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PREPARATION OF 4-CYANO-3-METHYL-1-PHENYL-1*H*-PYRAZOLE-5-(4-BROMOPHENYL)-NITRILE IMINE: REGIO- AND STEREOSELECTIVE SYNTHESIS OF A NEW CLASS OF SUBSTITUTED 3-PYRAZOLYL-2-PYRAZOLINES AND PYRAZOLES

Attreyee Mukherjee and Kumar K. Mahalanabis*

Department of Chemistry, Jadavpur University, Kolkata-700032, India

kumarmahalanabis@yahoo.in; kkmahalanabis@gmail.com

Abstract - A regio and stereoselective preparation of a new class of substituted 3-pyrazolyl-2-pyrazolines and pyrazoles in good to excellent yields has been developed by reacting 4-cyanopyrazole-5-nitrile imine with dipolarophiles.

INTRODUCTION

The present communication reports, for the first time, a regio and stereoselective synthesis of a new class of substituted 3-pyrazolyl-2-pyrazolines and pyrazoles required for our contemplated biological and photophysical study. Nitrile ylides have received extensive attention and synthetic use as reactive intermediate for the construction of heterocyclic systems.[1] Hydrazonoyl halides are stable precursor of nitrile imines which undergo facile 1,3-dipolar cycloaddition with a variety of alkenes and alkynes to produce pyrazolines and pyrazoles respecively[2] often accompanied by regio and stereoisomers. In our case, the major constraint for successful application of this widely used protocol is the lack of a straight-forward and efficient method to obtain 5-formyl pyrazole particularly in the presence of electron-withdrawing substitutents. This aldehyde is the key intermediate for the generation of the desired nitrile imine to undergo planned 1,3-dipolar cycloaddition with alkenes leading to formation of the 2-pyrazoline ring. Reported preparation of 3-carboethoxy-5-formyl pyrazole mixed with undesirable side products involves either hydrogenolysis of pyrazole-5-acid chloride or ozonolysis of the 5-olefinic side chain.[3] While seeking new methodologies for regiospecific synthesis of trisubstituted 1,2-azoles,[4-6] we have developed a high yielding synthesis of 5-dichloromethyl-3-methyl-1-phenyl-1*H*-pyrazole-4-carbonitrile **1**. 5-Dichloromethyl substituent present in **1** as masked formyl group**,** on mild acid hydrolysis, neatly afforded the desired 5-formyl pyrazole **2** in excellent yield. Easy availability of **2,** thus, allowed us a facile entry into *in situ* preparation of the key intermediate, 4-cyano-3-methyl-1-phenyl-1*H*-pyrazole-5-

(4-bromophenyl) nitrile imine **5** from **4** in the presence of triethylamine. Nitrile imine **5** was then treated with a series of dipolarophiles to give a new class of regio and stereocontrolled substituted 3-pyrazolyl-2-pyrazolines **6a-h** and 3-pyrazolylpyrazole **7** in good to excellent yields (Scheme 1, Table1).

Nitrogen containing heterocycles in general and pyrazole and pyrazolylpyrazoline derivatives specially possess important biological and pharmaceutical activities[7] and are also useful synthetic building blocks in organic chemistry including pyrazole-based bioactive materials.[8] 2-Pyrazoline derivatives, in particular, have been effectively utilized as antibacterial, antiviral, antiparasitic, antitubercular and insectidal agents.[9-12] Some of these compounds have also anti-inflammatory, anesthetic and analgesic properties,[13] and are also known to exhibit pronounced fluorescence.[14] In addition, the other most interesting property of 2-pyrazoline moiety is its use as nanoparticles.[15] Bipyrazoles are useful compounds and are used as cytotoxic, insecticide, herbicide and fungicide agents along with applications in the photographic and paint industry.[16]

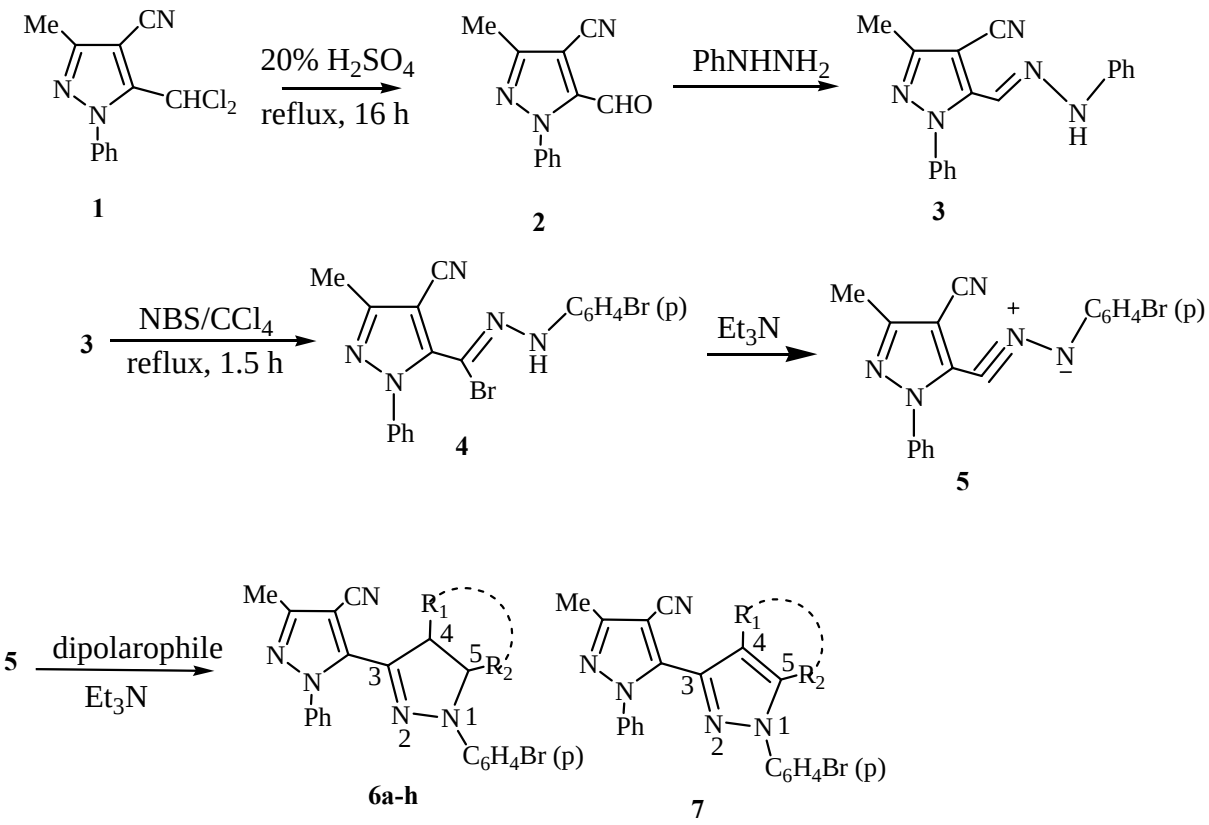
Aryl/heteryl pyrazolines are mostly derived from condensation of substituted chalcones with hydrazines.[17] Heteryl pyrazolines and pyrazoles have also been synthesized by the reaction of thienyl and pyridyl hydrazonoyl halides with alkenes and alkynes respectively.[18,19] A multi-step synthesis of 5-pyrazolyl-2-pyrazoline is reported.[20] Preparation of 3-pyrazolylpyrazoles by microwave assisted 1,3-dipolar cycloaddition has been described.[21] However, preparation of 3-pyrazolyl-2-pyrazolines are yet to be reported.

RESULTS AND DISCUSSION

Highly successful introduction of an aldehyde function in excellent yield and free from undesirable side products at C-5 of pyrazole ring in the presence of an electron-withdrawing group (-CN) allowed us to overcome the earlier difficulties encountered in formylation in good yield at C-5 of pyrazole particularly with electron withdrawing substituent. Pyrazole-5-aldehyde **2** thus obtained was then smoothly converted into hydrazone **3** by treatment with phenylhydrazine reagent.[22] Hydrazonoyl halides are generally prepared by direct halogenation[23-25] of hydrazone or treating the hydrazone with NBS/CCl_4[26] or Ph_3P/CX_4[27] (X = Cl, Br) respectively. In the present case, the best result was obtained when hydrazone **3** was treated with NBS in refluxing CCl_4 to afford **4**. The absence of -CH=N- proton signal in the ^{1}H-NMR spectrum of **4** is indicative of desired C-halogenation (-CBr=N-). Appearance of double doublets at δ 6.46 (J = 8.3 Hz) and δ 6.68 ppm (J = 8.8 Hz) respectively clearly demonstrates that spontaneous bromination also occurred in the para position of the N-phenyl ring during NBS treatment of **3**.

Terminal alkenes *i.e*. acrylonitrile, ethyl acrylate and styrene when reacted with nitrile imine **5**, in refluxing chloroform afforded 3-substituted-2-pyrazolines **6a-c** with complete control of regioselectivity in each case (Table 1). Selective incorporation of substituent at C-5 of pyrazoline ring is found to be in

compliance with the known observation that 1,3-cycloaddition of nitrile imines with terminal olefins generally produce 5-isomer regioselectively.



Scheme 1

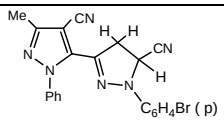
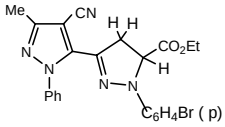
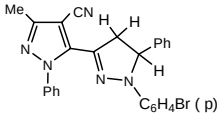
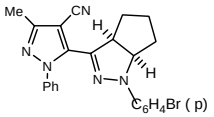
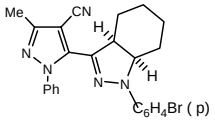
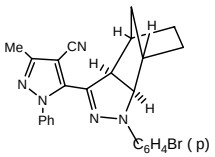
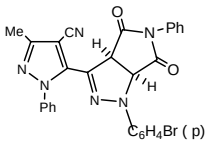
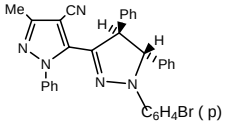
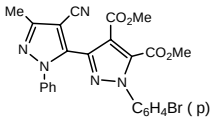
The effects of substituents on the shapes of the FOs have been elegantly derived[28] and union of the unsubstituted end of the dipolarophile with the carbon end of the dipole where larger HOMO and LUMO coefficients respectively are located, always favours the formation of 5-substituted heterocycles.

The chemical shift values of methine and methylene protons of **6a-c** in ^{1}H-NMR are well supported by the literature analogy.[29] For structural analyses of all new compounds please see Experimental section.

Huisgen[30] has demonstrated the reactivity of cyclic dipolarophiles with accurate comparisons of kinetic and thermodynamic data. The olefinic C-H bonds of norbornene are bent in the endo direction by 3.4°, and only a small expenditure of energy is necessary to effect the 10° *cis* bending to react in cycloaddition TS geometry. Similar deformations are also found in cyclopentene. On the other hand, the C=C bond of cyclohexene is bent in a *trans* fashion and considerable energy and even conformational changes are required to cause a *cis* bending - a fact borne out by the lower yield of the adduct **6e**.

The reaction of pyrazole-5-nitrile imine **5** with cyclic alkenes, namely norbornene, cyclopentene, cyclohexene and N-phenylmaleimide were found to be totally stereoselective and gave exclusive *cis*-

Table 1. Reaction of **5** with dipolarophiles

Entry no.	Dipolarophile	Structure		Yield (%)
1	CH_2=CH-CN		**6a**	70
2	CH_2=CH-CO_2Et		**6b**	75
3	CH_2=CH-Ph		**6c**	72
4	cyclopentene		**6d**	75
5	cyclohexene		**6e**	54
6	norbornene		**6f**	73
7	*N*-phenylmaleimide		**6g**	61
8	PhCH=CHPh (trans)		**6h**	70
9	DMAD		**7**	55

fused 2-pyrazoline products. Thus, in the ^{1}H-NMR spectrum of **6f**, protons (3a, 7a) appeared as doublet at δ 3.57 (J = 9.7 Hz) and δ 4.10 ppm (J = 9.7 Hz) respectively, and no splitting was observed between 3a and 4 and 7a and 7 protons indicating that the adduct is being produced by the attack of the dipolarophile from the *exo* side.[28] Similarly, *cis* fused adducts were also obtained with cyclopentene, cyclohexene and *N*-phenylmaleimide.

Reaction of pyrazole-5-nitrile imine **5** with *trans*-stilbene is expected to give the cycloadduct **6h** with retention of configuration. This was indeed the case[31] as evidenced from the coupling constant (J = 4.6 Hz) between C-4 and C-5 protons of **6h**.

Pyrazole-5-nitrile imine **5** when reacted with dimethyl acetylenedicarboxylate neatly produced 3-pyrazolyl pyrazole **7** in high yield.

Our interest on the photophysical study of these newly synthesized 2-pyrazoline derivatives in homogeneous solvents with Bhattacharya *et al.*[32] stems mainly for two reasons : to explore (i) potential biological applications of this class of compounds in pharmaceuticals, and (ii) their use as optical brightening agents for textile fibres, plastics and papers.[33] 2-Pyrazoline based nanoparticles have found applications in optical field.[34] Results of preliminary photophysical study with **6b** and **6f** have already been communicated.[32,35] These compounds show a strong tendency towards a hydrogen bonding interaction with protic solvents, are highly fluorescent with high fluorescence quantum yield and exhibit considerable solvatochromism. Presently we are exploring the photophysical behavior of these compounds in microheterogeneous medium.

In conclusion, we have developed an efficient new route for the synthesis of a new class of polysubstituted 3-pyrazolyl-2-pyrazolines with excellent control of regio and stereochemistry by employing, for the first time, cyanopyrazole-5-nitrile imine in 1,3-dipolar cycloaddition with different dipolarophiles. These compounds, in turn, on oxidative aromatization, could be easily converted to the corresponding pyrazoles which are known to exhibit a wide range of biological activities.[36, 37] Synthesis of this new class of pyrazole-substituted-2-pyrazolines with inbuilt bromo substituent allow them to be used as potential bromo organics in pharmaceuticals, intermediate for agrochemicals and industrially valuable new materials[38] and provides scope for elaboration to other functionality.[39-42] Further, 2-Pyrazoline derivatives are also considered to be important organic heterocyclic 'transition' materials and find use in organic molecular crystals.[43] Preliminary photophysical study[32,35] with some of these newly synthesized 2-pyrazoline derivatives clearly demonstrates their potential application as fluorescent probes in some chemosensors[44] and as nanoparticles in optoelectronic device.[45-48]

EXPERIMENTAL

Melting points (°C) were determined in open capillaries and are uncorrected . All compounds were crystallised from ethyl acetate- pet ether(60-80 °C). IR spectra (KBr, υ_{max}; cm^{-1}) were taken on Hitachi 270-30 spectrometer; UV spectra (EtOH ; λ_{max} (ε), nm) were taken on a Hitachi U-2000 spectrometer. ^{I}H NMR and ^{13}C NMR spectra (δ ppm ; *J* in Hz) in $CDCl_3$ (otherwise stated) were recorded on Bruker AV-300 and Spect-400 spectrometers with TMS as internal standard. Mass spectra [m/z(%)] were recorded by a Thermo Finnigan LCQ DUO . Elemental analyses were performed on a Perkin-Elmer 240C elemental analyser. All yields (%) refer to isolated , spectroscopically pure material.

5-Formyl-3-methyl-1-phenyl-1*H*-pyrazole-4-carbonitrile (2)

5-(Dichloromethyl)-3-methyl-1-phenyl-1*H*-pyrazole-4-carbonitrile[4] (**1**) (2.65 g, 10 mmol) in H_2SO_4 (20%, 30 mL) was taken in a round-bottomed flask (250 mL) and the mixture was refluxed for 16 h (monitored by TLC, EtOAc-pet. ether(1:3). Usual work up afforded white needle-shaped crystalline material.

Mp 134 – 135 °C. Yield (%): 75. IR (KBr): 2230, 1690, 1592, 1535 cm^{-1}. UV (EtOH): λ_{max} (ε) = 254 (9,769). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.48 (s, 3H, Me), 7.53 (m, 5H, Ar-*H*), 9.90 (s, 1H, C*H*O). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.60, 96.79, 111.78, 125.35, 129.50, 129.99, 137.09, 141.44, 153.53, 177.29. MS *m/z* (%): 211 (100) [M^+]. *Anal.* Calcd for $C_{12}H_9N_3O$ (%): C, 68.24; H, 4.29; N, 19.89. Found (%): C, 68.46; H, 4.32; N, 19.92.

(E)-1-((4-Cyano-3-methyl-1-phenyl-1*H*-pyrazol-5-yl)methylene)-2-phenylhydrazine (3)

A mixture of **2** (0.633 g, 3 mmol) and phenylhydrazine reagent[22] (13 mL, 9 mmol) was heated on a steam bath for a period of 30 min. The reaction mixture was cooled and extracted with EtOAC (3x20 mL). Usual work up afforded a yellow solid which was purified by column filtration (silica gel 60-120 mesh; EtOAc-pet.ether (1:1) when yellow shiny crystals were isolated.

Mp 148 – 149 °C. Yield (%): 75. IR (KBr): 3264, 2212, 1571, 1551, 1526, 1388, 1338 cm^{-1}. UV (EtOH): λ_{max} (ε) = 372 (14,639), 242 (15,843). ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.37 (s, 3H, Me), 6.85-7.58 (m, 10H, Ar-*H*), 7.72 (s, 1H, =C*H*) 11.02 (br, 1H, N*H*). ^{13}C NMR (75 MHz, DMSO-d_6): δ = 12.18, 87.89, 112.55, 114.90, 120.42, 122.27, 125.75, 129.15, 129.27, 129.59, 137.87, 144.01, 144.34, 152.30. MS *m/z* (%): 300 (100) [M^+]. *Anal.* Calcd for $C_{18}H_{15}N_5$ (%): C, 71.74; H, 5.02; N, 23.24. Found (%): C, 71.46; H, 4.99; N, 23.28.

(Z)-1-(Bromo(4-cyano-3-methyl-1-phenyl-1*H*-pyrazol-5-yl)methylene)-2-(4-bromophenyl)hydrazine (4)

A mixture of **3** (0.3 g, 1 mmol) and NBS (0.352 g, 2 mmol) was taken in dry carbon tetrachloride (30 mL) and refluxed for 1.5 h. The reaction mixture was filtered hot and the organic layer was washed with water, dried over anhydrous Na_2SO_4, and concentrated. The crude solid on recrystallization from a mixture (1:1)

of EtOAc and pet. ether afforded a grey solid.

Mp 160 -161 °C. Yield (%): 75. IR (KBr): 3072, 2212, 1568, 1533, 1475 cm^{-1}. UV (EtOH): λ_{max} (ε) = 341 (9,450), 245 (13,760). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.48 (s, 3H, Me), 6.46 (d, *J* = 8.3, 2*H*), 6.68 (d, *J* = 8.8, 2*H*), 7.13-7.47 (m, 5H, Ar-*H*), 8.15 (s, 1H, N*H*). MS *m/z* (%): 459 (94) [M^+], 461 (60) [MH^+ +1], 462 (50) [MH^+ + 2]. *Anal.* Calcd for $C_{18}H_{13}N_5Br_2$ (%): C, 47.09; H, 2.85; N, 15.25. Found (%): C, 47.37; H, 2.89; N, 15.28.

GENERAL PREPARATIVE METHOD OF 2-PYRAZOLINES 6a-h AND PYRAZOLE 7.

A mixture of **4** (0.459 g, 1 mmol), dipolarophile (1 mmol) and triethylamine (1 mmol) in dry $CHCl_3$ (10 mL) was refluxed for 12-16 h (monitored by TLC). The reaction mixture was then washed with water and the organic layer was dried over anhydrous Na_2SO_4. The crude solid, obtained on concentration of the organic layer, was purified by column filtration (silica gel 60-120 mesh ; EtOAc-pet.ether(1:3).

5-(1-(4-Bromophenyl)-5-cyano-4,5-dihydro-1*H*-pyrazol-3-yl)-3-methyl-1-phenyl-1*H*-pyrazole-4-carbonitrile (6a)

Yellowish-green sugar-cube crystals. Mp 199-200 °C. IR (KBr): 2224, 1575, 1355, 1124, 766, 692 cm^{-1}. UV (EtOH): λ_{max} (ε) = 389 (35902), 360 (21119), 248 (24437). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.50 (s, 3H, Me), 3.49-3.62 (m, 2H, H4), 4.95 (dd, *J* = 5.8 & 11.3, 1H, H5), 6.76 (d, *J* = 8.7, 2H, Ar-*H*), 7.39 (d, *J* = 8.6, 2H, Ar-*H*), 7.42-7.56 (m, 5H, Ar-*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.50, 39.28, 49.73, 93.59, 113.69, 115.33, 115.59, 116.07, 126.58, 129.49, 129.90, 132.38, 136.16, 138.98, 139.34, 140.99, 153.13. MS *m/z* (%): 431 (30) [MH^+], 432 (26) [MH^++1], 433 (30) [MH^++2], 406 (100) [MH^++2-HCN], 404 (92) (MH^+-HCN). *Anal.* Calcd for $C_{21}H_{15}N_6Br$ (%): C, 58.48; H, 3.51; N, 19.49. Found (%): C, 58.22; H, 3.53; N, 19.52;

Ethyl 1-(4-bromophenyl)-3-(4-cyano-3-methyl-1-phenyl-1*H*-pyrazol-5-yl)-4,5-dihydro-1*H*-pyrazole-5-carboxylate (6b)

Yellow needles. Mp 137-138 °C. IR (KBr) : 2220, 1740, 1590, 1479, 1366, 1199 cm^{-1}. UV (EtOH): λ_{max} (ε) = 377 (17903), 250 (19467). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.22 (t, *J* = 7.0, 3H, CH_2Me), 2.47 (s, 3H, Me), 3.35 (dd, *J* = 6.2 & 17.6, 1H, H4), 3.56 (dd, *J* = 12.9 & 17.6, 1H, H4), 4.21 (q, *J* = 7.0, 2H, C*H*$_2$Me), 4.77 (dd, *J* = 5.8 & 12.9, 1H, H5), 6.62 (d, *J* = 9.3, 2H, Ar-*H*), 7.30(d, *J* = 9.0, 2H, Ar-*H*), 7.45-7.46 (m, 2H, Ar-*H*), 7.53-7.54 (m, 3H, Ar-*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.49, 14.03, 38.67, 61.38, 62.20, 92.84, 113.39, 114.12, 114.95, 126.64, 129.14, 129.47, 131.96, 134.64, 139.73, 140.00, 141.98, 152.88, 169.72. MS *m/z* (%): 477 (30) [M^+], 478 (100) [MH^+], 480 (96) [M^++3]. *Anal.* Calcd for $C_{23}H_{20}N_5O_2Br$ (%): C, 57.75; H, 4.21; N, 14.64. Found (%): C, 57.52; H, 4.19; N, 14.85.

5-(1-(4-Bromophenyl)-4,5-dihydro-5-phenyl-1*H*-pyrazol-3-yl)-3-methyl-1-phenyl-1*H*-pyrazole-4-

carbonitrile (6c)

Yellowish green crystals. Mp 148-149 °C. IR (KBr) : 2214, 1589, 1483, 1347, 1130 cm^{-1}. UV (EtOH): λ_{max} (ε) = 373 (5752), 245 (5315). 1H NMR (400 MHz, $CDCl_3$): δ = 2.46 (s, 3H, Me), 3.00 (dd, *J* = 6.8 & 17.4, 1H, H4), 3.70 (dd, *J* = 12.5 & 17.5, 1H, H4), 5.23 (dd, *J* = 6.7 & 12.4, 1H, H5), 6.51-7.49 (m, 14H, Ar-*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.04, 43.25, 62.98, 91.34, 111.36, 113.34, 114.19, 115.22, 125.75, 126.71, 127.81, 128.85, 129.05, 129.60, 131.55, 135.55, 138.96, 140.69, 141.05, 141.91, 151.95. MS *m/z* (%): 481.9 (100) [M^+], 483.9 (88) [MH^+], 484.9 (25) [MH^++1], 505.9 (20) [MH^++Na^+]. *Anal.* Calcd for $C_{26}H_{20}N_5Br$ (%): C, 64.74; H, 4.18; N, 14.52. Found (%): C, 65.01; H, 4.20; N, 14.48.

5-((3a*S*,6a*R*)-1-(4-Bromophenyl)-1,3a,4,5,6,6a-hexahydrocyclopenta[*c*]pyrazol-3-yl)-3-methyl-1-phenyl-1*H*-pyrazole-4-carbonitrile (6d)

Yellowish brown shiny crystals. Mp 197-198 °C. IR (KBr): 2224, 1579, 1481, 1361, 1194, 1134, 914 cm^{-1}. UV (EtOH): λ_{max} (ε) = 253 (15833). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.37-2.08 (m, 6H, H-4,5,6), 2.50 (s, 3H, Me), 4.1 (m, 1H, $H3_a$), 4.66 (m, 1H, $H6_a$), 6.62 (d, *J* = 8.0, 2H, Ar-*H*), 7.29 (d, *J* = 8.0, 2H, Ar-*H*), 7.40-7.53 (m, 5H, Ar-*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.53, 24.44, 33.01, 33.61, 50.91, 65.68, 92.13, 112.30, 114.38, 114.79, 126.57, 129.08, 129.16, 131.83, 138.50, 140.21, 140.64, 141.42, 152.83. MS *m/z* (%): 445 (30) [M^+], 446 (100) [MH^+], 448 (98) [MH^++2], 449 (26) [MH^++3]. *Anal.* Calcd for $C_{23}H_{20}N_5Br$ (%)**:** C, 61.89; H, 4.52; N, 15.69. Found (%): C, 62.07; H, 4.54; N, 15.78.

5-((3a*S*,7a*R*)-1-(4-Bromophenyl)-3a,4,5,6,7,7a-hexahydro-1*H*-indazol-3-yl)-3-methyl-1-phenyl-1*H*-pyrazole-4-carbonitrile (6e)

Light green crystals. Mp 200-201 °C. IR (KBr): 2222, 1602, 1471, 1445, 1316, 1102 cm^{-1}. UV (EtOH): λ_{max} (ε) = 385 (30973), 340 (10081). ^{1}H NMR (400 MHz, $CDCl_3$): δ =1.18-2.04 (m, 8H, H-4,5,6,7), 2.55 (s, 3H, Me), 3.47 (m, 1H, $H3_a$), 4.27 (m, 1H, $H7_a$), 6.79-7.58 (m, 9H, Ar-*H*). MS *m/z* (%): 459.9 (92) [MH^+], 461.9 (100) [MH^++1], 462.9 (24) [MH^++2], 483.9 (17) [M+Na].$^+$ *Anal.* Calcd for $C_{24}H_{22}N_5Br$ (%): C, 62.61; H, 4.82; N, 15.21. Found (%): C, 62.38; H, 4.79; N, 15.19.

5-((3aS,7aR)-1-(4-Bromophenyl)-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methano-indazol-3-yl)-3-methyl-1-phenyl-1*H*-pyrazole-4-carbonitrile (6f)

Yellowish brown shiny crystals. Mp 202-203 °C. IR (KBr): 2224, 1575, 1484, 1367, 1295, 1152 cm^{-1}. UV (EtOH): λ_{max} (ε) = 341 (12272), 255 (17888). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.22-1.62 (m, 6H, H-5,6,8), 2.49 (s, 3H, Me), 2.50 & 2.72 (each s, 2H, H4,7), 3.57 (d, *J* = 9.7, 1H, $H3_a$), 4.09 (d, *J* = 9.7, 1H, $H7_a$), 6.59 (d, *J* = 9.0, 2H, Ar-*H*), 7.28 (d, *J* = 9.0, 2H, Ar-*H*), 7.42-7.53 (m, 5H, Ar-*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.52, 24.18, 27.09, 32.92, 40.71, 40.97, 55.11, 67.76, 112.18, 114.44, 114.51, 126.70, 129.07, 129.20, 131.84, 137.57, 140.28, 141.54, 152.81. MS *m/z* (%): 471 (38) [M^+], 472 (100) [MH^+], 474 (92) [MH^++3]. *Anal.* Calcd for $C_{25}H_{22}N_5Br$ (%)**:** C, 63.56; H, 4.69; N, 14.83. Found (%): C, 63.29; H,

4.72; N, 14.78.

5-((3a*S*,6a*S*)-1-(4-Bromophenyl)-1,3a,4,5,6,6a-hexahydro-4,6-dioxo-5-phenylpyrrolo[3,4-*c*]pyrazol-3-yl)- 3-methyl-1-phenyl-1*H*-pyrazole-4-carbonitrile (6g)

Yellowish green crystals. Mp 152-153 °C. IR (KBr) : 2224, 1721, 1586, 1487, 1368, 1187 cm^{-1}. UV (EtOH): λ_{max} (ε) = 373 (398441), 286 (29547). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.50 (s, 3H, Me), 4.81 (d, *J* = 11.2, 1H, $H3_a$), 5.23 (d, *J* = 11.2, 1H, $H6_a$), 7.21-7.51 (m, 14H, Ar-*H*). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.54, 29.67, 52.93, 64.20, 115.23, 116.26, 126.09, 126.60, 129.26, 129.32, 129.75, 130.69, 131.07, 132.10, 138.28, 139.28, 141.51, 153.14, 169.46, 170.21. MS *m/z* (%): 551 (40) [M^+], 552 (60) [MH^+], 553 (40) [MH^++1]. *Anal*.Calcd for $C_{28}H_{19}N_6O_2Br$ (%): C, 60.99; H, 3.47; N, 15.24.. Found (%): C, 60.74; H, 3.51; N, 15.32.

5-((4*S*,5*R*)-1-(4-Bromophenyl)-4,5-dihydro-4,5-diphenyl-1*H*-pyrazol-3-yl)-3-methyl-1-phenyl-1*H*-pyrazole-4-carbonitrile (6h)

Yellowish green crystals. Mp 170-171 °C. IR (KBr): 2208, 1589, 1548, 1485, 1360, 1303, 1199, 1135 cm^{-1}. UV (EtOH): λ_{max} (ε) = 370 (26832), 253 (31639). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.37 (s, 3H, Me), 4.18 (d, *J* = 4.6, 1H, H4), 5.03 (d, *J* = 4.6, 1H, H5), 6.66-7.42 (m, 19H, Ar-*H*). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.46, 62.32, 73.97, 113.09, 114.07, 115.38, 125.19, 126.10, 127.18, 128.19, 128.35, 129.08, 129.20, 129.38, 129.49, 131.62, 131.87, 137.27, 138.46, 139.37, 139.72, 140.43, 141.76, 152.90. MS *m/z* (%) : 557 (94) [M-H]$^-$, 559 (100) [M^+], 560 (22) [MH^+]. *Anal*. Calcd for $C_{32}H_{24}N_5Br$ (%)**:** C, 68.82; H, 4.33; N, 12.54. Found (%): C, 68.67; H, 4.23; N, 12.32.

Dimethyl 1-(4-b romophenyl)-3-(4-cyano-3-methyl-1-phenyl-1*H*-pyrazol-5-yl)-1*H*-pyrazole-4,5-dicarboxylate (7)

White amorphous solid. Mp 106-107 °C. IR (KBr): 2224, 1727, 1445, 1380, 1234, 1149 cm^{-1}. UV (EtOH): λ_{max} (ε) = 340 (9568), 256 (33384). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.53 (s, 3H, Me), 3.63 (s, 3H, CO_2Me), 3.80 (s, 3H, CO_2Me), 7.30-7.62 (m, 9H, Ar-*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.64, 52.22, 53.70, 96.53, 113.36, 115.40, 123.70, 124.30, 125.49, 128.53, 129.09, 132.64, 137.29, 138.00, 138.35, 138.87, 140.30, 152.65, 160.06, 160.56. MS *m/z* (%): 519 (18) [M^+], 520 (100) [MH^+], 522 (92) [MH^++1], 523 (26) [MH^++2]. *Anal*. Calcd for $C_{24}H_{18}N_5O_4Br$ (%)**:** C, 55.40; H, 3.48; N, 13.46. Found (%): C, 55.24; H, 3.41; N, 13.35.

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