A general and a simple synthesis of {4-[(*Z*)-4-(arylimino)-3,4-dihydroquinazolin-2(1*H*)-ylidene]cyclohexa-2,5-dien-1-ylidene} malononitrile from the reaction of 2-amino-N′-arylbenzimidamides with 7,7,8,8-tetracyanoquinodimethane

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A short and facile synthesis of a series of {4-[(*Z*)-4-(arylimino)-3,4-dihydroquinazolin-2(1*H*)-ylidene]cyclohexa-2,5-dien-1-ylidene}malononitrile was accomplished in moderate to good yields *via* Charge-transfer complexes between 2-amino-N′-aryl-benzimidamide derivatives and 7,7,8,8-tetracyanoquinodimethane. The structure of the products were established on the basis of their elemental analysis, IR, NMR (^{1}H and ^{13}C) and mass spectrometry data.

Keywords: CT-complexes, 2-amino-N′-arylbenzimidamides, 7,7,8,8-tetracyanoquinodimethane, quinazolines

Quinazolines occupy a prominent position among heterocyclic compounds[1] and their preparations are in demand because of their potential biological and pharmaceutical activities.[2–5] These findings prompted us to design different quinazoline derivatives for further pharmacological tests.[6–8] Unfortunately, synthetic methods for the elaboration of this system are not general in scope, and involve multistep, and often low-yielding, reaction sequences. Different one-pot syntheses for quinazoline derivatives have been described, but they require either high temperature or must be affected in a sealed tube at high temperature. We now describe a new method for the preparation of quinazoline derivatives using 2-amino-N′-arylbenzimidamides and 7,7,8,8-tetracyanoquinodimethane (TCNQ) as starting materials. The advantage of our method is carrying out the reaction at room temperature without using catalyst or hazardous compounds. We have used this method to synthesise novel 2,4-disubstituted quinazolines in good yields from the reaction of 2-amino-*N*′-arylbenzimidamides with tetracyanoethylene[9] and 2,3-dichloro-1,4-naphthoquinone.[10] This strategy is considered as an extension of our long-term interest in chemical reactions induced by charge-transfer complexation to obtain new heterocyclic systems.[11,12] TCNQ is a very known electron-acceptor molecule, which has been successfully used for preparation of electrically conducting salts and CT-complexes. The interest of TCNQ has been focused on its potential application on molecules rectifiers, non linear optical materials, organic ferromagents, and organic chromophores with electron accepting properties.

Results and discussion

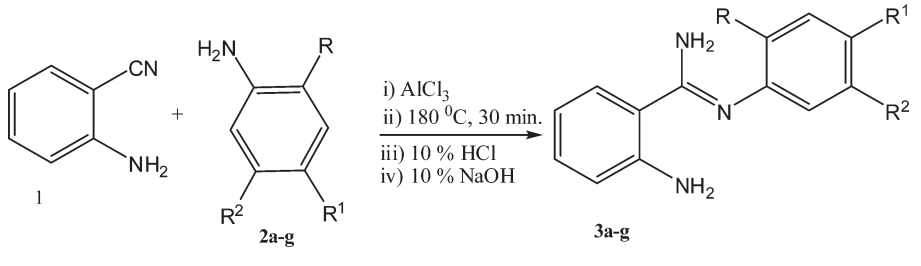
The starting materials of the present work (2-amino-*N*′-arylbenzimidamides, **3a–g**) were prepared in good yields by treatment of 2-aminobenzonitrile (**1**) with substituted aniline **2a–g** in the presence of aluminium chloride as a catalyst and they were all fully characterised (Scheme 1).[9]

As a part of our current studies we describe here the reaction between 2-amino-*N*′-arylbenzimidamides (**3a–g**) with 7,7,8,8-tetracyanoquinodimethane (**4**) producing {4-[(*Z*)-4-(arylimino)-3,4-dihydroquinazolin-2(1*H*)-ylidene]cyclohexa-2,5-dien-1-ylidene}-malononitrile (**5a–g**) derivatives. The reaction proceeded spontaneously in dry ethyl acetate at room temperature and was completed within a few hours (4–7 h), (Scheme 2).

The results obtained from elemental microanalysis and the IR, ^{1}H NMR, and ^{13}C NMR data as well as the mass spectra are in agreement with the assigned structures **5a–g**.

As an example IR spectrum of compound **5d** showed two strong absorptions at ν = 2183 and 2143 cm^{-1}, indicating the presence of two different cyano groups. While the C=N group absorbed in the IR spectrum at ν = 1636 cm^{-1}. However, the ^{1}H NMR spectrum of **5d** shows two broad resonances at δ = 10.99 and 7.92 ppm for exchangeable protons (NH). Moreover, there are four doublets at δ = 8.59, 7.81, 7.74 and 6.91 ppm with coupling constants *J* = 8.46, 8.95, 7.87 and 8.56 Hz, respectively characteristic for seven aromatic protons. In addition to two muliplets at δ = 8.04–7.96 and 7.72–7.65 characteristic for five aromatic protons. The ^{13}C NMR spectrum of **5d** showed 17 distinct resonances, where two of these 17 carbon atoms resonate at δ = 92.25 and 71.07 ppm assignable for the two the quaternary carbons (HN-C=C) and (C(CN)$_2$), respectively. While the cyano-group carbon atom resonates at δ = 112.10 ppm. The mass spectrum of this sample gives the molecular ion peak at *m/z* = 441/439 which is in accordance with the molecular weight of the compound **5d**. In addition to two fragmentations at *m/z* = 413 and 358 which are characteristic for both (M$^+$–CN) and (M$^+$–Br), respectively.

The ^{1}H and ^{13}C NMR spectra of the other compounds were similar to those of **5d** except for the substituents in the *o*- and *p*- position of the *N*-aryl group, which exhibited characteristic signals with appropriate chemical shifts.



Scheme 1 Synthesis of 2-aminoarylbenzimidamides (**3a–g**).

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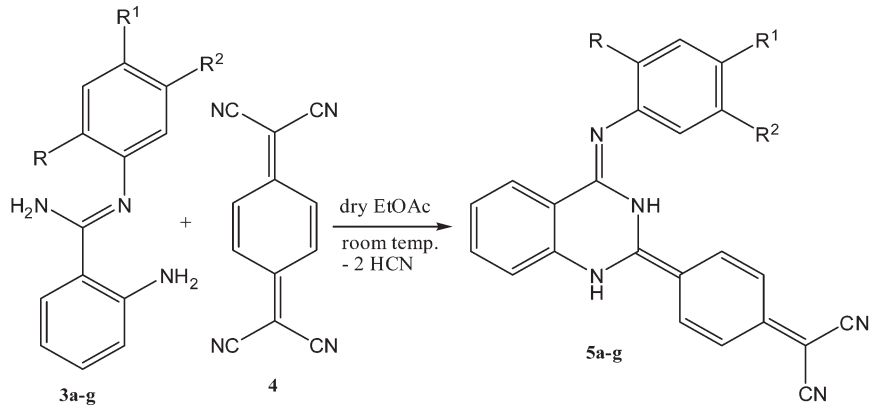

3,5

a, R = R^1 = R^2 = H **b**, R = R^2 = H, R^1 = CH_3 **c**, R = R^2 = H, R^1 = Cl
d, R = R^2 = H, R^1 = Br **e**, R = R^2 = H, R^1 = OCH_3 **f**, R = R^2 = CH_3, R^1 = H
g, R = R^1 = CH_3, R^2 = H

Scheme 2 Reaction of 2-amino-*N*′-arylbenzimidamides (**3a–g**) with TCNQ (**4**).

Conclusion

In conclusion, we have found a novel simple and efficient route for the synthesis of {4-[(*Z*)-4-(arylimino)-3,4-dihydroquinazolin-2(1*H*)-ylidene]cyclohexa-2,5-dien-1-ylidene}-malononitrile (**5a–g**) which are not obtained easily or as the sole products by other methods. These functionalised products are amenable to further transformations, and we anticipate that they may have important applications in industrial, medicinal and synthetic organic chemistry.

Experimental

All reagents were purchased from Alfa Aesar and Fluka and were used without further purification. 2-amino-*N*′-arylbenzimidamides (**3a–g**) were prepared according to ref.9. Melting points were measured in capillary tubes using a Büchi 530 melting point apparatus and are uncorrected. IR spectra were measured using a Bruker Tensor 27 instrument. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded in DMSO-d_6, on a Bruker AM 400 MHz spectrometer with TMS as internal standard. The mass spectral measurements (EI, 70 eV) were performed using a Finnigan MAT 8430 spectrometer. Elemental analyses have been determined by using automatic C,H,N (2400 P.E.).

*Reactions of 2-amino-N′-arylbenzimidamides (**3a–g**) with 7,7,8,8-tetracyanoquino-dimethane (**4**); general procedure*

To a well stirred solution of 7,7,8,8-tetracyanoquinodimethane (**4**) (0.11 mmol) dissolved in dry EtOAc (20 mL). A solution of 2-amino-*N*′-arylbenzimidamides (**3a–g**) (0.1 mmol) in dry EtOAc (15 mL) was added portionwise at room temperature. The colour of the solution changed to red. The reaction mixture was stirred at room temperature for 4-7 h. After completion of the reaction (the reaction was followed by TLC), the formed precipitate was collected by filtration, washed and recrystallised from DMF/EtOH to afford products **5a–g** in 45–60 % yield.

{4-[(Z)-4-(4-Phenylimino)-3,4-dihydroquinazolin-2(1H)-ylidene] cyclohexa-2,5-dien-1-ylidene}malononitrile (**5a**): Brownish-red solid; yield: (21 mg, 60 %); m.p. 130–131 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ = 10.94 (s, 1 H, NH), 8.60 (d, 1 H, *J* = 8.36 Hz), 8.07–7.93 (m, 3 H), 7.82 (d, 2 H, *J* = 7.49 Hz), 7.76–7.67 (m, 2 H), 7.55 (t, 3 H, *J* = 7.44 Hz), 7.36–7.29 (m, 1 H), 6.87 (d, 2 H, *J* = 8.68 Hz) ppm; ^{13}C NMR (100 MHz, d_6-DMSO): δ = 157.82, 157.77, 136.97, 135.64, 133.12, 131.02 (CH), 129.82 (CH), 129.60 (CH), 129.17 (2 CH), 128.58 (CH), 127.90 (CH), 126.53 (CH), 125.05 (CH), 124.01 (CH), 117.78 (CH), 114.74 (CH), 112.51 (CN), 92.27 (HN–C=C), 71.11 (C(CN)$_2$) ppm; IR (KBr): ν_{max} = 3256, 2180, 2135, 1633, 1599, 1560, 1537, 1520 cm^{-1}; MS (EI): *m/z* (%) = 361 (M^+, 64), 360 (M^+–1, 100), 335 (M^+–CN, 10), 295 (16), 242 (8), 236 (10), 218 (12), 192 (10), 166 (12), 153 (8), 114 (6), 102 (12), 93 (8), 77 (10), 57 (6), 44 (18); $C_{23}H_{15}N_5$ (361.40): Calcd: C, 76.44; H, 4.18; N, 19.38. Found: C, 76.29; H, 4.15; N, 19.27%.

{4-[(Z)-4-(4-p-Tolylimino)-3,4-dihydroquinazolin-2(1H)-ylidene] cyclohexa-2,5-dien-1-ylidene}malononitrile (**5b**): Red solid; yield: (21 mg, 57 %); m.p. > 310 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ = 10.98 (s, 1 H, NH) 7.99 (d, 2 H, *J* = 8.73 Hz), 7.96–7.92 (m, 2 H), 7.82–7.77 (m, 2 H), 7.71 (d, 2 H, *J* = 8.40 Hz), 7.41–7.35 (m, 2 H), 7.38 (s, 1 H, NH), 6.90 (d, 2 H *J* = 8.83 Hz), 2.39 (s, 3 H. CH_3) ppm; ^{13}C NMR (100 MHz, d_6-DMSO): δ = 157.82, 157.77, 136.97, 135.64, 133.12, 131.02 (CH), 129.82 (CH), 129.60 (CH), 129.17 (2 CH), 128.58 (CH), 127.90 (CH), 126.53 (CH), 125.05 (CH), 124.01 (CH), 117.78 (CH), 116.48 (CH), 112.13 (CN), 92.24 (HN–C=C), 71.09 (C(CN)$_2$), 20.68 (CH_3) ppm; IR (KBr): ν_{max} = 3260, 2171, 2121, 1636, 1596, 1564, 1536 cm^{-1}; MS (EI): *m/z* (%) = 375 (M^+, 48), 374 (M^+ –1, 100), 349 (M^+ – CN, 6), 309 (M^+ – (CH_3+2CN), 8), 269 (12), 232 96), 192 (6), 174 (8), 141 (6), 114 (4), 102 (10), 65 (8), 40 (6); $C_{24}H_{17}N_5$ (375.43): Calcd: C, 76.78; H, 4.56; N, 18.65. Found: C, 76.61; H, 4.52; N, 18.50%.

{4-[(Z)-4-(4-Chlorophenylimino)-3,4-dihydroquinazolin-2(1H)-ylidene] cyclohexa-2,5-dien-1-ylidene}malononitrile (**5c**): Red powder; yield: (19 mg, 49 %); m.p. > 310 °C. This sample is insoluble in the available deuterated solvents; IR (KBr): ν_{max} = 3257, 3188, 2183, 2143, 1636 cm^{-1}; MS (EI): *m/z* (%) = 397 (M^{+2}, 28), 395 (M^+, 80), 371 (M^+- CN, 12), 357 (10), 329 (8), 320 (2), 293 (4), 269 (20), 252 (4), 228 (2), 217 (8), 204 (4), 184 (8), 167 (10), 141 (10), 127 (2), 114 (4), 102 (18), 75 (12); $C_{23}H_{14}ClN_5$ (395.84): Calcd: C, 69.79; H, 3.56; Cl, 8.96; N, 17.69. Found: C, 69.61; H, 3.50; Cl, 8.80; N, 17.57%.

{4-[(Z)-4-(4-Bromophenylimino)-3,4-dihydroquinazolin-2(1H)-ylidene] cyclohexa-2,5-dien-1-ylidene}malononitrile (**5d**): Red crystals; yield: (24 mg, 55 %); m.p. 294–297 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ = 10.99 (s, 1 H, NH), 8.59 (d, 1 H, *J* = 8.46 Hz), 8.04–7.96. (m, 3 H), 7.92 (s, 1 H, NH), 7.81 (d, 2 H, *J* = 8.95 Hz), 7.74 (d, 2 H, *J* = 8.87 Hz), 7.72–7.65 (m, 2 H), 6.91 (d, 2 H, *J* = 8.56 Hz) ppm; ^{13}C NMR (100 MHz, d_6-DMSO): δ = 157.85, 136.49, 135.81 (CH), 131.64 (2 CH), 131.35 (CH), 129.69 (CH), 126.88 (CH), 126.23 (CH), 125.88 (CH), 124.03 (CH), 122.73, 118.19 (CH), 117.88 (CH), 112.10 (CN), 92.25 (HN-C=C), 71.07 (C(CN)$_2$) ppm; IR (KBr): ν_{max} = 3258, 2183, 2143, 1636, 1596, 1556, 1534 cm^{-1}; MS (EI): *m/z* (%) = 441 (M^{+2}, 70), 440 (M^{+1}, 100), 439 (M^+, 72), 438 (M^+-1, 90), 413 (M^+- CN, 6), 375 (6), 358 (M^+- Br,16), 315 (4), 293 (6), 269 (12), 217 (8), 192 (8), 166 (20), 147 (12), 114 (6), 102 (6), 75 (8), 63 (4), 43 (6); $C_{23}H_{14}BrN_5$ (440.29): Calcd: C, 62.74; H, 3.20; N, 15.91. Found: C, 62.60; H, 3.16; N, 15.79%.

{4-[(Z)-4-(4-Methoxyphenylimino)-3,4-dihydroquinazolin-2(1H)-ylidene]cyclohexa-2,5-dien-1-ylidene}malononitrile (**5e**): Red solid; yield: (20 mg, 51 %); m.p. 287–290 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ = 10.95 (s, 1 H, NH) 8.60 (d, 1 H, *J* = 8.09 Hz), 8.14–7.96 (m, 4 H), 7.78–7.67 (m, 4 H), 7.14 (d, 2 H, *J* = 8.92 Hz), 6.91 (d, 2 H, *J* = 8.68 Hz), 3.86 (s, 3 H, OCH_3) ppm; ^{13}C NMR (100 MHz, d_6-DMSO): δ = 159.23, 157.85, 136.49, 135.81 (CH), 131.54 (2 CH),

131.30 (CH), 129.63 (CH), 126.87 (CH), 126.23 (CH), 125.85 (CH), 124.03 (CH), 122.73, 117.21 (CH), 116.18 (CH), 112.15 (CN), 92.22 (HN–C=C), 71.12 ($\underline{C}(CN)_2$), 55.80 (OCH_3) ppm; IR (KBr): ν_{max} = 3257, 3198, 21753, 2137, 1635 cm^{-1}; MS (EI): *m/z* (%) = 391 (M^+, 100), 376 (M^+- CH_3, 84), 366 (12), 351 (8), 320 (10), 281 (2), 269 (64), 244 (8), 204 (6), 167 (6), 141 (16), 108 (10), 102 (10), 83 (8), 75 (10); $C_{24}H_{17}N_5O$ (391.42): Calcd: C, 73.64; H, 4.38; N, 17.89. Found: C, 73.49; H, 4.34; N, 17.75%.

{4-[(Z)-4-(2,5-Dimethylphenylimino)-3,4-dihydroquinazolin-2(1H)-ylidene]cyclohexa-2,5-dien-1-ylidene}malononitrile (**5f**): Red solid; yield: (22 mg, 57 %); m.p. 275–277 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ = 11.04 (s, 1 H, NH), 8.56 (d, 1 H, *J* = 8.12 Hz), 8.04–7.94. (m, 2 H), 7.80 (d, 2 H, *J* = 8.85 Hz), 7.75–7.63 (m, 1 H), 7.50 (s, 3 H, NH), 7.33–7.27 (m, 2 H), 7.18 (d, 1 H, *J* = 7.78 Hz), 6.80 (d, 2 H, *J* = 8.82 Hz), 2.36 (s, 3 H, CH_3), 2.21 (s, 3 H, CH_3) ppm; ^{13}C NMR (100 MHz, d_6-DMSO): δ = 158.71, 155.85, 135.79, 135.47 (CH), 134.98, 131.37, 130.46 (2 CH), 129.38 (2 CH), 128.32 (CH), 127.58 (CH), 126.69 (CH), 123.77 (CH), 122.72, 117.60 (2 CH), 111.62 (CN), 92.23 (HN-C=C), 71.05 ($\underline{C}(CN)_2$), 20.43 (CH_3), 17.40 (CH_3) ppm; IR (KBr): ν_{max} = 3259, 2185, 2142, 1637, 1598, 1561, 1536, 1509 cm^{-1}; MS (EI): *m/z* (%) = 389 (M^+, 100), 374 (M^+- CH_3, 70), 349 (10), 332 (4), 309 (8), 292 (4), 269 (8), 248 (10), 238 (4), 222 (48), 206 (12), 192 (8), 181 (16), 160 (8), 141 (8), 120 (16), 102 (12), 83 (8), 69 (12), 55 (16), 44 (24); $C_{25}H_{19}N_5$ (389.45): Calcd: C, 77.10; H, 4.92; N, 17.98. Found: C, 76.92; H, 4.89; N, 17.85%.

{4-[(Z)-4-(2,4-Dimethylphenylimino)-3,4-dihydroquinazolin-2(1H)-ylidene]cyclohexa-2,5-dien-1-ylidene}malononitrile (**5g**): Red solid; yield: (18 mg, 46 %); m.p. 211–213 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ = 10.90 (s, 1 H, NH), 8.61 (d, 1 H, *J* = 7.91 Hz), 8.08–7.94. (m, 2 H), 7.83 (d, 2 H, *J* = 7.90 Hz), 7.39–7.31 (m, 1 H), 7.26–7.22 (m, 2 H), 7.03 (d, 1 H, *J* = 8.48 Hz), 6.82 (d, 2 H, *J* = 8.63 Hz), 6.54 (d, 1 H, *J* = 8.33 Hz), 2.40 (s, 3 H, CH_3), 2.25 (s, 3 H, CH_3) ppm; ^{13}C NMR (100 MHz, d_6-DMSO): δ = 158.74, 136.73 (CH), 134.10, 132.64, 131.08 (CH), 129.24 (2 CH), 129.04 (CH), 127.00 (CH), 126.75 (CH), 123.92 (CH), 117.52 (CH), 116.42 (CH), 111.67 (CN), 92.19 (HN-C=C), 71.02 ($\underline{C}(CN)_2$), 20.59 (CH_3), 17.68 (CH_3) ppm; IR (KBr): ν_{max} = 3178, 3047, 2180, 2135, 1630 cm^{-1}; MS (EI): *m/z* (%) = 389 (M^+, 100), 374 (M^+- CH_3, 60), 308 (4), 269 (12), 222 (44), 206 (8), 181 (8), 159 (4), 141 (10), 120 (13), 102 (12), 91 (8), 77 (12), 60 (8); $C_{25}H_{19}N_5$ (389.45): Calcd: C, 77.10; H, 4.92; N, 17.98. Found: C, 76.89; H, 4.85; N, 17.79%.

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References

1 D.J. Brown, *The chemistry of heterocyclic compounds: Quinazolines.* Suppl. 1, John Wiley, New York, 1998.
2 S. Tamaoki, Y. Yamauchi, Y. Nakano, S. Sakano, A. Asagarasu and M. Sato, *J. Pharm. Exp. Ther*., 2007, **322**,1315.
3 S. Madapa, Z. Tusi, A. Mishra, K. Srivastava, S.K. Pandey, R. Tripathi, S.K. Puri and S. Batra, *Bioorg. Med. Chem*. 2009, **17**, 222.
4 G.M. Chinigo, M. Paige, S. Grindrod, E. Hamel, S. Dakshanamurthy, M. Chruszcz, W. Minor and M.L. Brown, *J. Med. Chem*., 2008, **51**, 4620.
5 S. Madapa, Z. Tusi, A. Mishra, K. Srivastava, S.K. Pandey, R. Tripathi, S.K. Puri and S. Batra, *Bioorg. Med. Chem.*, 2009, **17**, 2224.
6 K.M. El-Shaieb and P.G. Jones, *Z. Naturforsch.*, 2009, **64b**, 945.
7 K.M. El-Shaieb, H. Hopf and P.G. Jones, *Arkivoc*, 2009, **x**, 146.
8 K.M. El-Shaieb, H. Hopf and P.G. Jones, *Arkivoc*, 2010, **x**, 98.
9 K.M. El-Shaieb, H. Hopf and P.G. Jones, *Z. Naturforsch.*, 2009, **64b**, 858.
10 K. M. El-Shaieb, *J. Chem. Res.*, 2010, **34**, 137.
11 A.A. Aly, K.M. El-Shaieb, *Tetrahedron*, 2004, **60**, 3797.
12 K.M. El-Shaieb, A.-F.E. Mourad, A.A. Aly and H. Hopf, *Arkivoc*, 2006, **ii**, 193.