

Synthesis and structural properties of 2-([2.2]paracyclophanyl)-2,3-dihydroquinazolines by cyclocondensation of 2-aminoarylbenzimidamides with 4-formyl[2.2]paracyclophane catalyzed efficiently by iodine

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Abstract

Technical iodine was found to catalyze the condensation between 2-aminoarylbenzimidamide derivatives (**1a-i**) and 4-formyl[2.2]paracyclophane (**2**) in absolute ethanol under mild conditions to afford 2-([2.2]paracyclophanyl)-4-arylamino-2,3-dihydroquinazoline derivatives (**3a-i**) in good yields and with high diastereoselectivity. The obtained products were oxidized easily by KMnO₄ to yield the corresponding 2-([2.2]paracyclophanyl)-4-arylaminoquinazoline derivatives (**6a-g**). The structure of **3b** was conformed by X-ray crystallography.

Keywords: Aminoarylbenzimidamides, cyclocondensation, 4-formyl[2.2]paracyclophane, quinazolines

Introduction

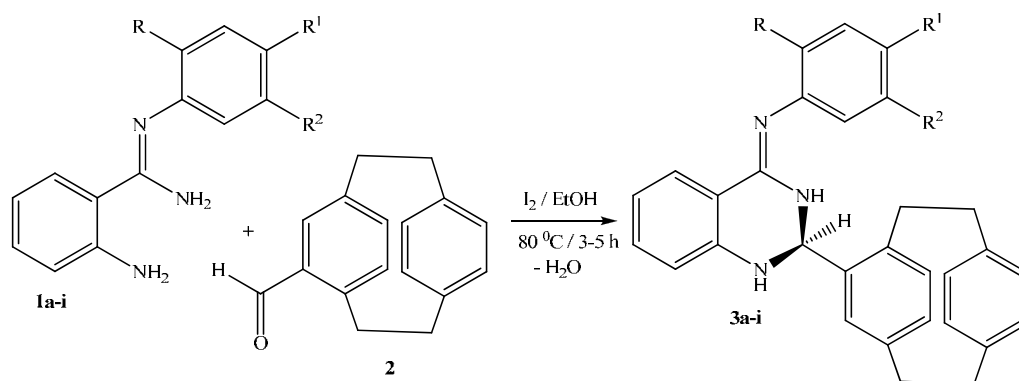
The quinazoline skeleton is an important part of many alkaloids and has been isolated from some plants, especially of the Rutacea family.^{1,2} Quinazoline moieties are considered to be pharmacophores because they show many types of pharmacological properties^{3,4} especially as antiinflammatory,⁵ antiallergic⁶ and antimalarial agents⁷ and in cancer treatment.⁸ Some quinazolines possess inhibiting properties for tyrosine kinase,⁹ which is useful in inhibiting tumour growth. Thus quinazolines are considered to be a privileged structure for drug

development. Quinazolines have been synthesized from the reaction of 2-aminobenzonitrile with Grignard reagents in presence of acyl halides, or by treating 2-aminobenzonitrile with Grignard reagent in presence of aldehydes or ketones or by heating 2-aminobenzonitrile with phenylisocyanate or lactic acid.^{10,11} They have also been synthesized by using low-valent titanium compounds as catalysts,¹² by using a tandem Aza-Wittig reaction,¹³ or by heating 2-aminobenzamide with aldehydes¹⁴ or, very recently, by reacting 2-aminoarylbenzimidamides with tetracyanoethylene.¹⁵

Results and Discussion

Because of the increasing importance of 2-substituted quinazolines, and as part of our program designed to expand the chemistry of 4-formyl[2.2]paracyclophane and other chiral phanes, a simpler approach to synthesize these heterocyclics was thought to be of value. Quinazolinophane and related compounds constitute an essentially unexplored area and this encouraged us to initiate a study of the chemistry of these compounds. Among the various catalysts that have been applied to cyclocondensation reactions, molecular iodine was found to be the best.¹⁶

2-Aminoarylbenzimidamides¹⁵ serve as convenient building blocks for the formation of heterocyclic moieties with two nitrogen atoms. The heterocyclization proceeds with the involvement of the N-C-C=C-N fragment of benzimidamide derivatives. Thus the condensation of the latter class of compounds with carbonyl compounds affords the 2,3-dihydroquinazoline system (**3a-i**). In the present study, we investigated the heterocyclization of 2-aminoarylbenzimidamides (**1a-i**) with 4-formyl[2.2]paracyclophane (**2**) in presence of a catalytic amount of commercial iodine. As shown in Scheme 1 this led to the formation of the title compounds in good yields. Since the products **3** have two elements of chirality (a center and a plane) one would expect the formation of diastereomeric mixtures. However, according to TLC analysis (one spot only) and NMR spectra (no sign of line doubling in the ¹³C NMR spectra) only one diastereoisomer appears to be formed: (*Z*)-aryl-N-(2-(*R*)-[2.2]paracyclophanyl)-2,3-dihydroquinazolin-4(*1H*)-ylidene)aniline. This means that the formation of the products **3** takes place with very high diastereoselectivity.



a, R = R¹ = R² = H

b, R = R² = H, R¹ = CH₃

c, R = R² = H, R¹ = Cl

d, R = R² = H, R¹ = Br

e, R¹ = R² = H, R = I

f, R¹ = H, R = R² = CH₃

g, R¹ = H, R = R² = Cl

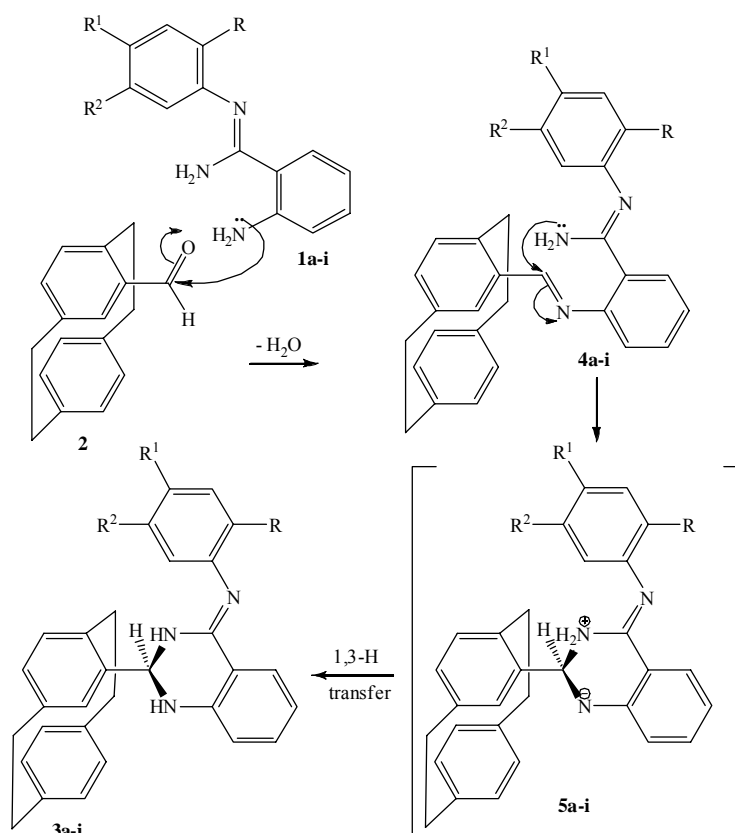
h, R = R¹ = H, R² = OCH₃

i, R = R² = H, R¹ = OCH₃

Scheme 1. Reaction of 2-aminoarylbenzimidamides (**1a-i**) with 4-formyl[2.2]paracyclophane (**2**).

The single crystal X-ray structure of the selected example **3b** (see below) supports this observation of very high diastereoselectivity.

The formation of the products (**3a-i**) may be rationalized according to the pathway shown in Scheme 2.



Scheme 2. Possible mechanism for the formation of compounds (**3a-i**).

The reaction begins by attack of the nucleophiles **1a-i** on the carbonyl group of **2**. We have previously shown that the oxygen atoms of several [2.2]paracyclophanes carrying a keto function in 4-position point towards the ethano bridge.¹⁷ Furthermore, we postulate that the bulky reagents **1** approach **2** only from the “outside” then the intermediate **4a-i** would result in the first step. It is easily conceivable that the intramolecular ring closure of **4a-i** could take place from the sterically less shielded outside also, resulting in the formation of the intermediate zwitterions **5a-i**. This, ultimately, will stabilize itself by a (formal) 1,3-proton transfer to the isolated products **3**.

The structures of the synthesized 2-([2.2]paracyclophanyl)-2,3-dihydroquinazoline derivatives (**3a-i**) were deduced from their IR and NMR spectra as well as their mass spectrometric properties. The IR spectra displayed (NH) absorption peaks at $\nu = 3490\text{--}3300\text{ cm}^{-1}$, in addition to the (C=N) absorption peaks at $\nu = 1640\text{--}1600\text{ cm}^{-1}$.

Taking **3g** as an example and with the help of 2D-NMR data we found that, its ^1H NMR spectrum showed in addition to the aliphatic protons of the bridge of the [2.2]paracyclophane unit which appeared as two multiplets at $\delta = 3.08\text{--}2.86$ and at $\delta = 3.51\text{--}3.43$ ppm characteristic for (H-14,15,20,21a) and (H-21b), respectively. However, the aromatic protons of the first paracyclophane ring resonated as two doublets at $\delta = 5.90, 6.39$ ppm with a coupling constant of 7.92 Hz for the protons H-23 and H-24, respectively. The protons of the second paracyclophanyl

ring protons (H-17,18,25,26) resonated as a multiplet at $\delta = 6.49$ - 6.44 ppm. Furthermore, the ^1H NMR spectrum revealed a doublet of doublets at $\delta = 5.63$ - 5.61 ppm with coupling constants ($J = 1.67, 3.31$ Hz) corresponding to the quinazoline C-2 carbon atom. The quinazoline C-2 carbon atom resonates in the ^{13}C NMR spectrum at $\delta = 62.36$ ppm as expected. Moreover, the two NH protons absorb in the ^1H NMR spectrum at $\delta = 6.30, 6.54$ ppm as a doublet and a singlet, respectively. While the protons of the 2,5-dichloroaniline moiety were registered in the ^1H NMR spectrum as two doublets at $\delta = 7.26, 7.60$ ($J = 2.50, J = 8.54$ Hz) and a doublet of doublets at $\delta = 7.14$ - 7.11 ppm related to H-28,31 and H-30, respectively. The carbon atoms of this aromatic ring moiety resonated in the ^{13}C NMR spectrum at $\delta = 123.14, 131.20$ ppm and the aromatic protons of the quinazoline substrate resonate in the ^1H NMR spectrum as a multiplet at $\delta = 6.67$ - 6.58 ppm for H-7,8 and a multiplet at $\delta = 7.14$ - 7.11 ppm backs to H-9. Whereas, the quinazoline proton (H-6) resonated as a doublet of doublets at $\delta = 7.91$ - 7.88 ppm with coupling constants ($J = 1.46, 7.81$ Hz). Finally, the mass spectra show the molecular ion peaks in accordance with the products **3a-i**. The intensities of the molecular ion peaks of compounds **3a-i** varied between 100 % (compound **3a**) and 12 % (compound **3f**); in other cases it lay between 60 % in compound **3d** and 80 % in compound **3g** depending on the aromatic moiety in the quinazoline C-4. Electron withdrawing substituents gave higher molecular ion peaks than electron donating substituents.

It has previously been claimed that of 2,4-diaryl-2,3-dihydroquinazoline derivatives are unstable^{14a} and change directly during silica-gel chromatography to the corresponding 2,4-diarylquinazolines. In our case, we found that the reaction was highly stereoselective leading to only one stereoisomer. Our product structures were confirmed by the representative single crystal X-ray structures of compound **3b** (Figure 1).

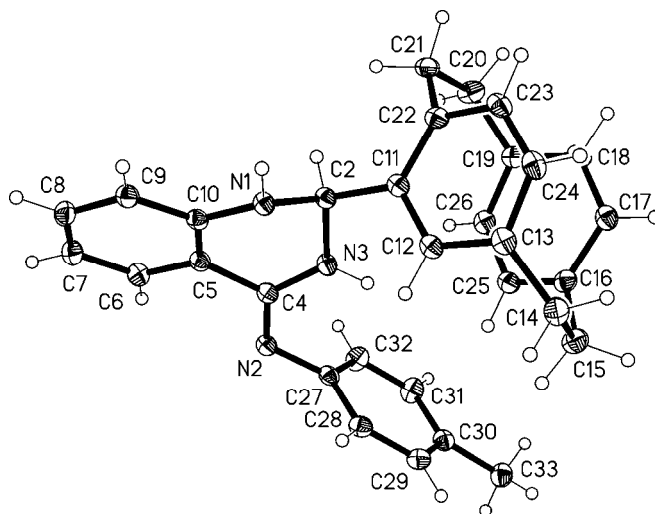


Figure 1. The single crystal X-ray structure of compound **3b**. Ellipsoids represent 30 % probability levels.

The packing of compound **3b** in the crystal lattice is as shown in Figure 2. It involves chains of molecules parallel to the *z* axis, linked by the hydrogen bond N1–HAN2.

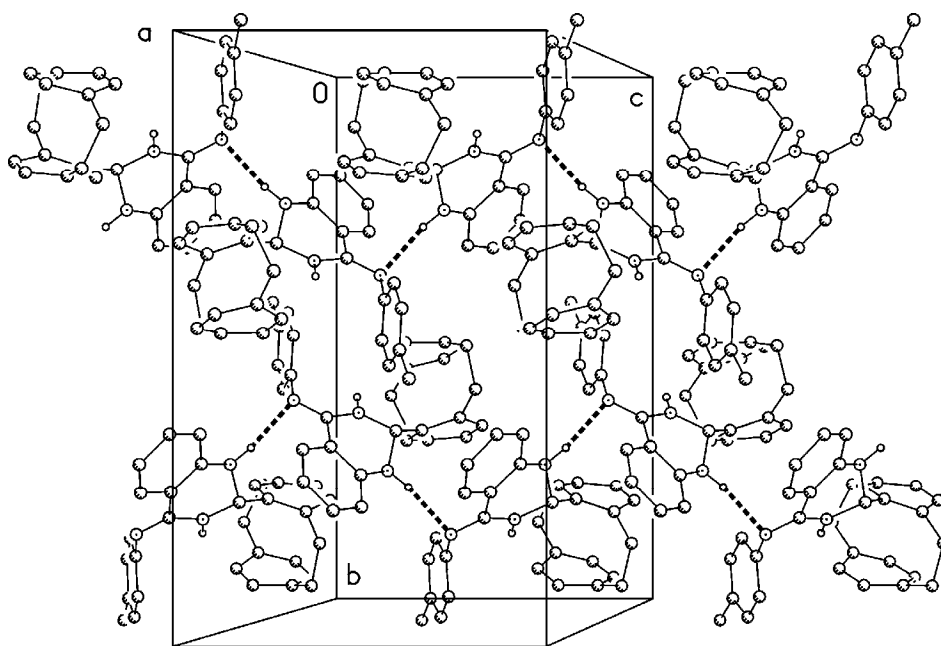
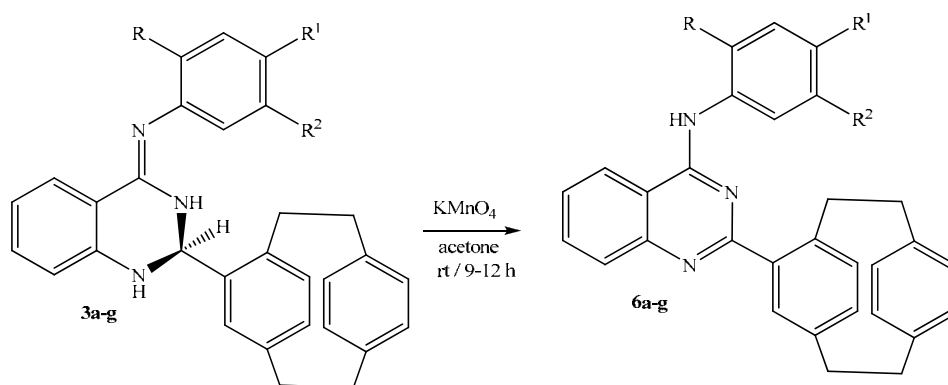


Figure 2. Packing diagram of **3b** viewed perpendicular to the *yz* plane in the region $x \approx 0$.

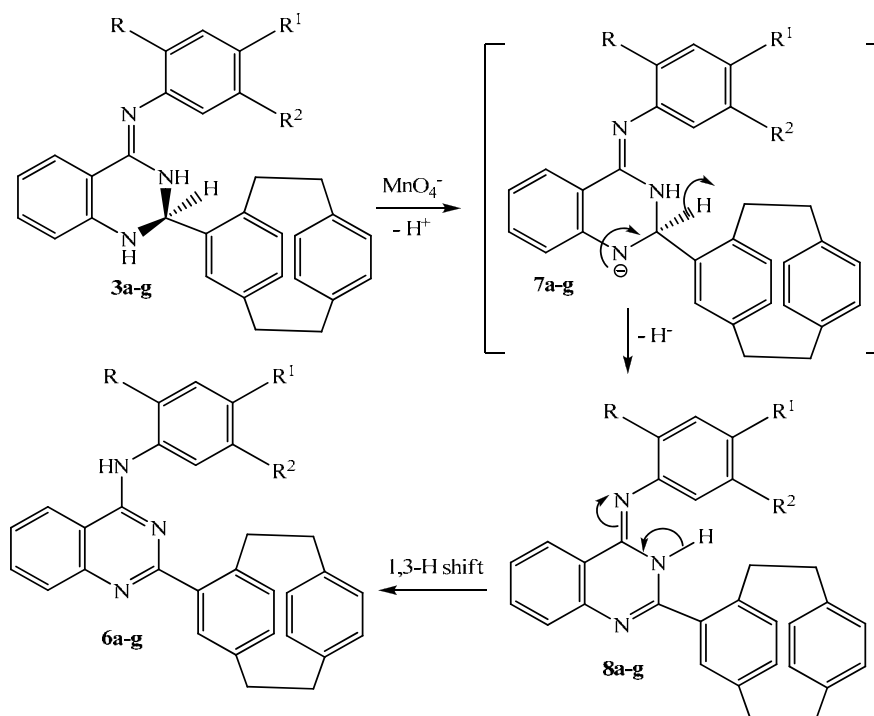
It has been described previously that oxidation of 2,3-dihydroquinazolines with KMnO_4 in acetone gave the corresponding quinazolines.^{14a,e} Thus, when using KMnO_4 as oxidant 2,3-dihydroquinazolines **3a-g** could be transformed into 2-([2.2]paracyclophanyl)quinazolines (**6a-g**) in good yields as shown in Scheme 3.



Scheme 3. Oxidation of 2-([2.2]paracyclophanyl)-2,3-dihydroquinazolines (**3a-g**) by KMnO_4 .

The formation of the 2-([2.2]paracyclophanyl)quinazoline derivatives (**6a-g**) can be rationalized according to the pathway shown in Scheme 4. In this pathway we expected the

formation of the anions **7a-g** under the influence of permanganate anion. The anions (**7a-g**) were neutralized to the intermediates (**8a-g**), thereby forming a double bond by loss of hydride from the adjacent carbon atom. After that a proton transfer (1,3-H shift) occurs from the amidic NH group to the exocyclic nitrogen atom to give the products (**6a-g**), which should be more stable than intermediates (**8a-g**) because of their aromaticity.



Scheme 4. Pathway for the formation of 2-([2.2]paracyclophanyl)quinazolines (**6a-g**) from **3a-g**.

The structures of the 2-([2.2]paracyclophanyl)quinazoline derivatives **6a-g** were elucidated by the usual spectral analyses (IR, NMR and MS). The IR spectrum shows an absorption maximum at $\nu = 3420\text{--}3300\text{ cm}^{-1}$ characteristic of NH groups. The NH protons resonated in the ¹H NMR as a singlet at $\delta = 8.29\text{--}7.27$ ppm depending on both the deuterated solvents that were used for measuring the NMR spectrum and the nature of the substituent at the quinazoline C-4 atom. The ¹H NMR spectrum of **6g** as an example revealed the paracyclophane bridge protons as five multiplets at $\delta = 2.70\text{--}2.60, 3.11\text{--}2.98, 3.26\text{--}3.18, 3.39\text{--}3.29, 4.61\text{--}4.52$ ppm corresponding to the protons H-21b, H-21a,20, H-14, H-15a, H-15b, respectively. The carbon atoms of these bridge protons resonated in the ¹³C NMR spectrum at $\delta = 36.13, 35.43, 35.41, 35.19$ ppm.

Whereas the ring protons of 2,5-dichloroaniline appeared in the ¹H NMR spectrum as two doublets at $\delta = 9.54$ and 7.42 ppm with $J = 2.49$ and 8.55 Hz related to H-28 and H-31, respectively. In addition to a doublet of doublets at $\delta = 7.14\text{--}7.09$ ppm with coupling constants $J = 2.51$ and 8.52 Hz related to H-30. The molecular ion peaks obtained from mass spectrometry were in accordance with the molecular weight of the products **6a-g** (see experimental section).

Experimental Section

General Procedures. All reagents were purchased from Alfa Aesar, Fluka and Aldrich companies and were used without further purification. 2-Aminoarylbenzimidamide derivatives **1a-i** were prepared according to ref¹⁵ and 4-formyl[2.2]paracyclophane (**2**) was synthesized according to ref¹⁸.

The m.p.s were measured in capillary tubes without corrections using a Büchi 530 melting point apparatus. IR spectra were run as KBr discs using a Bruker Tensor 27 instrument. The NMR spectra were recorded on a Bruker AM400 MHz spectrometer with TMS as internal standard; the coupling constants are given in Hz. The mass spectra (EI, 70 eV) were performed using a Finnigan MAT 8430 spectrometer.

Reactions of 2-aminoarylbenzimidamides (**1a-i**) with 4-formyl[2.2]paracyclophane (**2**).

General procedures

In a three necked-flask fitted with reflux condenser a solution of 0.25 mmol of 2-aminoarylbenzimidamides (**1a-i**) dissolved in 15 mL of absolute ethanol was added dropwise under nitrogen, to a solution of 4-formyl[2.2]paracyclophane (**2**) (59 mg, 0.25 mmol) dissolved in 20 mL of absolute ethanol at room temperature. A catalytic amount of commercial iodine (32 mg, 0.126 mmol) was added. The reaction mixture was heated under gentle reflux for 3-5 h. The progress of the reaction was monitored by TLC, and after completion the mixture was cooled to room temperature and sodium thiosulfate was added. The organic product was extracted by CH₂Cl₂. The aqueous phase was washed with CH₂Cl₂ and the combined organic layers were dried over MgSO₄. The solvent was removed and the residue was purified by silica gel chromatography using CH₂Cl₂ as the eluent to give the desired products (**3a-i**) in 70-82% yield.

(Z)-N-(2-R-[2.2]Pracyclophanyl-2,3-dihydroquinazolin-4(1H)-ylidene)aniline (3a). Yellow solid; Yield = (87 mg, 81 %); m.p. 180-182 °C; IR (KBr, cm⁻¹): 3413, 1616, 1585; ¹H NMR (400 MHz, CD₃OD): 3.03-2.80 (m, 7 H), 3.39-3.27 (m, 1H), 5.69 (m, 1 H, H-2), 6.29 (d, 1 H, *J* = 1.70 Hz), 6.47-6.34 (m, 6 H), 6.50 (s, 1H, NH), 6.62-6.60 (dd, 1 H, *J* = 0.71, 8.22 Hz), 7.12-7.08 (m, 1 H), 7.23-7.16 (m, 2 H), 6.76-6.71 (m, 1H), 7.52-7.35 (m, 3 H), 7.61-7.58 (dd, 1 H, *J* = 1.17, 8.13 Hz), 7.83-7.78 (m, 1 H); ¹³C NMR (100 MHz, CD₃OD): 148.77 (C-4), 141.85 (C), 141.73 (C), 140.93 (C), 140.66 (C), 140.47 (C), 138.55 (C), 137.70 (C), 137.24 (CH), 137.17 (CH), 134.97 (CH), 134.89 (C), 134.55 (CH), 134.24 (CH), 133.58 (CH), 132.58 (CH), 131.42 (CH), 131.33 (2 CH), 131.15 (2 CH), 129.70 (CH), 127.35 (CH), 125.24 (C), 124.43 (CH), 116.88 (CH), 65.19 (CH, C-2), 36.20, 36.01, 35.64, 33.86 (2 CH₂-CH₂); MS (*m/z*): 429 (M⁺, 100), 413 (8), 380 (4), 352 (8), 337 (20), 323 (M⁺ - CH₂-C₆H₅-CH₂, 94), 308 (18), 295 (4), 285 (8), 281 (20), 264 (8), 252 (4), 234 (74), 222 (54), 195 (22), 167 (20), 151 (8), 126 (24), 111 (22), 92 (42), 83 (44), 69 (34), 57 (20). Anal. Calcd For C₃₀H₂₇N₃ (429.57): C, 83.88; H, 6.34; N, 9.78. Found. C, 83.66; H, 6.30; N, 9.59.

(Z)-4-Methyl-N-(2-R-[2.2]paracyclophanyl-2,3-dihydroquinazolin-4(1H)-ylidne)aniline

(3b). Yellow crystals; Yield = (86 mg, 78 %); m.p. = 235-236 °C; IR (KBr, cm^{-1}): 3345, 1625, 1550, 1512; ^1H NMR (400 MHz, $\text{DMSO}-d_6$): 2.36 (s, 3 H, CH_3), 3.12-2.95 (m, 8 H), 6.25 (d, 1 H, $J = 7.37$ Hz, H-2), 6.32 (br, s, 1 H, NH), 6.58-6.48 (m, 7 H), 6.72-6.66 (m, 1 H), 6.82-6.74 (m, 1H), 7.15 (d, 2 H, $J = 8.10$ Hz), 7.33-7.37 (m, 1 H), 7.50-7.55 (m, 1 H), 7.82 (d, 2 H, $J = 8.11$ Hz), 7.95-7.91 (d, 1 H, $J = 7.72$ Hz); ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$): 148.15 (C-4), 139.66 (C), 139.55 (C), 139.13 (C), 139.05 (C), 138.93 (C), 137.51 (C), 136.40 (C), 136.18 (CH), 133.22 (CH), 133.06 (CH), 132.88 (CH), 132.81 (CH), 132.78 (CH), 132.03 (CH), 130.70 (CH), 130.38 (CH), 130.25 (CH), 129.58 (CH), 129.23 (CH), 127.94 (CH), 124.11 (C), 117.56 (CH), 115.88 (CH), 71.11 (CH, C-2), 34.40, 34.32, 33.37, 32.31 (2 $\text{CH}_2\text{-CH}_2$), 20.37 (CH_3); MS (m/z): 443 (M^+ , 24), 441 ($\text{M}^+ - 2$, 42), 427 ($\text{M}^+ - \text{CH}_3$, 2), 352 (4), 337 ($\text{M}^+ - \text{CH}_2\text{-C}_6\text{H}_4\text{-CH}_2$, 100), 320 (8), 248 (8), 231 (30), 209 (12), 192 (8), 161 (4), 129 (4), 107 (28), 91 (16), 77 (10), 65 (8), 51 (4), 44 (10). Anal. Calcd. For $\text{C}_{31}\text{H}_{29}\text{N}_3$ (443.60): C, 83.94; H, 6.59; N, 9.47. Found. C, 83.73; H, 6.60; N, 9.28.

(Z)-4-Chloro-N-(2-R-[2.2]paracyclophanyl-2,3-dihydroquinazolin-4(1H)-ylidne)aniline (3c).

Yellow solid; Yield = (94 mg, 82 %); m.p. = 181-182 °C; IR (KBr, cm^{-1}): 3414, 1612, 1551; ^1H NMR (400 MHz, $\text{DMSO}-d_6$): 3.10-2.98 (m, 8 H), 5.83-5.79 (m, 1 H, H-2), 6.33 (s, 1 H, NH), 6.42-6.38 (m, 1 H), 6.53-6.46 (m, 3 H), 6.56 (d, 2H, $J = 8.75$ Hz, H-29,31), 6.61-6.59 (m, 1H), 6.76-6.67 (m, 3 H), 7.02 (d, 2 H, $J = 8.76$ Hz, H-28,32), 7.25-7.17 (m, 1 H), 7.49-7.41 (m, 2 H), 7.57-7.52 (m, 1 H); ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$): 147.68 (C), 139.39 (C), 139.13 (C), 139.03 (C), 137.43 (C), 136.48 (C), 132.99 (C), 132.87 (CH), 132.74 (CH), 132.60 (2CH), 132.54 (CH), 132.45 (CH), 131.84 (CH), 130.66 (CH), 129.97 (CH), 129.28 (CH), 128.21 (2 CH), 118.66 (C), 115.16 (CH), 114.90 (2 CH), 33.39, 34.35, 34.15, 34.61 (2 $\text{CH}_2\text{-CH}_2$); MS (m/z): 465 (M^{+2} , 8), 464 (M^{+1} , 20), 463 (M^+ , 28), 426 (18), 357 ($\text{M}^+ - \text{CH}_2\text{-C}_6\text{H}_5\text{-CH}_2$, 100), 320 (22), 270 (4), 256 (8), 231 (40), 218 (4), 204 (4), 160 (6), 127 (12), 104 (8), 77 (12), 65 (6), 44 (10). Anal. Calcd. For $\text{C}_{30}\text{H}_{26}\text{ClN}_3$ (464.01): C, 77.66; H, 5.65; Cl, 7.64; N, 9.06. Found. C, 77.45; H, 5.62; Cl, 7.38; N, 8.87.

(Z)-4-Bromo-N-(2-R-[2.2]paracyclophanyl-2,3-dihydroquinazolin-4(1H)-ylidne)aniline (3d).

Yellowish white solid; Yield = (97 mg, 77 %); m.p. = 138-139 °C; IR (KBr, cm^{-1}): 3492, 1610, 1575, 1530; ^1H NMR (400 MHz, CDCl_3): 3.12-2.80 (m, 7 H), 3.33-3.12 (m, 1 H), 5.69 (m, 1 H, H-2), 5.92 (br, s, 1 H, NH), 6.62-6.45 (m, 7 H), 6.85-6.77 (m, 2 H), 6.75 (d, 2 H, $J = 8.58$ Hz), 7.18-7.09 (m, 2 H), 7.31-7.26 (m, 1 H), 7.43 (d, 2 H, $J = 8.55$ Hz); ^{13}C NMR (100 MHz, CDCl_3): 156.17 (C-4), 151.70 (C), 150.27 (C), 149.87 (C), 147.65 (C), 144.65 (C), 140.93 (C), 139.75 (C), 138.88 (C), 135.47 (CH), 133.75 (CH), 133.71 (CH), 133.22 (CH), 132.45 (2 CH), 132.25 (CH), 131.28 (CH), 127.29 (CH), 123.70 (2 CH), 118.70 (C), 117.11 (CH), 116.65 (CH), 115.88 (CH), 66.53 (CH, C-2), 35.25, 35.07, 34.80, 32.79 (2 $\text{CH}_2\text{-CH}_2$); MS (m/z): 509 (M^{+2} , 56), 507 (M^+ , 60), 491 (4), 426 ($\text{M}^+ - \text{Br}$, 32), 403 ($\text{M}^+ - \text{CH}_2\text{-C}_6\text{H}_5\text{-CH}_2$, 100), 352 (12), 336 (22), 329 (46), 320 (40), 300 (12), 274 (8), 231 (60), 218 (14), 171 (26), 160 (18), 129 (10), 92 (12), 65 (8), 40 (6). Anal. Calcd. For $\text{C}_{30}\text{H}_{26}\text{BrN}_3$ (508.47): C, 70.87; H, 5.15; N, 8.26; Br, 15.71. Found C, 70.64; H, 5.09; N, 8.01; Br, 15.39.

(Z)-2-iodo-N-(2-R-[2.2]paracyclophanyl-2,3-dihydroquinazolin-4(1H)-ylidene)aniline (3e).

Brownish solid, Yield = (98 mg, 71 %); m.p. = 208-211 °C; IR (KBr, cm^{-1}): 3387, 1618, 1569, 1518; ^1H NMR (400 MHz, CDCl_3): 3.22-2.86 (m, 8 H), 6.69-6.38 (m, 7 H), 7.49-7.38 (m, 4 H), 7.88-7.66 (m, 4 H); ^{13}C NMR (100 MHz, CDCl_3): 159.21 (C-4), 139.80 (C), 139.12 (C), 138.20 (C), 137.78 (C), 136.50 (C), 136.42 (C), 136.20 (C), 135.06 (C), 133.87 (CH), 133.44 (CH), 133.35 (CH), 133.00 (CH), 132.74 (CH), 132.50 (CH), 132.44 (CH), 132.22 (CH), 131.63 (CH), 129.37 (CH), 128.98 (CH), 123.30 (CH), 121.75 (CH), 120.50 (CH), 116.77 (C), 115.35 (CH), 63.36 (CH, C-2), 35.29, 35.23, 35.05, 33.69 (2 $\text{CH}_2\text{-CH}_2$); MS (m/z): 555 (M^+ , 20), 553 ($\text{M}^+ - 2$, 60), 456 (8), 449 (80), 427 ($\text{M}^+ - \text{I}$, 48), 402 (4), 352 (8), 323 [$\text{M}^+ - (\text{I} + \text{CH}_2\text{-C}_6\text{H}_5\text{-CH}_2)$, 100], 300 (4), 244 (4), 231 (20), 194 (18), 160 (16), 104 (8), 77 (8). Anal. Calcd. For $\text{C}_{30}\text{H}_{26}\text{IN}_3$ (555.47): C, 64.87; H, 4.72; N, 7.56. Found C, 64.59; H, 4.67; N, 7.37.

(Z)-2,5-dimethyl-N-(2-R-[2.2]paracyclophanyl-2,3-dihydroquinazolin-4(1H)-ylidene)aniline (3f).

Pale yellow solid; Yield = (82 mg, 72 %); m.p. = 132-133 °C; IR (KBr, cm^{-1}): 3462, 1627, 1565; ^1H NMR (400 MHz, CDCl_3): 2.37 (s, 3 H, CH_3), 2.45 (s, 3 H, CH_3), 2.80-2.93 (m, 1 H, H-21b), 3.01-3.22 (m, 6 H, H-14,15,20), 4.40-4.32 (m, 1H, H-21a), 5.34 (d, 1 H, $J = 2.89$ Hz, H-2), 5.60 (br, s, 1 H, NH), 6.25-6.30 (q, 2 H, $J = 7.82$ Hz), 6.51-6.62 (m, 5 H), 6.70-6.75 (m, 2 H), 7.03 (d, 1 H, NH, $J = 6.38$ Hz), 7.15-7.19 (m, 1 H), 7.35-7.41 (m, 1 H), 7.50 (t, 1 H, $J = 2.91$ Hz), 7.83-7.90 (m, 1 H), 8.02-8.06 (m, 1 H); ^{13}C NMR (100 MHz, CDCl_3): 158.09 (C-4), 148.05 (C), 140.28 (C), 139.04 (C), 136.90 (C), 136.16 (C), 135.21 (C), 133.60 (C), 132.91 (C), 132.53 (CH), 132.49 (CH), 132.43 (CH), 131.57 (CH), 130.96 (C), 130.34 (2 CH), 129.16 (CH), 128.14 (C), 126.08 (CH), 125.82 (CH), 125.59 (CH), 120.32 (CH), 117.83 (CH), 117.05 (CH), 115.06 (CH), 50.78 (CH, C-2), 35.58, 35.37, 35.31, 34.96 (2 $\text{CH}_2\text{-CH}_2$), 21.21 (CH_3), 17.57 (CH_3); MS: $m/z = 457$ (M^+ , 12), 455 ($\text{M}^+ - 2$, 60), 442 ($\text{M}^+ - \text{CH}_3$, 8), 380 (6), 351 ($\text{M}^+ - \text{CH}_2\text{-C}_6\text{H}_5\text{-CH}_2$, 100), 323 (20), 276 (8), 264 (20), 248 (40), 239 (60), 236 (74), 222 (44), 208 (28), 191 (6), 149 (8), 134 (22), 121 (60), 104 (86), 77 (26), 43 (40). Anal. Calcd. For $\text{C}_{32}\text{H}_{31}\text{N}_3$ (457.62): C, 83.99; H, 6.83; N, 9.18. Found C, 83.78; H, 6.81; N, 8.99.

(Z)-2,5-Dichloro-N-(2-R-[2.2]paracyclophanyl-2,3-dihydroquinazolin-4(1H)-ylidene)aniline (3g).

White crystals; Yield = (103 mg, 83 %); m.p. = 190-191 °C; IR (KBr, cm^{-1}): 3422, 1609, 1565, 1501; ^1H NMR (400 MHz, $\text{DMSO-}d_6$): 3.08-2.86 (m, 7 H, H-14,15,20,21a), 3.51-3.43 (m, 1 H, H-21b), 5.63-5.61 (dd, 1 H, $J = 1.67$, 3.31 Hz, H-2), 5.90 (d, 1 H, $J = 7.92$ Hz, H-23), 6.30 (d, 1 H, $J = 2.94$ Hz, NH, H-3), 6.39 (d, 1 H, $J = 7.92$ Hz, H-24), 6.49-6.44 (m, 4 H, H-12,18,25,26), 6.54 (s, 1 H, NH), 6.67-6.58 (m, 3 H, H-7,8,17), 7.14-7.11 (m, 2 H, H-9,30), 7.26 (d, 1 H, $J = 2.50$ Hz, H-28), 7.60 (d, 1 H, $J = 8.54$ Hz, H-31), 7.91-7.88 (dd, 1 H, $J = 1.46$, 7.81 Hz, H-6); ^{13}C NMR (100 MHz, $\text{DMSO } d_6$): 152.33 (C-4), 150.36 (C-32), 149.12 (C-29), 145.80 (C-5), 139.56 (C-10), 139.39 (C-27), 139.17 (C-11), 139.02 (C-22), 136.43 (C-19), 135.60 (CH, C-12), 133.35 (CH, C-23), 132.96 (CH, C-24), 132.10 (CH, C-18), 132.05 (CH, C-25), 131.38 (CH, C-9), 131.20 (CH, C-31), 130.43 (CH, C-26), 129.98 (CH, C-6), 126.65 (CH, C-17), 125.24 (C-13), 123.14 (2 CH, C28,30), 117.07 (CH, C-8), 115.05 (C-16), 115.00 (CH, C-7), 62.36 (CH, C-2), 34.70 (CH_2 , C-21), 34.58, 33.89 ($\text{CH}_2\text{-CH}_2$, C-14,15), 32.59 (CH_2 , C-20); MS (m/z): 501 (M^{+4} , 8), 499 (M^{+2} , 52), 497 (M^+ , 80), 462 ($\text{M}^+ - \text{Cl}$, 76), 393 ($\text{M}^+ - \text{CH}_2\text{-C}_6\text{H}_5\text{-CH}_2$,

100), 352 (22), 337 (26), 320 (14), 290 (44), 263 (36), 232 (90), 218 (22), 208 (6), 178 (12), 161 (16), 130 (10), 104 (20), 77 (32), 65 (14), 43 (18). Anal. Calcd. For $C_{30}H_{25}Cl_2N_3$ (498.46): C, 72.29; H, 5.06; N, 8.43; Cl, 14.23. Found C, 72.05; H, 4.97; N, 8.21; Cl, 13.95.

(Z)-3-Methoxy-N-(2-R-[2.2]paracyclophanyl-2,3-dihydroquinazolin-4(1H)-ylidene)aniline (3h). Yellowish brown solid; Yield = (80 mg, 70 %); m.p = 52-53 °C; IR (KBr, cm^{-1}): 3453, 1623, 1575; 1H NMR (400 MHz, $CDCl_3$): 3.22-2.79 (m, 8 H), 3.71 (s, 3 H, OCH_3), 5.60-5.54 (m, 1H, H-2), 5.91 (br, s, 1H, NH), 6.20-6.11 (m, 1 H), 6.32-6.24 (m, 1 H), 6.43-6.38 (m, 2 H), 6.54-6.46 (m, 3 H), 6.65-6.54 (m, 4 H), 6.74-6.68 (m, 1 H), 6.91-6.82 (m, 2 H), 7.34-7.27 (m, 4 H), ^{13}C NMR (100 MHz, $CDCl_3$): 160.43 (C-4), 150.21 (C), 149.60 (C), 147.52 (C), 146.60 (C), 140.59 (C), 139.43 (C), 137.28 (C), 136.04 (CH), 135.17 (CH), 133.67 (CH), 133.03 (CH), 131.93 (CH), 131.28 (CH), 130.82 (C), 130.03 (2 CH), 129.95 (C), 129.43 (CH), 127.21 (CH), 119.37 (CH), 117.51 (CH), 116.80 (2 CH), 115.34 (CH), 66.73 (CH, C-2), 54.89 (OCH_3), 34.94, 34.85, 34.76, 34.69 (2 CH_2-CH_2). Anal. Calcd. For $C_{31}H_{29}N_3O$ (459.60): C, 81.02; H, 6.36; N, 9.14. Found. C, 80.84; H, 6.37; N, 8.97.

(Z)-4-Methoxy-N-(2-R-[2.2]paracyclophanyl-2,3-dihydroquinazolin-4(1H)-ylidene)aniline (3i). Pale brown solid; Yield = (87 mg, 76 %); m.p. = 108-111 °C; IR (KBr, cm^{-1}): 3440, 1617, 1570, 1500; 1H NMR (400 MHz, $CDCl_3$): 2.91-3.25 (m, 7 H), 4.06-4.22 (m, 1 H), 3.80 (s, 3 H, OCH_3), 6.35-6.40 (m, 2 H), 6.47-6.51 (m, 3 H), 6.54-6.58 (m, 2 H), 6.67-6.73 (m, 2 H), 6.92 (s, 2 H), 7.01 (d, 1 H, $J = 1.93$ Hz), 7.16-7.21 (m, 2 H), 7.39-7.43 (dd, 1 H, 1.21, 7.86 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): 155.70 (C-4), 147.88 (C), 143.21 (C), 140.63 (C), 139.56 (C), 139.48 (C), 139.42 (C), 138.06 (CH), 136.56 (CH), 136.32 (C), 136.09 (CH), 133.23 (CH), 132.98 (CH), 132.89 (CH), 132.55 (C), 132.34 (CH), 132.13 (CH), 131.27 (C), 131.02 (CH), 127.29 (CH), 122.73 (CH), 117.09 (CH), 116.69 (C), 116.58 (CH), 114.88 (CH), 58.93 (CH, C-2), 55.50 (OCH_3), 35.64, 35.24, 35.13, 34.96 (2 CH_2-CH_2); MS (m/z): 459 (M^+ , 6), 457 ($M^+ - 2$, 20), 426 ($M^+ - OCH_3$, 26), 391 (12), 353 ($M^+ - CH_2-C_6H_5-CH_2$, 100), 322 (10), 252 (6), 208 (14), 191 (10), 165 (4), 144 (16), 132 (42), 104 (100), 78 (38), 63 (12). Anal. Calcd. For $C_{31}H_{29}N_3O$ (459.60) calcd. C, 81.02; H, 6.36; N, 9.14; Found. C, 80.86; H, 6.34; N, 8.93.

Oxidation of (Z)-aryl-N-(2-[2.2]paracyclophanyl-2,3-dihydroquinazolin-4(1H)-ylidene)-aniline (3a-g) by $KMnO_4$. General procedures

To a stirred solution of 0.25 mmol of (Z)-aryl-N-(2-[2.2]paracyclophanyl-2,3-dihydroquinazolin-4(1H)-ylidene)aniline (**3a-g**) dissolved in 15 mL of dry acetone and placed in a three-necked flask fitted with a dropping funnel, a solution of (53 mg, 0.30 mmol) of $KMnO_4$ dissolved in 15 mL of dry acetone was added dropwise. After complete addition, the reaction mixture was stirred at room temperature for 9-12 h. After completion of the reaction (monitored by TLC) it was poured onto ice- H_2O and 20 mL of saturated solution of sodium sulfite was added to reduce the permanganate. The product was extracted by CH_2Cl_2 , the organic layer was dried over $MgSO_4$. The solvent was removed and the products were purified by silica gel chromatography using CH_2Cl_2 . The products were obtained in yields of 65-77 %.

2-[2.2]Paracyclophanyl-*N*-phenylquinazolin-4-amine (6a). Yellow solid; Yield = (81 mg, 76 %); m.p. = 71-72 °C; IR (KBr, cm^{-1}): 3388, 1618, 1599, 1560, 1520; ^1H NMR (400 MHz, CDCl_3): 2.65-2.58 (m, 1 H), 2.88-2.81 (m, 2 H), 3.00-2.93 (m, 3 H), 3.11-3.02 (m, 1 H), 4.37-4.29 (m, 1H), 6.36-6.42 (m, 3 H), 6.46-6.57 (m, 4 H), 7.06-7.12 (m, 2 H), 7.33-7.40 (m, 3 H), 7.43 (br, s, 1 H, NH), 7.63-7.72 (m, 2 H), 7.84-7.91 (m, 2 H); ^{13}C NMR (100 MHz, CDCl_3): 161.93 (C-4), 157.36 (C), 150.96 (C), 140.19 (C), 139.98 (C), 139.61 (C), 139.16 (C), 139.04 (C), 138.90 (C), 136.47 (CH), 135.25 (CH), 133.85 (CH), 133.15 (CH), 132.77 (2 CH), 132.56 (CH), 131.80 (CH), 129.38 (CH), 129.02 (2 CH), 126.13 (CH), 124.20 (CH), 121.82 (2 CH), 120.45 (CH), 115.03 (C), 36.06, 35.75, 35.59, 35.34 (2 $\text{CH}_2\text{-CH}_2$); MS (m/z): 427 (M^+ , 40), 380 (20), 351 (8), 323 ($\text{M}^+ - \text{CH}_2\text{-C}_6\text{H}_4\text{-CH}_2$, 100), 308 (4), 287 (20), 276 (40), 248 (60), 236 (28), 213 (14), 195 (18), 161 (12), 129 (14), 104 (42), 77 (12), 51 (10). Anal. Calcd. For $\text{C}_{30}\text{H}_{25}\text{N}_3$ (427.55): C, 84.28; H, 5.89; N, 9.83. Found C, 84.08; H, 5.87; N, 9.66.

2-[2.2]Paracyclophanyl-*N*-*p*-tolylquinazolin-4-amine (6b). Yellow solid; Yield = (76 mg, 69 %); m.p. = 87-89 °C; IR (KBr, cm^{-1}): 3389, 1622, 1554; ^1H NMR (400 MHz, CDCl_3): 2.34 (s, 3 H, CH_3), 2.91-3.15 (m, 7 H), 3.54-3.61 (m, 1 H), 6.43-6.61 (m, 7 H), 7.08-7.18 (m, 2 H), 7.33 (br, s, 1 H, NH), 7.35-7.40 (m, 2 H), 7.68-7.82 (m, 3 H), 7.85-7.91 (m, 1 H); ^{13}C NMR (100 MHz, CDCl_3): 162.02 (C), 157.56 (C), 150.99 (C), 140.16 (C), 139.51 (C), 139.14 (C), 138.98 (C), 136.59 (C), 136.22 (CH), 136.06 (C), 135.04 (C), 133.53 (CH), 132.93 (CH), 132.56 (CH), 132.52 (CH), 132.43 (CH), 132.37 (CH), 132.22 (C), 131.62 (CH), 129.98 (CH), 129.12 (CH), 127.93 (CH), 125.75 (CH), 121.78 (CH), 120.61 (CH), 113.23 (C), 35.57, 35.39, 35.11, 34.49 (2 $\text{CH}_2\text{-CH}_2$), 20.87 (CH_3); Anal. Calcd For $\text{C}_{31}\text{H}_{27}\text{N}_3$ (441.58): C, 84.32; H, 6.16; N, 9.52. Found C, 84.10; H, 6.13; N, 9.34.

***N*-(4-Chlorophenyl)-2-[2.2]paracyclophanylquinazolin-4-amine (6c).** Yellow solid; Yield = (86 mg, 75 %), m.p. = 108-109 °C; IR (KBr, cm^{-1}): 3301, 1621, 1601, 1564, 1522; ^1H NMR (400 MHz, CDCl_3): 2.63-2.67 (m, 1 H), 2.83-3.03 (m, 4 H), 3.11-3.17 (m, 1 H), 3.65-3.70 (m, 1H), 4.30-4.37 (m, 1H), 6.35-6.40 (m, 3 H), 6.50-6.55 (m, 4 H), 7.33 (br, s, 1 H, NH), 7.43 (d, 2 H, J = 8.88 Hz), 7.43-7.50 (m, 2 H), 7.71-7.79 (m, 1 H), 7.82-7.90 (d, 2 H, J = 8.84 Hz), 7.93-7.96 (m, 1 H); ^{13}C NMR (100 MHz, CDCl_3): 161.80 (C-4), 157.14 (C-30), 151.06 (C), 141.31 (C), 140.02 (C), 139.44 (C), 139.25 (C), 137.61 (C), 136.39 (CH), 134.96 (CH), 133.78 (CH), 132.98 (CH), 132.78 (CH), 132.67 (CH), 132.62 (CH), 132.30 (CH), 131.51 (CH), 129.41 (CH), 129.06 (C), 128.87 (CH), 127.03 (C), 126.15 (CH), 123.67 (CH), 122.62 (CH), 120.11 (CH), 113.02 (C), 35.94, 35.63, 35.59, 35.44 (2 $\text{CH}_2\text{-CH}_2$); MS (m/z): 463 (M^{+2} , 12), 461 (M^+ , 34), 426 ($\text{M}^+ - \text{Cl}$, 18), 380 (4), 357 ($\text{M}^+ - \text{CH}_2\text{-C}_6\text{H}_4\text{-CH}_2$, 100), 320 (20), 275 (6), 248 (10), 231 (8), 203 (4), 174 (8), 161 (6), 129 (6), 111 (10), 104 (10), 91 (6), 77 (8), 69 (10), 57 (6). Anal. Calcd. For $\text{C}_{30}\text{H}_{24}\text{ClN}_3$ (462.00): C, 77.99; H, 5.24; N, 9.10; Cl, 7.67. Found C, 77.75; H, 5.13; N, 8.97; Cl, 7.43.

***N*-(4-Bromophenyl)-2-[2.2]paracyclophanylquinazolin-4-amine (6d).** Off-white solid; Yield = (78 mg, 62 %); m.p. = 77-78 °C; IR (KBr, cm^{-1}): 3318, 1609, 1570; ^1H NMR (400 MHz, CDCl_3): 2.64-2.69 (m, 2 H), 2.83-3.01 (m, 5 H), 3.12-3.18 (m, 1 H), 6.35-6.40 (m, 2 H), 6.50-6.55 (m, 5 H), 7.45 (br, s, 1 H, NH), 7.36-7.41 (m, 2 H), 7.43-7.50 (m, 2 H), 7.71-7.79 (m, 1 H),

7.82-7.90 (m, 2 H), 7.93-7.96 (m, 1 H); ^{13}C NMR (100 MHz, CDCl_3): 157.40 (C), 151.26 (C), 141.15 (C), 140.09 (C), 139.56 (C), 139.44 (C), 139.25 (C), 139.19 (C), 137.61 (C), 136.39 (CH), 134.96 (CH), 133.78 (CH), 132.98 (CH), 132.78 (CH), 132.67 (CH), 132.62 (CH), 132.30 (CH), 131.51 (CH), 129.41 (CH), 129.06 (C), 129.00 (C), 128.87 (CH), 127.03 (C), 126.15 (CH), 123.67 (C), 122.62 (CH), 122.27 (C), 120.11 (CH), 113.02 (C), 35.94, 35.36, 35.09, 34.46 (2 $\text{CH}_2\text{-CH}_2$); MS (m/z): 507 (M^{+2} , 22), 505 (M^+ , 26), 426 ($\text{M}^+ - \text{Br}$, 44), 321 [$\text{M}^+ - (\text{Br} + \text{CH}_2\text{-C}_6\text{H}_4\text{-CH}_2)$, 100], 320 (32), 275 (6), 248 (20), 231 (18), 207 (14), 174 (8), 161 (26), 129 (6), 111 (8), 104 (30), 91 (6), 77 (8), 69 (10), 57 (6). Anal. Calcd. For $\text{C}_{30}\text{H}_{24}\text{BrN}_3$ (506.45): C, 71.15; H, 4.78; N, 8.30; Br, 15.78. Found C, 70.91; H, 4.73; N, 8.13; Br, 15.63.

***N*-(2-Iodophenyl)-2-[2.2]paracyclophanylquinazolin-4-amine (6e).** Brown solid; Yield = (84 mg, 61 %); m.p. = 121-122; IR (KBr, cm^{-1}): 3336, 1614, 1587, 1548; ^1H NMR (400 MHz, CDCl_3): 2.68-2.63 (m, 1 H), 3.32-2.91 (m, 7 H), 6.63-6.42 (m, 7 H), 7.54-7.34 (m, 4 H), 7.96-7.84 (m, 4 H); ^{13}C NMR (100 MHz, CDCl_3): 140.31 (C), 140.03 (C), 139.41 (C), 139.20 (C), 137.75 (C), 136.32 (C), 136.09 (C), 135.08 (C), 133.79 (CH), 133.71 (CH), 133.09 (CH), 132.90 (CH), 132.62 (CH), 132.38 (CH), 132.32 (CH), 131.51 (CH), 129.37 (CH), 129.00 (C), 128.92 (CH), 128.18 (CH), 126.04 (C), 124.07 (CH), 123.30 (CH), 121.75 (CH), 120.50 (CH), 35.60, 35.45, 35.19, 30.91 (2 $\text{CH}_2\text{-CH}_2$); Anal. Calcd. For $\text{C}_{30}\text{H}_{24}\text{IN}_3$ (553.45): C, 65.11; H, 4.37; N, 7.59. Found C, 64.87; H, 4.31; N, 7.37.

***N*-(2,5-Dimethylphenyl)-2-[2.2]paracyclophanylquinazolin-4-amine (6f).** Pale yellow solid; Yield = (71 mg, 63 %); m.p. = 39-41 $^\circ\text{C}$; IR (KBr, cm^{-1}): 3307, 1617, 1565; ^1H NMR (400 MHz, CDCl_3): 2.39 (s, 3 H, CH_3), 2.41 (s, 3 H, CH_3), 2.83-2.97 (m, 1 H, CH_2), 3.03-3.18 (m, 7 H, 3 CH_2), 6.25-6.30 (m, 2 H), 6.51-6.62 (m, 5 H), 6.70-6.75 (m, 2 H), 7.27 (br, s, 1 H, NH), 7.15-7.19 (m, 1 H), 7.35-7.41 (m, 2 H), 7.83-7.90 (m, 2 H); ^{13}C NMR (100 MHz, CDCl_3): 148.05 (C), 140.28 (C), 139.04 (C), 136.90 (C), 136.16 (C), 135.21 (C), 133.60 (C), 132.91 (C), 132.53 (CH), 132.49 (CH), 132.43 (CH), 131.57 (CH), 130.96 (C), 130.34 (2 CH), 129.16 (CH), 128.14 (C), 126.08 (CH), 125.82 (CH), 125.59 (CH), 120.32 (CH), 117.83 (CH), 117.05 (CH), 115.06 (CH), 34.96, 35.31, 35.37, 35.58 (2 $\text{CH}_2\text{-CH}_2$), 21.62 (CH_3), 17.35 (CH_3); MS (m/z): 455 (M^+ , 18), 440 ($\text{M}^+ - \text{CH}_3$, 34), 326 (4), 351 ($\text{M}^+ - \text{CH}_2\text{-C}_6\text{H}_4\text{-CH}_2$, 100), 323 (22), 276 (18), 264 (12), 248 (24), 239 (10), 236 (44), 222 (44), 208 (32), 191 (6), 149 (8), 134 (22), 121 (60), 104 (48), 77 (26), 43 (40). Anal. Calcd. For $\text{C}_{32}\text{H}_{29}\text{N}_3$ (455.61): C, 84.36; H, 6.42; N, 9.22. Found C, 84.11; H, 6.41; N, 9.01.

***N*-(2,5-Dichlorophenyl)-2-[2.2]paracyclophanylquinazolin-4-amine (6g).** White crystals; Yield = (95 mg, 77 %); m.p. = 225-227 $^\circ\text{C}$; IR (KBr, cm^{-1}): 3422, 1619, 1594, 1565, 1518; ^1H NMR (400 MHz, CDCl_3): 2.70-2.60 (m, 1 H, H-21b), 3.11-2.98 (3 H, H-21a, 20), 3.26-3.18 (2 H, H-14), 3.39-3.29 (m, 1 H, H-15a), 4.61-4.52 (m, 1 H, H-15b), 6.37 (d, 1 H, $J = 7.86$ Hz), 6.57 (t, 2 H, $J = 1.05$ Hz), 6.68-6.61 (m, 2 H), 6.75-6.72 (m, 1H), 7.14-7.09 (dd, 1 H, $J = 2.51, 8.52$ Hz, H-30), 7.42 (d, 1 H, $J = 8.55$ Hz, H-31), 7.59 (d, 1 H, $J = 1.74$ Hz), 7.64-7.61 (m, 1 H), 7.89-7.83 (m, 1 H), 7.98-7.95 (dd, 1 H, $J = 0.67, 8.40$ Hz), 8.06-8.03 (dd, 1 H, $J = 0.66, 8.43$ Hz), 8.29 (s, 1 H, NH), 9.54 (d, 1 H, $J = 2.49$ Hz, H-28); ^{13}C NMR (100 MHz, CDCl_3): 161.48 (C-4), 156.43 (C-32), 151.15 (C-29), 140.55 (C), 139.93 (C), 139.51 (C), 139.49 (C), 139.22 (C), 136.76 (CH),

136.53 (CH), 134.98 (CH), 134.00 (CH), 133.40 (C), 133.13 (CH), 132.88 (CH), 132.57 (CH), 132.36 (CH), 131.60 (CH), 129.75 (C), 129.62 (CH), 126.77 (CH), 123.37 (CH), 121.62 (CH), 121.09 (C), 119.93 (CH), 113.43 (C), 36.13, 35.43, 35.41, 35.19 (2 CH₂-CH₂); MS (m/z): 499 (M⁺, 6), 497 (M⁺, 24), 495 (M⁺, 36), 460 (M⁺- Cl, 44), 391 (M⁺- CH₂-C₆H₄-CH₂, 100), 354 (28), 320 (16), 293 (2), 231 (8), 178 (4), 159 (8), 102 (4), 77 (6), 43 (18). Anal. Calcd. For C₃₀H₂₃Cl₂N₃ (496.44): C, 72.58; H, 4.67; N, 8.46; Cl, 14.28. Found C, 72.35; H, 4.63; N, 8.27; Cl, 14.03.

X-Ray structure determination of 3b

Crystal data: C₃₁H₂₉N₃, *M_r* = 443.57, monoclinic, *P*2₁/*c*, *T* = -170°C, *a* = 12.8695(4), *b* = 17.8784(5), *c* = 10.8119(4) Å, β = 107.722(4)°, *U* = 2367.77 Å³, *Z* = 4, *F*(000) = 944, λ(Cu Kα) = 1.54184 Å, μ = 0.56 mm⁻¹, *D_x* = 1.244 g cm⁻³. *Data collection:* A yellow plate ca. 0.25 × 0.15 × 0.01 mm was mounted in inert oil on a glass fibre and transferred to the cold gas stream of an Oxford Diffraction Nova Atlas diffractometer. Data were recorded to 2θ 140°. *Structure refinement:* The structure was refined using SHELXL-97.¹⁹ NH hydrogen atoms were refined freely, other H were included using a riding model. The final *wR*2 (all reflections) was 0.114 for 4372 intensities and 316 parameters, with *R*1 (*I* > 2σ(*I*)) 0.042; *S* 1.04, max. Δρ 0.22 e Å⁻³.

X-ray crystallographic data (excluding structure factors) were deposited under the number CCDC-720312 and can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Conclusions

In the present study we report a simple, inexpensive, and efficient one-pot synthesis of 2-([2.2]paracyclophanyl)-2,3-dihydroquinazoline derivatives using a catalytic amount of technical iodine with good product yields. Their preparation entails cyclocondensation of 2-aminoarylbenzimidamides with 4-formyl[2.2]paracyclophane. The reaction was found to be highly diastereoselective, and is presumably caused by the layered structure of the paracyclophane unit. This protocol leads to new heterocyclic systems that might possess interesting pharmacological properties. The mechanisms of formation of the products **3** and **6** have been rationalized

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