-amine (3). The structure of (3) was established and confirmed as the reaction product on the basis of their elemental analysis and spectral data. The IR spectrum showed absorption band in the region 3285 cm\(^{-1}\) assignable for NH\(_2\), in addition to disappearance of cyano function signal. Its \(^1\)H NMR spectrum revealed the presence of singlet signals at 6.93 ppm, 10.31 ppm assignable for the NH proton and singlet signal at 10.53 ppm, respectively. Its mass spectrum showed a molecular ion peak at \(m/z = 335\) corresponding to a molecular formula C\(_{18}\)H\(_{17}\)N\(_5\)S. (Scheme 1)

Treatment of 4-(1-methyl-1H-benzo[d]imidazol-2-yl)-3-(methylthio)-1-phenyl-1H-pyrazol-5-amine (3) (with 3,5-dimethyl-1H-pyrazol -1-yl)-3-oxopropanitrile as cyanoacetylation reagent in dry toluene afforded 2-cyano-N-(4-(1-methyl-1H-benzo[d]imidazol-2-yl)-3-(methylthio)-1-phenyl-1H-pyrazol-5-yl)acetamide (4). The structure of (4) was established on the basis of spectral data. The IR spectrum revealed absorption bands at 1615, 1662 cm\(^{-1}\) assignable to carbonyl group. Its \(^1\)H NMR spectrum revealed the presence of singlet signals at 6.22 ppm in addition to multiplet signal for aromatic protons at 7.37-8.12 ppm. Its mass spectrum showed a molecular ion peak at \(m/z = 638\) corresponding to a molecular formula (C\(_{35}\)H\(_{26}\)N\(_8\)O\(_2\)S\(_2\)).

In similar manner compound (6) reacted with equimolar amounts of C-acetyl-N-phenylhydrazonoyl chloride (7b) and C-ethyl carbamyl-N-phenylhydrazonoyl chloride (7c) which converted to cyano function and absorption band at 1662 cm\(^{-1}\) assignable to carbonyl group. Its \(^1\)H NMR spectrum revealed singlet signal for NH at \(6 \pm 9.98\) ppm in addition to multiplet signal for aromatic protons at \(6 \pm 7.37-8.12\) ppm. Its mass spectrum showed a molecular ion peak at \(m/z = 638\) corresponding to a molecular formula (C\(_{35}\)H\(_{26}\)N\(_8\)O\(_2\)S\(_2\)).

Thus, reaction of compound (6) with C-phenyl-N-phenylhydrazonoyl chloride (7a) in refluxing ethanol solution containing triethylamine as basic catalyst afforded solely the corresponding 3,4-thiadiazole derivatives (9a-c). Formation of the latter structures is assumed proceed via elimination of aniline molecule from the non-isolable intermediate (8) as outlined in scheme 2. The 1, 3, 4-thiadiazole structure derivative (9a-c) was confirmed from the elemental analyses and spectral data of the isolated product. The IR spectrum of (9a) revealed absorption band at 2208 cm\(^{-1}\) assignable to cyano function and absorption band at 1662 cm\(^{-1}\) assignable to carbonyl group. Its \(^1\)H NMR spectrum revealed singlet signal for NH at \(6 \pm 9.98\) ppm in addition to multiplet signal for aromatic protons at \(6 \pm 7.37-8.12\) ppm. Its mass spectrum showed a molecular ion peak at \(m/z = 638\) corresponding to a molecular formula (C\(_{35}\)H\(_{26}\)N\(_8\)O\(_2\)S\(_2\)). In similar manner compound (6) reacted with equimolar amounts of C-acetyl-N-phenylhydrazonoyl chloride (7b) and C-ethyl carbamyl-N-phenylhydrazonoyl chloride (7c) which at the next stage were functionalized with different halocarbonyl reagents and obtained single products for which the IR and \(^1\)H NMR spectra (as outlined in scheme 2).

Thus, reaction of compound (6) with C-phenyl-N-phenylhydrazonoyl chloride (7a) in refluxing ethanol solution containing triethylamine as basic catalyst afforded solely the corresponding 1,3,4-thiadiazole derivatives (9a-c). Formation of the latter structures is assumed proceed via elimination of aniline molecule from the non-isolable intermediate (8) as outlined in scheme 2. The 1, 3, 4-thiadiazole structure derivative (9a-c) was confirmed from the elemental analyses and spectral data of the isolated product. The IR spectrum of (9a) revealed absorption band at 2208 cm\(^{-1}\) assignable to cyano function and absorption band at 1662 cm\(^{-1}\) assignable to carbonyl group. Its \(^1\)H NMR spectrum revealed singlet signal for NH at \(6 \pm 9.98\) ppm in addition to multiplet signal for aromatic protons at \(6 \pm 7.37-8.12\) ppm. Its mass spectrum showed a molecular ion peak at \(m/z = 638\) corresponding to a molecular formula (C\(_{35}\)H\(_{26}\)N\(_8\)O\(_2\)S\(_2\)). In similar manner compound (6) reacted with equimolar amounts of C-acetyl-N-phenylhydrazonoyl chloride (7b) and C-ethyl carbamyl-N-phenylhydrazonoyl chloride (7c) which at the next stage were functionalized with different halocarbonyl reagents and obtained single products for which the IR and \(^1\)H NMR spectra (as outlined in scheme 2).
methylthio)-1-phenyl-1H-Pyrazol-5-yl)acetamide (4) underwent Gewald thiophene synthesis via its reaction with cyanomethylene derivatives (15a,b) and elemental sulfur in refluxing dioxane containing triethylamine as basic catalyst afforded the 3,5-diamino thiophene derivatives (18a,b), respectively. Formation of (18a,b) proceed via non-isolable intermediates (16) and (17). The analytical and spectral data of compounds (18a,b) are consistent with the proposed structures. The IR spectrum of (18a) displayed absorption bands at 3316, 3218 cm⁻¹ and 2198 cm⁻¹ for the NH₂ and cyano function and carbonyl absorption band at 1662 cm⁻¹. Its ¹H NMR spectrum two singlet signals at δ 4.42 ppm and δ 5.56 ppm for NH₂ protons and singlet signal at δ 10.21 ppm assignable to the NH group. Its mass spectrum showed a molecular ion peak at m/z = 500 corresponding to a molecular formula (C₂₄H₂₀N₈OS₂).

On the other hand reaction of (4) with phenyl isothiocyanate and elemental sulfur afforded the 4-amino-2,3-dihydro-N-(4-(1-methyl-1H-benzo[d]imidazol-2-yl)-3-(me-thylthio)-1-phenyl-1H-pyrazol-5-yl)-3-phenyl-2-thioxothiazole-5-carboxamide (20) which proceed via intermediacy (16) and (19). The analytical and spectral data of compounds (18a,b) and (20) are consistent with the proposed structures (scheme 4).

Scheme 1. Synthesis of 5-aminopyrazole derivative 3

Scheme 2. Synthesis of 1,3,4-thiadiazole derivatives 9a-c
Scheme 3. Reactions of halocarbonyl compounds 10a-c with enaminonitriles 11a-c

Scheme 4. Synthesis of polysubstituted thiophene 18a,b and thiazole 20 derivatives
The reaction of 2-cyano-N-(4-(1-methyl-1H-benzo[d]imidazol-2-yl)-3-(methylthio)-1-phenyl-1H-pyrazol-5-yl)acetamide (4) with benzaldehyde yielded the phenyl-methylidene derivative (21). The latter showed interesting reactivity towards cyanomethylene reagent (15a,b) afforded the 2-(4-(1-methyl-1H-benzo[d]imidazol-2-yl)-3-(methylthio)-1-phenyl-1H-pyrazol-5-ylamino)-6-amino-4-phenyl-4H-pyran-3,5-dicarbonitrile (22a) and ethyl 6-(4-(1-methyl-1H-benzo[d]imidazol-2-yl)-3-(methylthio)-1-phenyl-1H-pyrazol-5-ylamino)-2-amino-5-cyano-4-phenyl-4H-pyran-3-carboxylate (22b), respectively.

Also, when compound (21) reacted with hydrazine derivatives (23a, b) afforded the 3-amino-N-(4-(1-methyl-1H-benzo[d]imidazol-2-yl)-3-(methylthio)-1-phenyl-1H-pyrazol-5-yl)-1-phenyl-1H-pyrazol-5-yl)-5-phenyl-1H-pyrazole-4-carboxamide (25a) and 3-amino-N-(4-(1-methyl-1H-benzo[d]imidazol-2-yl)-3-(methylthio)-1-phenyl-1H-pyrazol-5-yl)-1-phenyl-1H-pyrazol-5-yl)-1,5-diphenyl-1H-pyrazol e-4-carboxamide (25b) as the major products. The formation of the pyrazole derivatives (25a, b) proceed via β-attack on the C=C moiety in (21) to give the non-isolable intermediate (24) which underwent 1,5-intramolecular dipolar cyclization and concomitant aromatization. Minor product (26) was obtained in the mother liquor which proceed via the condensation with the carbonyl followed by addition on the cyano function afforded the pyrazole derivatives (26) (Scheme 5). The analytical and spectral data of compounds (22a, b), (25a, b) and (26) are consistent with the proposed structures.

3. Experimental

All organic solvents were purchased from commercial sources and used as received or dried using standard procedures, unless otherwise stated. All chemical were purchased from Aldrich or Across and used without purification. Melting points were measured on a Cä llenkamp apparatus and are uncorrected. IR spectra were recorded on Shimadzu FT-IR 8101 PC infrared spectrophotometer. The 1H NMR and 13C NMR spectra were determined in DMSO-δ6 at 300 MHz on a Varian Mercury VX 300 NMR spectrometer as an internal standard. Mass spectra were measured on a GCMS-QP1000 EX spectrometer at 70 eV. Elemental analyses were carried out at the Microanalytical Center of Cairo University. (3,5-Dimethyl-1H-pyrazol-1-yl)-3-oxopropanenitrile was prepared according to the reported literature[60]. Hydrazonyl halides (7a) and (7b,c) were prepared according to the reported literature[61] and[62,63], respectively. 4-(1-methyl-1H-benzo[d]imidazol-2-yl)-3-(methylthio)-1-Phenyl-1H-pyrazol-5-5-amine (3) was prepared according to the reported literature[64].

2).2-Cyano-N-(4-(1-methyl-1H-benzo[d]imidazol-2-5-yl)-3-(methylthio)-1-phenyl-1H-pyrazol-5-yl)acetamide (4),
A solution of 4-(1-methyl-1H-benzomega[d]imidazol-2-yl)-3-(methylthio)-1-phenyl-1H-pyrazol-5-ylacetamide (13) in dry toluene (30 ml) was added to solution of 2-cyano-N-(4-(1-methyl-1H-benzo[d]imidazol-2-yl)-3-(methylthio)-1-phenyl-1H-pyrazol-5-yl)-3-phenylamino acrylamide (6) in dry toluene (30 ml). The reaction mixture was refluxed for about 1h. After evaporation of the solvent, the solid product was collected by filtration and recrystallised from dry DMF to afford (83%, yield) of (4), mp 293-295°C, IR νmax / cm⁻¹ (KBr) 3237 (NH), 2208 (CN), 1662 (CO), 1632 (C=N); ¹H NMR (DMSO-d6) δ 2.68 (s, 3H, CH3), 3.10 (3H, NCH3), 4.12 (s, 2H, CH2), 7.51-8.07 (m, 14H, Ar-H), 10.15 (s, 1H, NH); m/z 604 (M⁺, 21.45). Anal. Calcd. For C31H24N8O2S2 (604.70): C, 61.57; H, 4.00; N, 18.53; S, 10.51%. Found: C, 61.55; H, 4.10; N, 18.51; S, 10.58%.

3.2. General Procedure for the synthesis of 2-Cyano-N-(4-(1-methyl-1H-benzo[d]imidazol-2-yl)-3-(methylthio)-1-phenyl-1H-pyrazol-5-yl)-2-(4-oxo-3-phenylthiazolidin-2-ylidene)-4,5-dihydro-4-phenyl-1,3,4-thiadiazole-2-carboxylate (9a).

To stirred solution of potassium hydroxide (10 mmol) in dimethylformamide (20ml), 2-cyano-N-(4-(1-methyl-1H-benzo[d]imidazol-2-yl)-3-(methylthio)-1-phenyl-1H-pyrazol-5-yl)-3-phenylamino acrylamide (6) (0.01 mol) was added. After stirring for 30 min., phenyl isothiocyanate (0.01 mol) was added to the resulting mixture. Stirring was continued overnight then poured onto crushed ice containing hydrochloric acid. The solid product so-formed was collected by filtration, washed with water, dried and finally recrystallized from ethanol/dimethylformamide to afford (72%, yield) of (6), mp 239-241°C; IR νmax / cm⁻¹ (KBr) 3362, 3215 (NH), 2206 (CN), 1653 (CO), 1635 (C=N); ¹H NMR (DMSO-d6) δ 2.68 (s, 3H, CH3), 3.10 (3H, NCH3), 4.12 (s, 2H, CH2), 7.35-7.89 (m, 14H, Ar-H), 10.15 (s, 1H, NH), 10.14 (s, 1H, SH); m/z 538 (M⁺, 1.26). Anal. Calcd. For C34H30N6O2S2 (573.66): C, 62.55; H, 4.31; N, 18.24; S, 11.99%. Found: C, 62.53; H, 4.28; N, 18.19; S, 11.99%.

3.1. General Procedure for the Reaction of 2-Cyano-3-mercapto-N-(4-(1-methyl-1H-benzo[d]imidazol-2-yl)-3-methylthio-1-phenyl-1H-pyrazol-5-yl)-3-phenylamino acrylamide (6) with Hydrazonoyl Chlorides (7 a-c)

To a solution of 4-(1-methyl-1H-benzo[d]imidazol-2-yl)-3-(methylthio)-1-phenyl-1H-pyrazol-5-yl)acetamide (9a) (1 mmol of each), α and then the appropriate halocarbonyl compounds (10 mmol of each) was added. After stirring for 30 min., phenyl isothiocyanate (10 mmol) was added to the resulting mixture. Stirring was continued 6h., then the appropriate α-halocarbonyl compounds (10a-c) (10 mmol of each) was added. Stirring continued for additional overnight. Then, the reaction mixture was poured onto crushed ice water. The solid product that formed was filtered off, dried and recrystallized from the suitable solvent to afford the corresponding thiazole derivatives (12) and (13b,c), respectively.

1.2-Cyano-N-(4-(1-methyl-1H-benzo[d]imidazol-2-yl)-3-(methylthio)-1-phenyl-1H-pyrazol-5-yl)-2-(4-oxo-3-phenylthiazolidin-2-ylidene)acetamide (13c).

To stirred solution of potassium hydroxide (10 mmol) in dimethylformamide (20ml), 2-cyano-N-(4-(1-methyl-1H-benzo[d]imidazol-2-yl)-3-(methylthio)-1-phenyl-1H-pyrazol-5-yl)acetamide (4) (10 mmol) was added. After stirring for 30 min., phenyl isothiocyanate (10 mmol) was added to the resulting mixture. Stirring was continued 6h., then the appropriate α-halocarbonyl compounds (10a-c) (10 mmol of each) was added. Stirring continued for additional overnight. Then, the reaction mixture was poured onto crushed ice water. The solid product that formed was filtered off, dried and recrystallized from the suitable solvent to afford the corresponding thiazole derivatives (12) and (13b,c), respectively.
3.3. General Procedure for the synthesis of 3,5-Diamino-4-cyano-N-(4-(1-methyl-1H-benzo[d]imidazol-2-yl)-3-(methylthio)-1-phenyl-1H-pyrazol-5-yl)thiophene-2-carboxamide (18a) and Ethyl 5-(4-(1-methyl-1H-benzo[d]imidazol-2-yl)-3-(methylthio)-1-phenyl-1H-pyrazol-5-yl)carbamoyl)-2,4-diaminothiophene-3-carboxylate (18b).

To a solution of compound (4) (0.01 mol) in 1,4-dioxane (30 ml) containing triethylamine (1 ml), either malononitrile (0.01 mol) or ethyl cyanoacetate (0.01 mol) was added. The reaction mixture was heated under reflux for 3 h., then cooled and neutralized by pouring onto ice/water mixture containing few drops of hydrochloric acid. The solid product formed was collected by filtration and crystallized from dimethylformamide and ethanol.

White powder, (52%, yield), mp 295-297°C; IR $\nu_{\text{max}}$/ cm$^{-1}$ (KBr) 3436-3385 (NH$_2$), 3256 (NH), 2205 (CN), 1696, 1650 (CO), 1592 (C=N); 1H NMR (DMSO-$d_6$) $\delta$ 2.57 (s, 3H, CH$_3$), 3.1 (2s, 2H, NH$_2$), 4.69 (2s, 2H, NH$_2$), 7.23-7.76 (m, 9H, Ar-H), 10.23 (s, 1H, NH); m/z 547 (M$^+$, 27.32). Anal. Calcd. For C$_{26}$H$_{25}$N$_7$O$_3$S$_2$ (547.65): C, 63.96; H, 4.09; N, 17.82; S, 16.88%. Found: C, 63.90; H, 4.06; N, 17.10; S, 16.79%

3.4. General Procedure for the synthesis of 2-(4-(1-Methyl-1H-benzo[d]imidazol-2-yl)-3-(methylthio)-1-phenyl-1H-pyr-azol-5-yl)-3-phenyl-2-thioxothiazole-5-carboxamide (20).

To a solution of compound (4) (0.01 mol) in absolute ethanol (30 ml) containing triethylamine (1 ml) and elemental sulfur (0.01 mol) was added followed by the addition of an equimolar amount of phenyl isothiocyanate (0.01 mol). The reaction mixture was heated under reflux for 1 h., at 75°C with continuous stirring and then cooled and neutralized by pouring onto ice/water mixture containing few drops of hydrochloric acid. The solid product formed was collected by filtration and crystallized from dimethylformamide and ethanol.

To a solution of compound (4) (0.01 mol) in 1,4-dioxane (30 ml) containing piperidine (0.5 ml), benzaldehyde (0.01 mol) was added. The reaction mixture was heated under reflux for 3 h., then left to cool. The solid product so formed was collected by filtration and crystallized from dimethylformamide and ethanol.

Purple crystals, (56%, yield), mp >300°C; IR $\nu_{\text{max}}$/ cm$^{-1}$ (KBr) 3436-3385 (NH$_2$), 3256 (NH), 2205 (CN), 1696, 1650 (CO), 1592 (C=N); 1H NMR (DMSO-$d_6$) $\delta$ 2.57 (s, 3H, CH$_3$), 3.1 (2s, 2H, NH$_2$), 4.69 (2s, 2H, NH$_2$), 7.23-7.76 (m, 9H, Ar-H), 10.23 (s, 1H, NH); m/z 547 (M$^+$, 27.32). Anal. Calcd. For C$_{26}$H$_{25}$N$_7$O$_3$S$_2$ (547.65): C, 63.90; H, 4.06; N, 17.10; S, 16.79%.
was added. The reaction mixture was heated in each case under reflux for 6h., then the excess solvent was evaporated under reduced pressure. The solid product formed in each case was collected by filtration and crystallized from dimethylformamide/ethanol (2:1).

1).2-(4-(1-Methyl-1H-benz[d]imidazol-2-yl)-3-(methyliodo)-1-phenyl-1H-pyrazol-5-ylamino)-6-amino-4-phenyl-1H-pyranyl-3,5-dicarboximide (25a).

White crystals, (52%, yield), mp 267-269°C; IR \( \nu_{\text{max}} \) / cm\(^{-1} \) (KBr) 3442, 3259 (2NH and NH\( \_2 \)), 1645 (CO), 1629 (q, 2H, J = 6.78 Hz, \( CH\_2 \)), 4.83 (s, 2H, NH\( \_2 \)), 6.62 (s, 1H, pyran H-4), 7.21-7.84 (m, 14H, Ar-H), 10.23 (s, 1H, NH); m/z 556 (M\(^+\), 53.11). Anal. Calcld. For C\(_28\)H\(_{24}\)N\(_8\)S (556.61): C, 66.65; H, 4.79; N, 22.21; S, 6.35%. Found: C, 66.61; H, 4.78; N, 22.19; S, 6.36%.

2).Ethyl 6-(4-(1-Methyl-1H-benz[d]imidazol-2-yl)-3-(methyliodo)-1-phenyl-1H-pyrazol-5-ylamino)-2-amino-5-cyano-4-phenyl-1H-pyranyl-3-carboxylate (25b).

Pale yellow crystals, (51%, yield), mp 201-203°C; IR \( \nu_{\text{max}} \) / cm\(^{-1} \) (KBr) 3368 (NH\( \_2 \)), 3255 (NH), 2222, 2219 (2CN), 1650 (CO), 1635 (C=N); \(^1\)H NMR (DMSO-d\(_6 \)) \( \delta \) 2.72 (s, 3H, SCH\(_3 \)), 3.90 (s, 3H, NCH\(_3 \)), 4.11 (s, 2H, NH\( \_2 \)), 7.31-7.81 (m, 19H, Ar-H), 10.21 (s, 1H, NH); m/z 603 (M\(^+\), 32.54). Anal. Calcld. For C\(_{31}\)H\(_{24}\)N\(_8\)S (569.63): C, 66.69; H, 4.31; N, 20.12; S, 5.75%.

3).3-Aminoo-N-(4-(1-Methyl-1H-benzo[d]imidazol-2-yl)-3-(methyliodo)-1-phenyl-1H-pyrazol-5-ylamino)-1,5-diphenyl-1H-pyranyl-4-carboxamide (25c).

Pale orange crystals, (48%, yield), mp 297-300°C; IR \( \nu_{\text{max}} \) / cm\(^{-1} \) (KBr) 3368 (NH\( \_2 \)), 3255 (NH), 2222 (CN), 1650 (CO), 1635 (C=N); \(^1\)H NMR (DMSO-d\(_6 \)) \( \delta \) 2.72 (s, 3H, SCH\(_3 \)), 3.90 (s, 3H, NCH\(_3 \)), 4.11 (s, 2H, NH\( \_2 \)), 7.31-7.81 (m, 19H, Ar-H), 10.29 (s, 1H, NH); m/z 596 (M\(^+\), 19.83). Anal. Calcld. For C\(_{34}\)H\(_{32}\)N\(_8\)OS (596.7) C, 64.42; H, 4.73; N, 18.78; S, 5.30%. Found: C, 64.2; H, 4.70; N, 18.77; S, 5.21%.

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