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Tetrahedron 60 (2004) 3457–3464
Tetrahedron

α-Oxoketene dithioacetals mediated heteroaromatic annulation protocol for benzoheterocycles: an efficient regiocontrolled synthesis of highly substituted and annulated indazoles

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Received 23 November 2003; revised 26 January 2004; accepted 12 February 2004

Abstract—An efficient regiocontrolled synthesis of highly substituted and annulated indazoles involving base induced addition–elimination of 1,3-diphenyl-5-cyanomethylpyrazole to a variety of acyclic and cyclic α-oxoketene, followed by acid assisted cycloaromatization of the resulting conjugate adducts has been reported.

1. Introduction

Indazole and its derivatives have gained considerable importance in medicinal chemistry in view of their promising pharmacological properties.[1,2] Several indazoles are found to exhibit significant levels of activity as HIV protease inhibitors,[3,4] serotonin 5-$HT_{1\alpha}$, 5-HT_2[5] and 5-HT_3 receptor antagonists,[6,7] acetylcholinesterase inhibitors[8] and aldol reductase inhibitors,[9] whereas 1-[3-(dimethylamino)-propyl]-5-methyl-3-phenyl-1*H*-indazole (FS-32) has been shown to be a potent antidepressant drug candidate.[2] Several methods for the synthesis of indazoles and their derivatives have been reported in the literature,[1–3,10–12] most of them involving construction of the pyrazole moiety on pre-constructed benzenoid derivatives. On the other hand, the methods based on the more easily accessible pyrazole precursors are scantily described in the literature.[13] During the course of our heteroaromatic annulation[14] studies involving [3+3] cyclocondensation of α-oxoketene dithioacetals (1,3-bielectrophilic components) with various heteroallyl anions (1,3-binucleophilic components), we had demonstrated earlier that it is possible to tune up the reactivity of ambident heteroallyl anions derived from various methyl-substituted heterocycles towards α-oxoketene dithioacetals in either regiospecific 1,2-addition fashion or conjugate 1,4-addition–elimination pathway.[15] In general, the heteroallyl anions stabilized by electron withdrawing group such as nitrile are shown to add to α-oxoketene dithioacetals initially in conjugate addition–elimination fashion,[5h–i,15b] whereas the corresponding lithiomethyl species generated by deprotonation of methyl-substituted heterocycles were found to be less discriminate displaying either 1,2- or 1,4-addition pattern.[15d,e,15g,15j–m] Subsequent acid induced (or spontaneous) cycloaromatization of these adducts leads to the formation of either linearly substituted/annulated (1,2-addition) or angularly substituted/annulated (conjugate addition–elimination) benzoheterocycles (or bridged azaheterocycles) in highly regiospecific fashion.[14,15] We have shown in our earlier studies that the lithium 5-lithiomethyl-3-methylpyrazole-1-carboxylate generated by deprotonation-protection of 3,5-dimethylpyrazole undergoes 1,2-addition with various α-oxoketene dithioacetals to give carbinol acetals[15e] which on acid induced cycloaromatization afford the pyrazolo[1,5-*a*]pyridines instead of the expected indazoles via intramolecular cyclization at electron-rich nitrogen of the pyrazole ring rather than at C-4 position. We have also reported in our earlier work, the regiospecific deprotonation of 2,3-dimethyl-1-phenyl-pyrazolin-5-one (antipyrine) to give the corresponding 3-lithiomethyl species which was shown to undergo highly regioselective γ-1,4 addition to α-oxoketene dithioacetals followed by cycloaromatization in the presence of $BF_3{\cdot}Et_2O$ to afford a range of novel substituted and condensed indazolones in good yields.[13a] Also in a recent paper, we have developed another approach for substituted and fused indazolones by anionic [4+2] cycloaddition of dihydro-pyrazolin-5-one dienolate (generated by deprotonation of 2,3-dimethyl-4-formyl-1-phenylpyrazolin-5-one) with a variety of dienophiles.[13b] In continuation of these studies, we now report an efficient synthesis of angularly substituted

Keywords: α-Oxoketene dithioacetals; Heteroaromatic annulation; Benzoheterocycles; Indazoles.
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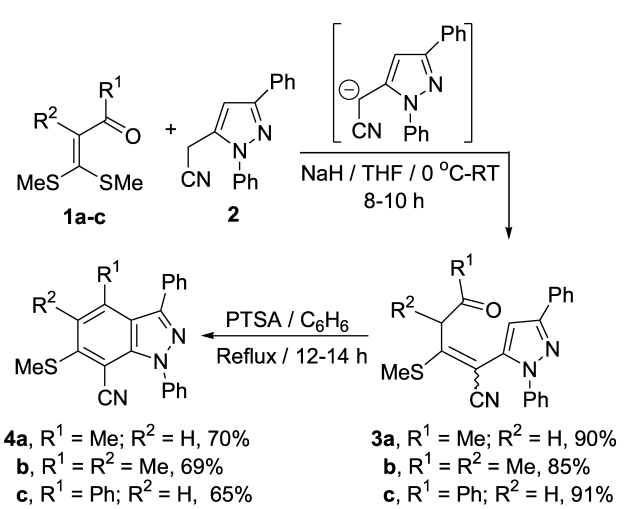
doi:10.1016/j.tet.2004.02.029

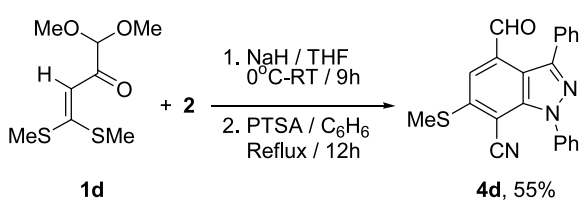
and fused indazoles involving base-induced conjugate addition of 1,3-diphenyl-5-cyanomethylpyrazole **2** with α-oxoketene dithioacetals followed by acid induced cycloaromatization of the resulting conjugate adducts.

2. Results and discussion

Our previous studies on the synthesis of carbazoles,[15i] indoles[15h] and benzothiophenes[15b] via [3+3] cycloaromatization of α-oxoketene dithioacetals with various heteroallyl anions have demonstrated that the cyano group is especially useful for stabilizing the negative charge on the heterocyclic side chain of 1,3-binucleophilic component. We therefore selected 1,3-diphenyl-5-cyanomethylpyrazole (**2**) as an anionic component in the present benzoannulation process. Thus in a typical experiment, the α-oxoketene dithioacetal **1a** was reacted with **2** in the presence of sodium hydride in THF at 0 °C to give the adduct **3a** (R^1=Me, R^2=H) in 90% yield. The adduct **3a** was purified by crystallization for spectral characterization which showed it to exist in the tautomeric β,γ-unsaturated keto form **3a** exclusively. The adduct **3a** was subjected to cycloaromatization in the presence of various protic (H_3PO_4, TFA, PTSA) and Lewis acids ($BF_3{\cdot}Et_2O$, $SnCl_4$), when the cyclization was found to be most efficient (in terms of yield and work-up) in the presence of *p*-toluenesulfonic acid (PTSA) in refluxing benzene yielding 7-cyano-1,3-diphenyl-4-methyl-6-(methylthio)indazole (**4a**) in 70% yield (Scheme 1). This reaction sequence could also be extended for the synthesis of other substituted indazole derivatives **4b-c** from the respective α-oxoketene dithioacetals **1b-c** in good yields with full regiocontrol of the substitutent positions (Scheme 1). Cycloaromatization of

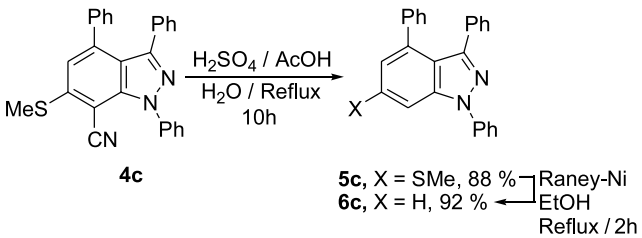


Scheme 1.



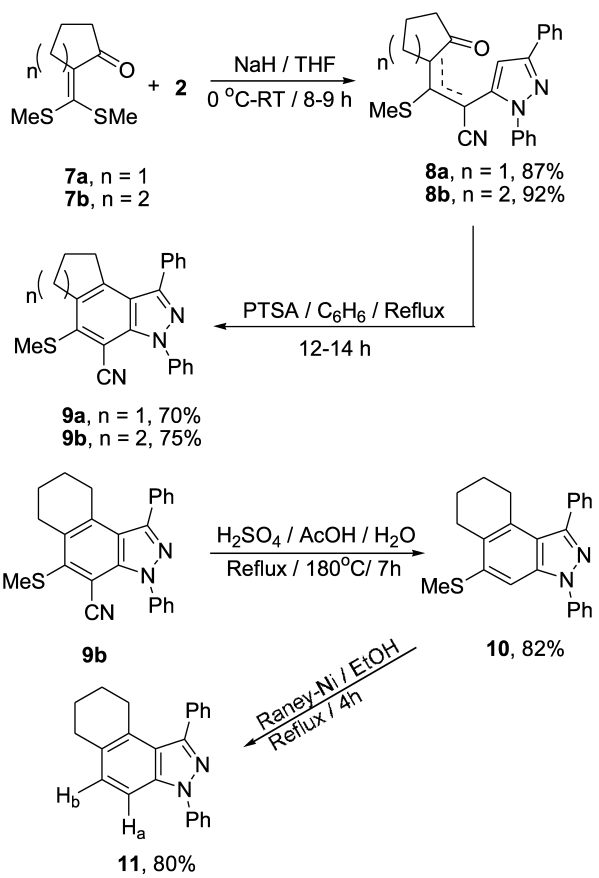
Scheme 2.

α-oxoketene dithioacetal **1d** (from pyruvaldehyde dimethylacetal) with **2** under similar conditions furnished directly the corresponding 7-cyano-4-formylindazole **4d** in 55% yield via in situ hydrolysis of the acetal group (Scheme 2). The structures of all these newly synthesized indazoles **4a-d** were established with the help of spectral and analytical data. In one of the experiments, the 7-cyanoindazole **4c** was subjected to acid induced hydrolysis–decarboxylation to give the corresponding 1,3,4-tris(phenyl)-6-(methylthio)indazole **5c** (88%), which on Raney-Ni dethiomethylation afforded the corresponding sulfur free indazole **6c** in 92% yield (Scheme 3).

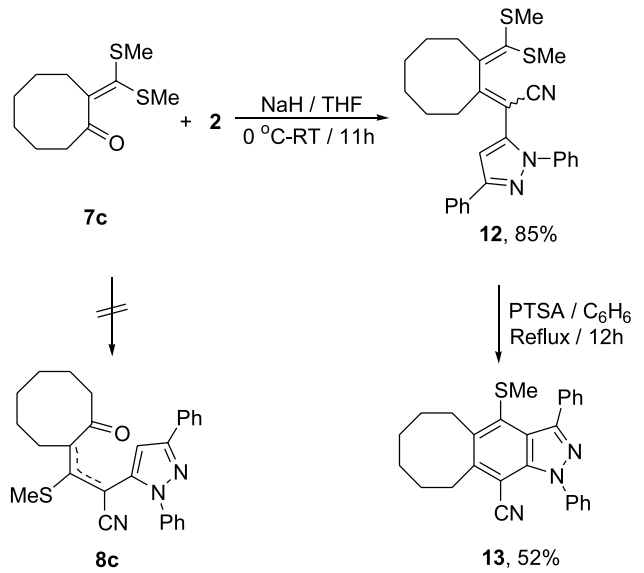


Scheme 3.

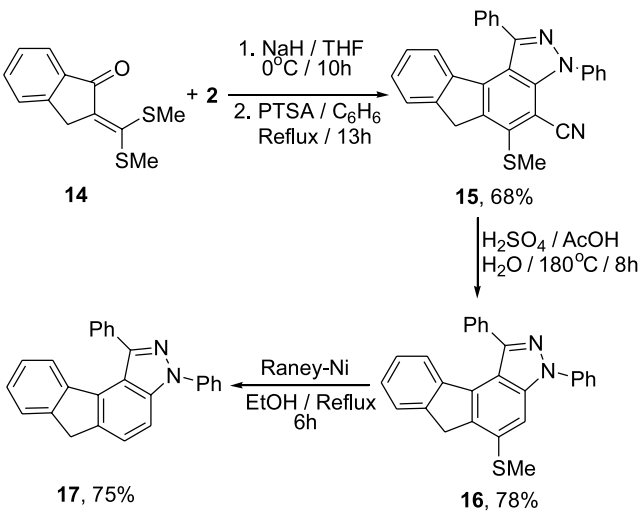
The conjugate addition–cycloaromatization protocol was next extended for the synthesis of annulated indazoles and the results are shown in Schemes 4–7. Thus, the base-induced conjugate addition of **2** with cyclic ketene dithioacetals **7a-b** from cyclopentanone and cyclohexanone, respectively, proceeded smoothly to give the respective adducts **8a-b** in high yields, these underwent facile



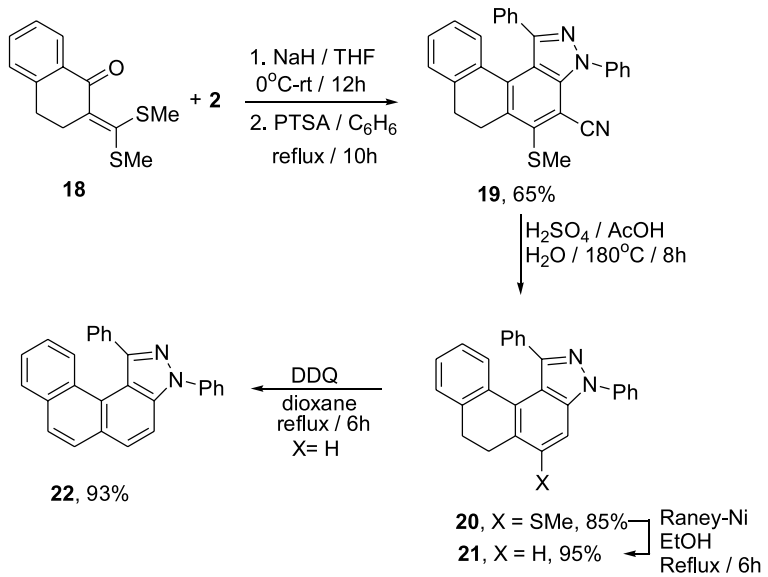
Scheme 4.



Scheme 5.



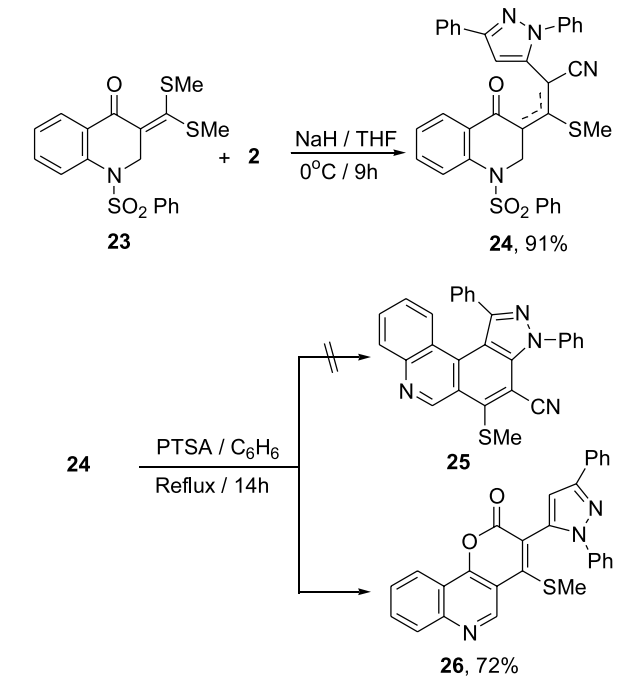
Scheme 6.



Scheme 7.

cyclization in the presence of PTSA/benzene yielding the corresponding tricyclic indazoles **9a**-**b** in 70 and 75% yields, respectively. The regiochemistry of one of the annulated indazole **9b** was established by its acid-induced hydrolysis–decarboxylation followed by reductive dethiomethylation of the resulting **10** to furnish 1,3-diphenyl-6,7,8,9-tetrahydrobenzo[*e*] indazole **11** in 80% yield (Scheme 4). The ^{1}H NMR spectrum of **11** displayed signals due to the two aromatic protons (H_a and H_b) as *ortho* coupled doublets (J=8.8 Hz) at δ 7.16 and 7.50, respectively, which unequivocally established the angular regiochemistry of the product **9b** formed through conjugate 1,4-addition–elimination of the carbanion from **2** with **7b**. Interestingly, the base-induced addition of the pyrazole **2** with ketene dithioacetal **7c** from cyclooctanone did not give the expected conjugate adduct **8c** and the product isolated (85%) was characterized as the adduct **12** formed by aldol condensation of pyrazoleacetonitrile **2** with **7c**. Apparently, the conformationally flexible cyclooctane ring of **7c** disturbs the planar structure of its enone functionality resulting in the nucleophilic attack of the carbanion derived from **2** on more electrophilic carbonyl group to give the aldol condensation product **12** exclusively. Subsequent cycloaromatization of **12** (via electrocyclization) on prolonged refluxing in benzene in the presence of PTSA afforded the corresponding linearly fused indazole **13** in 52% yield (Scheme 5). The structure of **13** was fully established with help of spectral and analytical data.

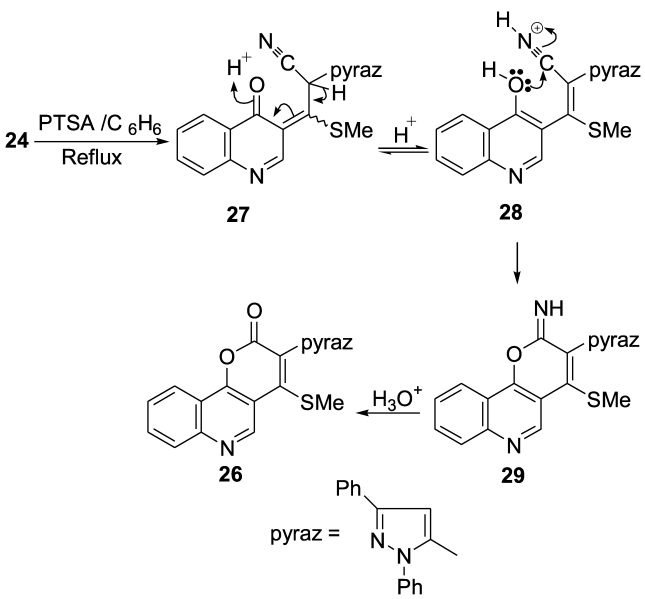
The versatility of our heteroaromatic annulation protocol was further demonstrated by the synthesis of tetracyclic angularly fused indazoles **15** and **19** by extrapolation of this reaction sequence under standard conditions to α-oxoketene dithioacetals **14** and **18** derived from indan-1-one and α-tetralone, respectively (Schemes 6 and 7). The annulated indazoles **15** and **19** on sequential hydrolysis–decarboxylation and Raney-Ni dethiomethylation of the resulting **16** and **20** under earlier reported conditions afforded the corresponding sulfur free tetracyclic angularly fused indazoles **17** and **21** in overall high yields (Schemes 6 and 7). The dihydroindazole **21** was transformed into the



Scheme 8.

corresponding fully aromatic tetracyclic indazole **22** (93%) by dehydrogenation with DDQ (Scheme 7). The structures of all the newly synthesized indazoles **15**-**17** and **19**-**22** were established with the help of spectral and analytical data.

Finally, we have extended our studies to oxoketene dithioacetal **23** obtained from *N*-(benzenesulfonyl)-4-quinolone with a view to synthesize the tetracyclic azaindazole framework **25** (Scheme 8). Thus, the ketene dithioacetal **23** underwent facile base-induced conjugate-addition–elimination with **2** to afford the corresponding adduct **24** in nearly quantitative yield. However, the acid-induced cycloaromatization of **24** under earlier described conditions did not yield the expected tetracyclic azaindazole



Scheme 9.

25, the product (72%) isolated after work-up was characterized as the pyrano[3,2-*c*]quinoline **26** on the basis of its spectral and analytical data. Our attempts to obtain indazole **25** from **24** in the presence of other protic and Lewis acids were not successful yielding only intractable reaction mixtures. The possible mechanism for the formation of the observed product **26** from **24** is shown in Scheme 9. The hydroxyquinoline intermediate **28** formed by debenzenesulfonylation[16] and tautomerization of the adduct **24** (via intermediate **27**) undergoes intramolecular nucleophilie attack of hydroxy group on nitrile functionality to give imine intermediate **29** which on subsequent hydrolysis affords the pyrano[3,2-*c*]quinoline **26** (Scheme 9).

3. Conclusion

In summary, the two steps [3+3] annulation of 1,3-diphenyl-5-cyanomethylindazole (**2**) with a range of α-oxoketene dithioacetals affords a variety of novel substituted and annulated indazoles in good yields with high regioselectivity. The above study has clearly demonstrated that the α-oxoketene dithioacetal mediated aromatic and heteroaromatic annulation protocol[14a] provides a general route for the construction of complex heteroaromatics from easily available precursors in highly regioselective manner. In view of the wide range of biological activities displayed by indazole derivatives, the above methodology can be extended for generating library of substituted indazoles. Our efforts in this direction are in progress.

4. Experimental

4.1. General

^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded in $CDCl_3$ and TMS was used as an internal standard. Melting points were uncorrected. Chromatographic purification was conducted by column chromatography using 100–200 mesh silica gel obtained from standard firms. Raney-Nickel was prepared according to the reported method.[17] The 1,3-diphenyl-5-cyanomethylpyrazole (**2**) was prepared according to literature method.[18] The known α-oxoketene dithioacetals were prepared according to the earlier reported procedure.[14a,19]

4.2. General procedure for base induced addition of 1,3-diphenyl-5-cyanomethylpyrazole (2) to α-oxoketene dithioacetals

A solution of 1,3-diphenyl-5-cyanomethylpyrazole (**2**) (0.57 g, 2.2 mmol) in THF (15 mL) was added dropwise to a stirring suspension of NaH (0.1 g, 2.4 mmol, 60%) in THF (15 mL) at 0 °C under N_2 atmosphere. After 1 h, a solution of the appropriate α-oxoketene dithioacetal (2 mmol) in THF (15 mL) was slowly added at 0 °C and the reaction mixture was allowed to warm to room temperature with stirring during 8–10 h. It was then poured into cold saturated ammonium chloride solution (50 mL) and extracted with DCM (3×20 mL). The organic layer was washed with H_2O (3×50 mL), brine (50 mL), dried

(Na_2SO_4) and the solvent evaporated in vacuo. A few of the adducts **3a**, **3c** and **12** were purified by crystallization (ether–DCM) for characterization and their spectral and analytical data are given below. The other adducts were used as such for further cyclization.

4.2.1. 2-(1,3-Diphenyl-1*H*-5-pyrazolyl)-3-methylthio-5-oxo-hexen-2-carbonitrile (3a). Yield (0.56 g, 75%, isolated yield) as a pale yellow solid, mp 151–2 °C; [found: C, 70.78; H, 5.11; N, 11.29. $C_{22}H_{19}N_3SO$ requires C, 70.75; H, 5.13; N, 11.25%]; R_f (20% EtOAc/hexane) 0.38; ν_{max}(KBr) 3066, 2924, 2201, 1719, 1498 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.81–7.87 (2H, m, ArH), 7.57–7.60 (2H, m, ArH), 7.49–7.45 (2H, m, ArH), 7.39–7.43 (3H, m, ArH), 7.30–7.34 (1H, m, ArH), 6.87 (1H, s, ArH), 3.89 (2H, s, C*H*$_2$), 2.23 (3H, s, SC*H*$_3$), 2.22 (3H, s, C*H*$_3$); δ_C (100 MHz, $CDCl_3$) 200.8 (C=O), 160.2 (*C*(SCH$_3$)=C(CN)), 152.1 (C), 139.1 (C), 134.0 (C), 132.4 (C), 129.2 (CH), 128.6 (CH), 128.3 (CH), 128.2 (CH), 125.7 (CH), 124.3 (CH), 115.9 (CN), 107.2 (CH), 98.9 (C(SCH$_3$)=*C*(CN)), 48.7 (CH_2), 29.5 (CH_3), 15.0 (SCH_3); *m*/*z* 374 (100 MH^+).

4.2.2. 2-(1,3-Diphenyl-1*H*-5-pyrazolyl)-3-methylthio-5-oxo-5-phenyl-penten-2-carbonitrile (3c). Yield (0.61 g, 70%) as a colourless solid, mp 169–170 °C; [found: C, 74.41; H, 4.90; N, 9.68. $C_{27}H_{21}N_3SO$ requires C, 74.46; H, 4.86; N, 9.65%]; R_f (20% EtOAc/hexane) 0.30; ν_{max} (KBr) 3059, 2923, 2199, 1680, 1593, 1535 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 8.00 (2H, d, *J*=8.0 Hz, ArH), 7.90 (2H, d, *J*=8.0 Hz, ArH),7.69 (2H, d, *J*=8.3 Hz, ArH), 7.64 (1H, t, *J*=7.8 Hz, ArH), 7.51 (4H, dt, *J*=1.7, 7.8 Hz, ArH), 7.40–7.45 (3H, m, ArH), 7.33–7.38 (1H, m, ArH), 6.96 (1H, s, ArH), 4.52 (2H, s, C*H*$_2$), 2.22 (3H, s, SC*H*$_3$); δ_C (100 MHz, $CDCl_3$) 192.6 (C=O), 160.8 (*C*(SCH$_3$)=C(CN)), 152.0 (C), 139.2 (C), 135.5 (C), 134.17 (CH), 134.11 (C), 132.6 (C), 129.2 (CH), 128.9 (CH), 128.7 (CH), 128.20 (CH), 128.18 (CH), 128.08 (CH), 125.8 (CH), 124.2 (CH), 115.9 (CN), 107.5 (CH), 99.4 (C(SCH$_3$)=*C*(CN)), 44.1 (CH_2), 15.2 (SCH_3); *m*/*z* 436 (100 MH^+).

4.2.3. 2-[2-Bis(methylthio)methylenecyclooctylidene]-2-(1,3-diphenyl-1*H*-5-pyrazolyl) acetonitrile (12). Yield (0.80 g, 85%) as a yellow solid, mp 158–9 °C; [found: C, 71.33; H, 6.16; N, 8.95. $C_{28}H_{29}N_3S_2$ requires C, 71.30; H, 6.20; N, 8.91%]; R_f (40% EtOAc/hexane) 0.28; ν_{max}(KBr) 2919, 2210, 1666, 1595 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.92 (2H, d, *J*=7.8 Hz, ArH), 7.78 (2H, d, *J*=7.8 Hz, ArH), 7.39–7.50 (4H, m, ArH), 7.29–7.33 (2H, m, ArH), 6.85 (1H, s, ArH), 2.56–2.62 (1H, m, C*H*), 2.44–2.49 (1H, m, C*H*), 2.26–2.32 (1H, m, C*H*$_2$), 2.24 (3H, s, SC*H*$_3$), 2.09–2.14 (1H, m, C*H*$_2$), 1.96 (3H, s, SCH_3), 1.76–1.79 (2H, m, C*H*$_2$), 1.52–1.73 (6H, m, C*H*$_2$); δ_C (100 MHz, $CDCl_3$) 166.8 (C), 155.6 (C), 151.9 (C), 140.0 (C), 139.2 (C), 134.8 (C), 133.0 (C), 131.9 (C), 128.7 (CH), 128.5 (CH), 127.9 (CH), 127.5 (CH), 125.8 (CH), 124.4 (CH), 118.8 (CN), 106.4 (CH), 34.3 (CH_2), 29.1 (CH_2), 28.9 (CH_2), 28.0 (CH_2), 27.1 (CH_2), 24.8 (CH_2), 14.8 (SCH_3), 14.3 (SCH_3).

4.3. General procedure for the synthesis of substituted indazoles 4a-d, 9a-b, 13, 15, 19 and pyranoquinoline 26

To a solution of adduct (ca. 1 mmol) in dry benzene (25 mL), *p*-toluenesulphonic acid (0.35 g, 2 mmol) was added and the reaction mixture was refluxed with stirring for 10–14 h (monitored by TLC). It was neutralized with $NaHCO_3$ solution and extracted with benzene (3×20 mL). The combined extracts were washed with H_2O (3×100 mL), brine (100 mL), dried (Na_2SO_4) and the solvent evaporated at reduced pressure. The crude product was purified by column chromatography using EtOAc/hexane (1:9) as eluent to give pure indazole.

4.3.1. 7-Cyano-1,3-diphenyl-4-methyl-6-methylthio-1*H*-indazole (4a). Yield (0.25 g, 70%) as a colourless solid, mp 167–8 °C; [found: C, 74.39; H, 4.84; N, 11.80. $C_{22}H_{17}N_3S$ requires C, 74.34; H, 4.82; N, 11.82%]; R_f (20% EtOAc/hexane) 0.58; ν_{max}(KBr) 2918, 2211, 1514, 1433 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.53–7.59 (6H, m, ArH), 7.50–7.52 (2H, m, ArH), 7.45–7.46 (2H, m, ArH), 6.91 (1H, s, ArH), 2.60 (3H, s, SC*H*$_3$), 2.39 (3H, s, C*H*$_3$); δ_C (100 MHz, $CDCl_3$) 148.1 (C), 146.6 (C), 139.8 (C), 138.7 (C), 138.0 (C), 132.9 (C), 129.9 (CH), 129.4 (CH), 128.8 (CH), 128.7 (CH), 128.0 (CH), 127.3 (CH), 121.2 (C), 120.4 (CH), 113.7 (CN), 90.3 (C), 20.7 (CH_3), 16.2 (SCH_3); *m*/*z* 355 (80 M^+), 352 (100 $M-3^+$).

4.3.2. 7-Cyano-4,5-dimethyl-1,3-diphenyl-6-methylthio-1*H*-indazole (4b). Yield (0.26 g, 69%) as a colourless solid, mp 165–6 °C; [found: C, 74.73; H, 5.21; N, 11.40. $C_{23}H_{19}N_3S$ requires C, 74.77; H, 5.18; N, 11.37%]; R_f (20% EtOAc/hexane) 0.54; ν_{max}(KBr) 2922, 2219, 1653, 1573, 1497 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.57–7.59 (4H, m, ArH), 7.51–7.56 (4H, m, ArH), 7.46–7.49 (2H, m, ArH), 2.62 (3H, s, SC*H*$_3$), 2.48 (3H, s, C*H*$_3$), 2.36 (3H, s, C*H*$_3$); δ_C (100 MHz, $CDCl_3$) 147.7 (C), 142.9 (C), 138.3 (C), 138.1 (C), 137.3 (C), 133.5 (C), 133.4 (C), 130.2 (CH), 129.4 (CH), 128.8 (CH), 128.6 (CH), 128.2 (CH), 127.5 (CH), 123.8 (C), 114.9 (CN), 98.2 (C), 19.8 (CH_3), 18.16 (CH_3), 17.4 (SCH_3); *m*/*z* 369 (100 M^+), 354 (21).

4.3.3. 7-Cyano-6-methylthio-1,3,4-tris(phenyl)-1*H*-indazole (4c). Yield (0.27 g, 65%) as a colourless solid, mp 201–2 °C; [found: C, 77.71; H, 4.61; N, 10.02. $C_{27}H_{19}N_3S$ requires C, 77.67; H, 4.59; N, 10.06%]; R_f (20% EtOAc/hexane) 0.59; ν_{max}(KBr) 3060, 2920, 2214, 1496, 1425 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.62–7.64 (2H, m, ArH), 7.57–7.59 (2H, m, ArH), 7.56 (1H, s, ArH), 7.22 (1H, t, *J*=7.1 Hz, ArH), 7.12–7.18 (4H, m, ArH), 7.08–7.10 (4H, m, ArH), 7.01–7.05 (2H, m, ArH), 2.63 (3H, s, SC*H*$_3$); δ_C (100 MHz, $CDCl_3$) 148.0 (C), 146.6 (C), 142.1 (C), 140.6 (C), 138.1 (C), 137.5 (C), 132.1 (C), 129.6 (CH), 129.3 (CH), 129.1 (CH), 128.9 (CH,), 128.2 (CH), 127.8 (CH), 127.7 (CH), 127.6 (CH), 127.4 (CH), 120.2 (CH), 119.1 (C), 113.6 (CN), 91.2 (C), 16.3 (SCH_3); *m*/*z* 417 (100, M^+), 370 (20).

4.3.4. 7-Cyano-1,3-diphenyl-4-formyl-6-methylthio-1*H*-indazole (4d). Yield (0.20 g, 55%) as a yellow solid, mp 200–1 °C; [found: C, 71.49; H, 4.11; N, 11.42. $C_{22}H_{15}N_3SO$ requires C, 71.52; H, 4.09; N, 11.37%]; R_f (20% EtOAc/hexane) 0.45; ν_{max}(KBr) 2922, 2854, 2212, 1695, 1570, 1496 cm^{-1}; δ_H (400 MHz, $CDCl_3$), 10.34 (1H, s, C*H*O), 7.74 (1H, s, ArH), 7.66–7.69 (2H, m, ArH), 7.58–7.61 (5H, m, ArH), 7.52–7.55 (3H, m, ArH), 2.70 (3H, s, SC*H*$_3$); δ_C (100 MHz, $CDCl_3$) 188.8 (*C*HO), 147.8 (C), 146.6 (C),

141.1 (C), 137.5 (C), 133.1 (C), 131.9 (C), 130.1 (CH), 129.5 (CH), 129.4 (CH), 129.1 (CH), 129.0 (CH), 127.63 (CH), 127.59 (C), 120.5 (C), 117.5 (CH), 112.6 (CN), 16.1 (SCH_3); *m/z* 370 (100 MH^+), 342 (20).

4.3.5. 4-Cyano-1,3-diphenyl-5-methylthio-3,6,7,8-tetrahydrocyclopenta[*e*]indazole (9a). Yield (0.29 g, 70%) as a colourless solid, mp 197–8 °C; [found: C, 75.59; H, 5.04; N, 11.08. $C_{24}H_{19}N_3S$ requires C, 75.56; H, 5.02; N, 11.01%]; R_f (20% EtOAc/hexane) 0.59; ν_{max}(KBr) 2980, 2949, 2831, 2217, 1586, 1553, 1498 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.68 (2H, dd, *J*=2.0, 8.0 Hz, ArH), 7.56–7.60 (3H, m, ArH), 7.52–7.55 (2H, m, ArH), 7.43–7.51 (3H, m, ArH), 3.13 (4H, quint, *J*=7.8, CH_2–CH_2–CH_2), 2.56 (3H, s, SCH_3), 2.14 (2H, q, *J*=7.6 Hz, CH_2–CH_2–CH_2); δ_C (100 MHz, $CDCl_3$) 147.2 (C), 142.9 (C), 141.3 (C), 140.4 (C), 139.9 (C), 138.3 (C), 132.2 (C), 129.5 (CH), 129.4 (CH), 128.8 (CH), 128.7 (CH), 128.3 (CH), 127.5 (CH), 120.7 (C), 114.7 (CN), 96.5 (C), 34.3 (CH_2), 32.8 (CH_2), 24.8 (CH_2), 18.9 (SCH_3); *m/z* 381 (100 M^+), 366 (40), 333 (26), 289 (20).

4.3.6. 4-Cyano-1,3-diphenyl-5-methylthio-6,7,8,9-tetrahydro-3*H*-benzo[*e*]indazole (9b). Yield (0.30 g, 70%) as a colourless solid, mp 198–9 °C; [found: C, 75.95; H, 5.39; N, 10.64. $C_{25}H_{21}N_3S$ requires C, 75.92; H, 5.35; N, 10.62%]; R_f (20% EtOAc/hexane) 0.42; ν_{max}(KBr) 2941, 2856, 2217, 1595, 1569, 1496 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.54–7.60 (5H, m, ArH), 7.50–7.52 (3H, m, ArH), 7.45–7.47 (2H, m, ArH), 3.06 (2H, t, *J*=6.4 Hz, CH_2), 2.75 (2H, t, *J*=6.4 Hz, CH_2), 2.51 (3H, s, SCH_3), 1.82–1.88 (2H, m, CH_2), 1.63–1.69 (2H, m, CH_2); δ_C (100 MHz, $CDCl_3$) 147.7 (C), 143.9 (C), 138.19 (C), 138.16 (C), 138.0 (C), 133.8 (C), 133.3 (C), 130.1 (CH), 129.4 (CH), 128.8 (CH), 128.6 (CH), 128.1 (CH), 127.5 (CH), 122.9 (C), 114.7 (CN), 98.4 (C), 28.9 (CH_2), 28.6 (CH_2), 22.9 (CH_2), 21.8 (CH_2), 19.6 (SCH_3); *m/z* 396 (100 MH^+), 380 (43), 348 (20).

4.3.7. 11-Cyano-1,3-diphenyl-4-methylthio-5,6,7,8,9,10-hexahydro-1*H*-cycloocta[*f*]indazole (13). Yield (0.22 g, 52%) as a colourless solid, mp 197–8 °C; [found: C, 76.51; H, 5.99; N, 9.97. $C_{27}H_{25}N_3S$ requires C, 76.56; H, 5.95; N, 9.92%]; R_f (20% EtOAc/hexane) 0.52; ν_{max}(KBr): 2924, 2218, 1594, 1499 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.60–7.62 (2H, m, ArH), 7.52–7.58 (5H, m, ArH), 7.43–7.49 (3H, m, ArH), 3.24 (2H, t, *J*=6.1 Hz, CH_2), 2.94 (2H, t, *J*=6.1 Hz, CH_2), 2.55 (3H, s, SCH_3), 1.76–1.78 (2H, m, CH_2), 1.40–1.43 (2H, m, CH_2), 1.26–1.32 (4H, m, CH_2); δ_C (100 MHz, $CDCl_3$) 147.6 (C), 143.2 (C), 142.5 (C), 138.6 (C), 138.2 (C), 137.5 (C), 133.9 (C), 130.1 (CH), 129.4 (CH), 128.83 (CH), 128.78 (CH), 128.1 (CH), 127.5 (CH), 123.1 (C), 114.9 (CN), 98.8 (C), 31.3 (CH_2), 31.1 (CH_2), 28.8 (CH_2), 28.5 (CH_2), 26.5 (CH_2), 25.9 (CH_2), 20.8 (SCH_3); *m/z* 424 (100, MH^+).

4.3.8. 4-Cyano-1,3-diphenyl-5-methylthio-3,6-dihydroindeno[1,2-*e*]indazole (15). Yield (0.29 g, 68%) as a colourless solid, mp 267–8 °C; [found: C, 79.25; H, 4.49; N, 9.80. $C_{28}H_{19}N_3S$ requires C, 79.29; H, 4.46; N, 9.78%]; R_f (20% EtOAc/hexane) 0.60; ν_{max}(KBr) 3054, 2919, 2214, 1555, 1497 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.64–7.67 (4H, m, ArH), 7.56–7.61 (5H, m, ArH), 7.51–754 (2H, m, ArH), 7.31 (1H, t, *J*=7.8 Hz, ArH), 6.99 (1H, t, *J*=7.8 Hz, ArH), 6.57 (1H, d, *J*=7.8 Hz, ArH), 4.15 (2H, s, CH_2), 2.66 (3H, s, SCH_3); δ_C (100 MHz, $CDCl_3$) 147.0 (C), 145.2 (C), 141.3 (C), 140.6 (C), 139.8 (C), 139.5 (C), 139.4 (C), 138.3 (C), 134.1 (C), 130.5 (CH), 129.8 (CH), 129.2 (CH), 128.9 (CH), 128.5 (CH), 128.2 (CH), 127.8 (CH), 126.6 (CH), 126.4 (CH), 124.6 (CH), 118.7 (C), 113.8 (CN), 96.6 (C), 38.3 (CH_2), 19.2 (SCH_3); *m/z* 430 (100 MH^+), 414 (20), 279 (20).

4.3.9. 4-Cyano-1,3-diphenyl-5-methylthio-6,7-dihydro-3*H*-naphtho[1,2-*e*]indazole (19). Yield (0,29 g, 65%) as a colourless solid, mp 220–1 °C; [found: C, 78.49; H, 4.81; N, 9.50. $C_{29}H_{21}N_3S$ requires C, 78.53; H, 4.77; N, 9.47%]; R_f (20% EtOAc/hexane) 0.50; ν_{max}(KBr) 3210, 3062, 2924, 2214, 1594, 1539 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.62–7.66 (2H, m, ArH), 7.54–7.62 (3H, m, ArH), 7.24–7.29 (4H, m, ArH), 7.16–7.19 (2H, m, ArH), 7.12 (1H, t, *J*=7.6 Hz, ArH), 6.83 (1H, d, *J*=7.6 Hz, ArH), 6.59 (1H, t, *J*=7.6Hz, ArH), 3,23 (2H, t, *J*=6.8 Hz, CH_2), 2.92 (2H, t, *J*=6.8 Hz, CH_2), 2.51 (3H, s, SCH_3); δ_C (100 MHz, $CDCl_3$) 147.3 (C), 141.4 (C), 140.5 (C), 138.9 (C), 138.3 (C), 136.6 (C), 135.7 (C), 133.2 (C), 131.2 (CH), 130.9 (C), 129.7 (CH), 129.5 (CH), 128.9 (CH), 128.7 (CH), 128.0 (CH), 127.9 (CH), 127.8 (CH), 126.7 (CH), 125.0 (CH), 119.2 (C), 114.7 (CN), 98.7 (C), 29.2 (CH_2), 27.4 (CH_2), 19.6 (SCH_3); *m/z* 444 (MH^+).

4.3.10. 3-(1,3-Diphenyl-1*H*-5-pyrazolyl)-4-methylthio-2*H*-pyrano[3,2-*c*]quinolin-2-one (26). Yield (0.33 g, 72%) as a yellow solid, mp 224–225 °C; [found: C, 72.91; H, 4.19; N, 9.12. $C_{28}H_{19}N_3O_2S$ requires C, 72.87; H, 4.15; N, 9.10%]; R_f (20% EtOAc/hexane) 0.35; ν_{max}(KBr) 3048, 2928, 1723, 1594, 1567 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 9.37 (1H, s, ArH), 8.47 (1H, d, *J*=8.3 Hz, ArH), 8.17 (1H, d, *J*=8.3 Hz, ArH), 7.94 (2H, d, *J*=7.6 Hz, ArH), 7.89 (1H, t, *J*=7.7 Hz, ArH), 7.71 (1H, t, *J*=7.7 Hz, ArH), 7.56 (2H, d, *J*=7.6 Hz, ArH), 7.40–7.46 (2H, m, ArH), 7.36–7.39 (2H, m, ArH), 7.29–7.34 (2H, m, ArH), 6.99 (1H, s, ArH), 2.18 (3H, s, SCH_3); δ_C (100 MHz, $CDCl_3$) 157.2 (C=O), 155.1 (C), 154.9 (C), 152.3 (C), 148.8 (C), 147.0 (CH), 140.1 (C), 135.6 (C), 132.58 (CH), 132.53 (CH), 129.3 (CH), 129.0 (C), 128.7 (CH), 128.3 (CH), 128.2 (CH), 127.9 (CH), 125.9 (CH), 123.4 (CH), 122.5 (CH), 117.4 (C), 117.1 (C), 110.7 (C), 108.6 (CH), 17.1 (SCH_3); *m/z* 462 (100 MH^+), 414 (20) 386 (20).

4.4. General procedure for acid induced hydrolysis–decarboxylation indazoles 4c, 9b, 15 and 19

A solution of the respective indazole (1 mmol) in glacial AcOH/H_2O/conc. H_2SO_4 (1:1:1, 10 mL) was refluxed at 180 °C for 7–10 h (monitored by TLC). It was cooled and neutralized with sat. $NaHCO_3$ solution and extracted with DCM (3×25 mL), and the extract washed with H_2O (50 mL), brine (50 mL), dried (Na_2SO_4) and the solvent evaporated in vacuo to give crude product which was purified by column chromatography over silica gel using EtOAc/hexane (1:20) as eluent.

4.4.1. 6-Methylthio-1,3,4-tris(phenyl)-1*H*-7-indazole (5c). Yield (0.35 g, 88%) as a colourless solid, mp 189–190 °C; [found: C, 79.58; H, 5.17; N, 7.19. $C_{26}H_{20}N_2S$ requires C, 79.56; H, 5.14; N, 7.14%]; R_f (20% EtOAc/

hexane) 0.65; ν_{max}(KBr) 3048, 2919, 1962, 1592, 1493 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.79 (2H, d, J=7.3 Hz, ArH), 7.55–7.59 (3H, m, ArH), 7.40 (1H, t, J=7.6 Hz, ArH), 7.13–7.19 (6H, m, ArH), 7.12 (1H, d, J=1.4 Hz, ArH), 7.09 (2H, d, J=7.3 Hz, Ar H), 7.05 (2H, d, J=7.6 Hz, ArH), 2.57 (3H, s, SCH_3); δ_C (100 MHz, $CDCl_3$) 147.6 (C), 141.3 (C), 139.8 (C), 138.7 (C), 138.5 (C), 137.4 (C), 133.1 (C), 129.5 (CH), 129.32 (CH), 129.30 (CH), 127.6 (CH), 127.33 (CH), 127.28 (CH), 127.23 (CH), 127.0 (CH), 123.5 (CH), 122.43 (CH), 118.9 (C), 105.8 (CH), 16.1 (SCH_3); *m/z* 393 (100 MH^+), 392 (80, M^+).

4.4.2. 1,3-Diphenyl-5-methylthio-6,7,8,9-tetrahydro-3*H*-benzo[*e*]indazole (10). Yield (0.30 g, 82%) as a colourless solid, mp 151–152 °C; [found: C, 77.71; H, 5.94; N, 7.60. $C_{24}H_{22}N_2S$ requires C, 77.80; H, 5.98; N, 7.56%]; R_f (20% EtOAc/hexane) 0.58; ν_{max}(KBr) 3053, 2937, 1956, 1588, 1497 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.75 (2H, d, J=7.6 Hz, ArH), 7.59–7.62 (2H, m, ArH), 7.53 (2H, t, J=7.8 Hz, ArH), 7.43–7.48 (3H, m ArH), 7.35 (1H, t, J=7.8 Hz ArH), 7.32 (1H, s, ArH), 2.75 (2H, t, J=6.3 Hz CH_2), 2.69 (2H, t, J=6.3 Hz, CH_2) 2.49 (3H, s, SCH_3), 1.83–1.87 (2H, m, CH_2), 1.64–1.68 (2H, m, CH_2); δ_C [100 MHz, $CDCl_3$] 147.6 (C), 140.4 (C), 139.9 (C), 138.7 (C), 134.8 (C), 131.2 (C), 130.2 (CH), 129.5 (CH), 128.2 (CH), 127.9 (CH), 127.6 (C), 126.6 (CH), 123.2 (CH), 120.2 (C), 102.3 (CH), 28.4 (CH_2), 26.6 (CH_2), 22.9 (CH_2), 22.3 (CH_2), 15.3 (SCH_3); *m/z* 372 (100, MH^+) 323 (25).

4.4.3. 1,3-Diphenyl-5-methylthio-3,6-dihydroindeno[1,2-*e*]indazole (16). Yield (0.32 g, 78%) as a colourless solid, mp 172–3 °C; [found: C, 80.13; H, 5.01; N, 6.94. $C_{27}H_{20}N_2S$ requires C, 80.16; H, 4.98; N, 6.92%]; R_f (20% EtOAc/hexane) 0.60; ν_{max}(KBr) 3042, 2914, 1592, 1497 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.80 (2H, d, J=8.0 Hz, ArH), 7.69 (2H, d, J=6.4 Hz, ArH), 7.50–7.59 (6H, m, ArH), 7.48 (1H, s, ArH), 7.41 (1H, t, J=7.3 Hz, ArH), 7.21 (1H, t, J=7.8 Hz, ArH), 6.96 (1H, t, J=7.8 Hz, ArH), 6.56 (1H, d, J=7.8 Hz, ArH), 3.89 (2H, s, CH_2), 2.60 (3H, s, SCH_3); δ_C (100 MHz, $CDCl_3$) 146.9 (C), 144.1 (C), 141.5 (C), 140.9 (C), 140.0 (C), 135.9 (C), 135.6 (C), 135.2 (C), 134.4 (C), 130.6 (CH), 129.6 (CH), 128.8 (CH), 128.2 (CH), 127.0 (CH), 126.3 (CH), 126.2 (CH), 125.1 (CH), 124.3 (CH), 123.7 (CH), 116.8 (C), 103.5 (CH), 36.6 (CH_2), 15.0 (SCH_3); *m/z* 406 (100, M2H^+), 405 (90, MH^+), 357 (20).

4.4.4. 1,3-Diphenyl-5-methylthio-6,7-dihydro-3*H*-naphtho[1,2-*e*]indazole (20). Yield (0.36 g, 85%) as colourless solid, mp 192–3 °C; [found: C, 80.39; H, 5.27; N, 6.72. $C_{28}H_{22}N_2S$ requires C, 80.35; H, 5.30; N, 6.69%]; R_f (20% EtOAc/hexane) 0.65; ν_{max}(KBr) 3046, 2950, 2833, 1595, 1544, 1494 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.8 (2H, d, J=8.0 Hz, ArH), 7.57 (2H, t, J=8.0 Hz, ArH), 7.52 (1H, s, ArH), 7.37–7.43 (2H, m, ArH), 7.19–7.28 (5H, m, ArH), 7.05 (1H, t, J=7.6 Hz, ArH), 6.82 (1H, d, J=7.6 Hz, ArH), 6.59 (1H, t, J=7.6 Hz, ArH), 2.89–2.96 (4H, m, CH_2–CH_2), 2.52 (3H, s, SCH_3); δ_C (100 MHz, $CDCl_3$) 147.1 (C), 141.0 (C), 139.9 (C), 137.9 (C), 137.8 (C), 134.3 (C), 131.8 (C), 131.6 (C), 130.7 (CH), 130.0 (C), 129.6 (CH), 129.5 (CH), 127.7 (CH), 127.6 (CH), 127.0 (CH), 126.9 (CH), 126.5 (CH), 124.8 (CH), 123.6 (CH), 116.6 (C), 105.0 (CH), 29.1 (CH_2), 25.7 (CH_2), 16.0 (SCH_3); *m/z* 419 (100 MH^+), 418 (90, M^+), 370 (25).

4.5. General procedure for dethiomethylation of indazoles 5c, 10, 16 and 20 with Raney Nickel

To a solution of corresponding indazole (1 mmol) in ethanol (30 mL), was added Raney Nickel (W4, four times by weight) and the suspension was stirred at 70–80 °C for 2–6 h (monitored by TLC). The reaction mixture was filtered through sintered funnel and the residue was washed with ethanol. The filtrate was concentrated in vacuo and passed through small silica gel column using 2% EtOAc/hexane as eluent.

4.5.1. 1,3,4-Tris(phenyl)-1*H*-7-indazole (6c). Yield (0.32 g, 92%) as a colourless solid, mp 159–60 °C; [found: C, 86.71; H, 5.21; N, 8.11. $C_{25}H_{18}N_2$ requires C, 86.68; H, 5.24; N, 8.09%]; R_f (20% EtOAc/hexane) 0.68; ν_{max}(KBr) 3071, 1591, 1563, 1495, 1444 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.76–7.82 (3H, m, ArH), 7.53–7.57 (2H, m, ArH), 7.48–7.52 (1H, m, ArH), 7.37 (1H, dt, J=1.2, 7.6 Hz, ArH), 7.13–7.22 (7H, m, ArH), 7.03–7.09 (4H, m, ArH); δ_C (100 MHz, $CDCl_3$) 147.6 (C), 140.6 (C), 139.9 (C), 139.2 (C), 137.3 (C), 133.3 (C), 129.42 (CH), 129.40 (CH), 129.37 (CH), 127.5 (CH), 127.3 (CH), 127.2 (CH), 127.1 (CH), 126.9 (CH), 126.8 (CH), 123.4 (CH), 123.0 (CH) 120.7 (C), 109.3 (CH); *m/z* 347 (100, MH^+), 346 (60, M^+).

4.5.2. 1,3-Diphenyl-6,7,8,9-tetrahydro-3*H*-benzo[*e*]indazole (11). Yield (0.26 g, 80%) as a colourless solid, mp 116–7 °C; [found: C, 85.18; H, 6.19; N, 8.59. $C_{23}H_{20}N_2$ requires C, 85.15; H, 6.21; N, 8.63%]; R_f (20% EtOAc/hexane) 0.61; ν_{max}(KBr) 3046, 2935, 1592, 1495, 1442 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.75 (2H, d, J=7.8 Hz, ArH), 7.60–7.63 (2H, m, ArH), 7.51–7.54 (2H, m, ArH), 7.50 (1H, d, J=8.8 Hz), 7.41–7.47 (3H, m, ArH), 7.33 (1H, t, J=7.3 Hz, ArH), 7.16 (1H, d J=8.8 Hz, ArH), 2.87 (2H, t, J=6.4 Hz, CH_2), 2.68 (2H, t, J=6.4 Hz, CH_2), 1.78–1.84 (2H, m, CH_2), 1.66–1.72 (2H, m, CH_2); δ_C (100 MHz, $CDCl_3$) 147.5 (C), 140.1 (C), 138.5 (C), 134.9 (C), 130.9 (C), 130.3 (CH), 129.8 (CH), 129.7 (C), 129.3 (CH), 128.1 (CH), 127.8 (CH), 126.5 (CH), 123.1 (CH), 122.8 (C), 107.9 (CH), 29.4 (CH_2), 27.8 (CH_2), 23.0 (CH_2), 22.9 (CH_2); *m/z* 325 (100 MH^+), 324 (70, M^+).

4.5.3. 1,3-Diphenyl-3,6-dihydroindeno[1,2-*e*]indazole (17). Yield (0.27 g, 75%) as a colourless solid, mp 135–6 °C; [found: C, 87.16; H, 5.09; N, 7.79. $C_{26}H_{18}N_2$ requires C, 87.12; H, 5.06; N, 7.82%]; R_f (20% EtOAc/hexane) 0.65; ν_{max}(KBr) 3051, 2920, 1952, 1592, 1495 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.81 (2H, d, J=7.8 Hz, ArH), 7.73 (1H, d, J=8.8 Hz, ArH), 7.71 (2H, d, J=7.8 Hz, ArH), 7.63 (1H, d, J=8.8 Hz, ArH), 7.51–7.58 (6H, m, ArH), 7.39 (1H, t, J=7.6 Hz, ArH), 7.19 (1H, t, J=7.6 Hz, ArH), 6.96 (1H, t, J=7.6 Hz, ArH), 6.55 (1H, d, J=7.6 Hz, ArH), 3.99 (2H, s, CH_2); δ_C (400 MHz, $CDCl_3$) 146.8 (C), 144.5 (C), 141.2 (C), 140.5 (C), 140.0 (C), 137.9 (C), 135.4 (C), 134.8 (C), 130.6 (CH), 129.4 (CH), 128.7 (CH), 128.2 (CH), 126.9 (CH), 126.2 (CH), 125.9 (CH), 124.9 (CH), 124.3 (CH), 124.1 (CH), 123.7 (CH), 118.9 (C), 108.9 (CH), 37.5 (CH_2); *m/z* 359 (100, MH+), 358 (60, M^+), 281 (20) 254 (30).

4.5.4. 1,3-Diphenyl-6,7-dihydro-3*H*-naphtho[1,2-*e*]indazole (21). Yield (0.35 g, 95%) as a colourless solid, mp

63–65 °C; [found: C, 87.10; H, 5.39; N, 7.48. $C_{27}H_{20}N_2$ requires C, 87.07; H, 5.41; N, 7.52%]; R_f (20% EtOAc/hexane) 0.69; ν_{max}(KBr) 3045, 2954, 2935, 2886, 1591, 1493, 1450 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.80 (2H, d, J=7.8 Hz, ArH), 7.66 (1H, d, J=8.5 Hz, ArH), 7.55 (2H, t, J=7.8 Hz, ArH), 7.40 (2H, d, J=7.8 Hz, ArH), 7.38 (1H, d, J=8.5 Hz, ArH), 7.21–7.28 (5H, m, ArH), 7.05 (1H, t, J=7.6 Hz, ArH), 6.82 (1H, d, J=7.6 Hz, ArH), 6.60 (1H, t, J=7.6 Hz, ArH), 2.90 (4H, s, CH_2–CH_2); δ_C (100 MHz, $CDCl_3$) 146.9 (C), 141.1 (C), 139.9 (C), 138.2 (C), 134.7 (C), 133.2 (C), 131.9 (C), 130.6 (CH), 129.6 (CH), 129.4 (CH), 127.75 (CH), 127.7 (CH), 127.6 (CH), 126.89 (C), 126.86 (CH), 126.83 (CH), 126.6 (CH), 124.8 (CH), 123.61 (CH), 118.7 (C), 109.2 (CH), 29.5 (CH_2), 29.4 (CH_2); m/z 373 (100 MH^+), 372 (80 M^+).

4.5.5. Dehydrogenation of indazole 21 with DDQ. A solution of **21** (0.37 g, 1 mmol) and DDQ (0.45 g, 2 mmol) was refluxed in dioxane for 6 h. The reaction mixture was cooled and poured into ice-cold water and extracted with DCM (3×20 mL). The organic layer was washed with brine (30 mL), dried (Na_2SO_4) and evaporated under reduced pressure. The crude product was passed through small silica gel column using 2% EtOAc/hexane as eluent to give **22** (0.34 g, 93%) as a colourless solid, mp 153–154 °C; [found: C, 87.56; H, 4.93; N, 7.59. $C_{27}H_{18}N_2$ requires C, 87.54; H, 4.90; N, 7.56%]; R_f (20% EtOAc/hexane) 0.69; ν_{max}(KBr) 3047, 1950, 1886, 1589, 1499, 1450 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.86–7.93 (5H, m, ArH), 7.82–7.85 (3H, m, ArH), 7.59 (2H, t, J=7.7 Hz, ArH), 7.52–7.55 (2H, m, ArH), 7.39–7.46 (2H, m, ArH), 7.32–7.38 (3H, m, ArH), 6.95 (1H, dt, J=1.2, 7.7 Hz, ArH); δ_C (100 MHz, $CDCl_3$) 148.6 (C), 140.5 (C), 139.6 (C), 136.1 (C), 133.1 (C), 130.6 (CH), 129.5 (CH), 129.3 (CH), 129.2 (CH), 128.8 (C), 128.2 (CH), 127.9 (CH), 127.8 (C), 127.5 (CH), 127.3 (CH), 126.9 (CH), 126.2 (CH), 125.8 (CH), 125.7 (C), 124.2 (CH), 124.1 (CH), 117.1 (C), 110.7 (CH); m/z 371 (100 MH^+), 370 (90, M^+), 267 (20).

References and notes

1. Caron, S.; Vazquez, E. *Synthesis* **1999**, *4*, 588, and references cited therein.
2. Yeu, J.-P.; Yeh, J.-T.; Chen, T.-Y.; Uang, B.-J. *Synthesis* **2001**, *1775*, and references cited therein.
3. Sun, J.-H.; Teleha, C. A.; Yan, J.-S.; Rodgers, J. D.; Nugiel, D. A. *J. Org. Chem.* **1997**, *62*, 5627.
4. Rodgers, J. D.; Johnson, B. L.; Wang, H.; Greenberg, R. A.; Erickson-Viitanen, S.; Klabe, R. M.; Cordova, B. C.; Rayner, M. M.; Lam, G. N.; Chang, C.-H. *Biorg. Med. Chem. Lett.* **1996**, *6*, 2919.
5. Norman, M. H.; Navas, F., III; Thompson, J. B.; Rigdon, G. C. *J. Med. Chem.* **1996**, *39*, 4692.
6. Yoshida, T.; Matsuura, N.; Yamamoto, K.; Doi, M.; Shimada, K.; Morie, T.; Kato, S. *Heterocycles* **1996**, *43*, 2701.
7. Robertson, D. W.; Bloomquist, W.; Cohen, M. L.; Reid, L. R.; Schenck, K.; Wong, D. T. *J. Med. Chem.* **1990**, *33*, 3176.
8. Villalobos, A.; Blake, J. F.; Biggers, C. K.; Butler, T. W.; Chapin, D. S.; Chen, Y. L.; Ives, J. L.; Jones, S. B.; Liston, D. R.; Nagel, A. A.; Nason, D. M.; Nielsen, J. A.; Shalaby, I. A.; White, W. F. *J. Med. Chem.* **1994**, *37*, 2721.
9. Mylari, B. L.; Zembrowski, W. J.; Beyer, T. A.; Aldinger, C. E.; Siegel, T. W. *J. Med. Chem.* **1992**, *35*, 2155.
10. (a) Elguero, J. Pyrazole and their benzo derivatives. *Comprehensive heterocyclic chemistry*; Katritzkey, A. R., Rees, C. W., Potts, K. T., Eds.; Pergamon: New York, 1984; Vol. 5, p 167. (b) Behr, L. C.; Fusco, R.; Jarobe, C. H. In *Pyrazoles, pyrazolines, pyrazolidines, indazoles and condensed rings*; Wiley, R. H., Ed.; Wiley Science: New York, 1969; p 289. (c) Sainsbury, M.; 2nd ed. *Rodd's chemistry of carbon compounds*; Caffey, S., Ansell, M. F., Eds.; Elsevier: New York, 1986; Vol. 4, p 93 part C.
11. (a) Ruechardt, C.; Hassmann, V. *Liebigs Ann. Chem.* **1980**, 908. (b) Dell'Erba, C.; Novi, M.; Petrillo, G.; Tavani, C. *Tetrahedron* **1992**, *48*, 325.
12. (a) Kunka, C. P. A.; Warkentin, J. *Can. J. Chem.* **1990**, *68*, 575. (b) Huisgen, R.; Bast, K. *Organic syntheses. Collect. vol. V*; Wiley: New York, 1973; p 650. (c) Boudreault, N.; Leblanc, Y. *Org. Synth.* **1996**, *74*, 241.
13. (a) Reddy, K. R.; Roy, A.; Ila, H.; Junjappa, H. *Tetrahedron* **1995**, *51*, 10941. (b) Roy, A.; Reddy, K. R.; Ila, H.; Junjappa, H. *J. Chem. Soc., Perkin Trans. 1* **1999**, 3001. (c) Barluenga, J.; Aznar, F.; Palomero, M. A. *Chem. Eur. J.* **2001**, *7*, 5318. (d) Mediò-Simon, M.; Alvarez de Laviada, M. J.; Sequlveda Arques, J. *J. Chem. Soc., Perkin Trans. 1* **1990**, 2749.
14. Review: (a) Ila, H.; Junjappa, H.; Mohanta, P. K. *Progress in heterocyclic chemistry*; Gribble, G. W., Gilchrist, T. L., Eds.; Pergamon: Oxford, 2001; Vol. 13, p 1 Chapter 1. (b) Junjappa, H.; Ila, H.; Asokan, C. V. *Tetrahedron* **1990**, *46*, 5423. (c) Junjappa, H.; Ila, H.; Patro, B.; Rao, Ch. S. *J. Indian Chem. Soc.* **1994**, *71*, 501.
15. (a) Suresh, J. R.; Syam Kumar, U. K.; Ila, H.; Junjappa, H. *Tetrahedron* **2001**, *57*, 781. (b) Suresh, J. R.; Barun, O.; Ila, H.; Junjappa, H. *Tetrahedron* **2000**, *56*, 8153. (c) Barun, O.; Patra, P. K.; Ila, H.; Junjappa, H. *Tetrahedron Lett.* **1999**, *40*, 3797. (d) Basveswara Rao, M. V.; Syam Kumar, U. K.; Ila, H.; Junjappa, H. *Tetrahedron* **1999**, *55*, 11563. (e) Kishore, K.; Reddy, K. R.; Suresh, J. R.; Ila, H.; Junjappa, H. *Tetrahedron* **1999**, *55*, 7645. (f) Patra, P. K.; Suresh, J. R.; Ila, H.; Junjappa, H. *Tetrahedron* **1998**, *54*, 10167. (g) Syam Kumar, U. K.; Patra, P. K.; Ila, H.; Junjappa, H. *Tetrahedron Lett.* **1998**, *39*, 2029. (h) Suresh, J. R.; Patra, P. K.; Ila, H.; Junjappa, H. *Tetrahedron* **1997**, *53*, 14737. (i) Patra, P. K.; Suresh, J. R.; Ila, H.; Junjappa, H. *Tetrahedron Lett.* **1997**, *38*, 3119. (j) Satyanarayana, J.; Reddy, K. R.; Ila, H.; Junjappa, H. *Tetrahedron Lett.* **1992**, *33*, 6173. (k) Reddy, K. R.; Ila, H.; Junjappa, H. *Synthesis* **1995**, 929. (l) Balu, M. P.; Pooranchand, D.; Ila, H.; Junjappa, H. *Tetrahedron Lett.* **1988**, *29*, 501. (m) Pooranchand, D.; Satyanarayana, J.; Ila, H.; Junjappa, H. *Synthesis* **1993**, 241.
16. Sangwan, N. K.; Kelkar, P. M.; Rastogi, S. N.; Anand, N. *Ind. J. Chem.* **1985**, *24B*, 639.
17. Vogel, A. I. *Textbook of practical organic chemistry*; 5th ed. ELBS: London, 1989; p 1149.
18. Kumar, A.; Malhotra, S.; Vats, A.; Himanshu; Singh, S. K.; Sharma, S. K.; Prasad, A. K.; Errington, W.; Olsen, C. E.; Jain, S. C.; Parmar, V. S. *Ind. J. Chem.* **2002**, *41B*, 360.
19. Chauhan, S. M. S.; Junjappa, H. *Tetrahedron* **1976**, *32*, 1779.