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Syntheses and crystal structures of guanidine hydrochlorides with two Schiff base functions as efficient colorimetric and selective sensors for fluoride

https://doi.org/10.1515/znb-2018-0102
Received May 11, 2018; accepted June 28, 2018

Abstract: A series of guanidinium chloride derivatives have been synthesized by condensation of 1,3-diaminoguanidine monohydrochloride with heteroaromatic formaldehydes in good yields. All compounds were characterized by nuclear magnetic resonances and infrared spectroscopies, and the molecular structures of four compounds were determined by single crystal X-ray diffraction. The optical properties of these guanidinium chloride derivatives with fluoride anions were investigated, showing selective color changes from colorless to yellow or orange, red-shifted in the ultraviolet/visible absorption spectra.

Keywords: fluoride sensor; guanidinium chloride; Schiff base; selective chemosensor; X-ray structure.

1 Introduction

Both Schiff bases and guanidine derivatives are interesting nitrogen-containing heterocyclic molecules that possess various types of physical, chemical, and biological properties [1–4], which have resulted in wide applications in the fields of agrochemicals and pharmaceuticals, such as anti-inflammatory [5], antimicrobial [3, 6], antifungal [7], antitumor [8, 9], and antimalarial agents [10, 11]. The guanidinium moiety of the guanidine derivatives is widely used as an anion binding site in biology as well as in colorimetric molecular probes [12–16]; for example, the detection of citrate using guanidinium-based tripodal receptors [17, 18], a colorimetric biosensor based on guanidinium recognition for the detection of protein tyrosine phosphatase 1B and its inhibitor [19], and efficient colorimetric anion sensors for fluoride [20]. The compounds with an indole functionality was used for selective sensing of fluoride by the naked eye and with a near infrared (IR) signature signal at ~930 nm [20]. With these observations in mind, we functionalized guanidine hydrochloride with Schiff bases in order to arrive at efficient colorimetric and selective sensors for fluoride anion via naked eye detection of a pattern of color changes as well as a range of absorption signals in the near IR range in this paper.

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2 Experimental

2.1 Materials and methods

1,3-Diaminoguanidine hydrochloride and all tetrabutylammonium salts of other anions were purchased from Sigma-Aldrich and were used as supplied. 2-Hydroxybenzaldehyde (99%), 5-chloro-2-hydroxybenzaldehyde (98%), 2-hydroxy-5-nitrobenzaldehyde (98%), 3,5-di-bromo-2-hydroxybenzaldehyde (98%), 4-(diethylamino)-2-hydroxybenzaldehyde (99%), 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde, 4-*iso*-propylbenzaldehyde (97%), 2-nitrobenzaldehyde (99%), 3-hydroxybenzaldehyde (98%), 3-hydroxy-4-methoxybenzaldehyde (97%), 4-(methyl-sulfonyl)benzaldehyde (98%), 4-(dimethylamino)benzaldehyde (98%), 4-methoxybenzaldehyde (98%), 4-bromobenzaldehyde (98%), benzaldehyde (99%), cinnamaldehyde (98%), 1-naphthaldehyde (98%), nicotinaldehyde (98%), thiophene-2-carbaldehyde (98%), thiophene-3-carbaldehyde (98%), and 5-bromothiophene-2-carbaldehyde (97%) were purchased from Alfa Aesar Ltd. and used as received without further purification. Melting points were determined in capillaries using an X4 digital melting-point apparatus and are uncorrected. The infrared spectra were recorded on a Nicolet 6700 spectrophotometer with the use of pressed KBr pellets. The ultraviolet absorption spectra were recorded on a Shimadzu UV-2501 PC spectrophotometer. ^{1}H and ^{13}C nuclear magnetic resonance (NMR) spectra were recorded on a Bruker AV400-MHz Advance NMR spectrometer at 400 MHz for ^{1}H NMR and at 100 MHz for ^{13}C NMR.

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2.2 General synthesis procedure

N,*N*′-Diaminoguanidine hydrochloride (0.628 g, 5.00 mmol) was taken up in 64 mL ethanol-water (5:1, *v*/*v*) solution, and the mixture was stirred for 15 min until complete dissolution. To this solution, the respective substituted aldehyde (10.00 mmol) in 10 mL ethanol solution was added, and the mixture was stirred at room temperature for 2 h, and then the solution was continuously refluxed at 80°C for 6–8 h. The product was precipitated from the solution. It was cooled, filtered, washed with methanol and ether, and finally air dried to obtain a solid.

2.2.1 1,3-Bis(2-hydroxyphenyl-methylideneamino) guanidine hydrochloride (DG1)

White solid, yield: 1.305 g (78%), m.p.: 259–261°C. – ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.90 (br, 2H, –NH · HCl), 10.31 (s, 2H, –OH), 9.08 (s, 2H, –NH–N), 8.31 (s, 2H, –CH=N), 8.04 (dd, J = 14.7 and 3.1 Hz, 2H, –C_6H_4), 7.31 (dd, J = 15.0 and 3.3 Hz, 2H, –C_6H_4), 6.90 (td, J = 10.8 and 3.1 Hz, 2H, –C_6H_4), 6.86 (dd, J = 14.8 and 3.2 Hz, 2H, –C_6H_4) ppm. – ^{13}C NMR (100 MHz, DMSO-d_6): δ = 159.19, 156.99, 144.20, 133.55, 128.72, 120.06, 119.63, 117.00 ppm. – IR (KBr disc, cm^{-1}): 3412, 2881, 1641, 1606, 1488, 1414, 1358, 1269, 1149, 1034, 964, 784, 751, 668, 646, 571, 473.

2.2.2 1,3-Bis(5-chloro-2-hydroxyphenyl-methylideneamino)guanidine hydrochloride (DG2)

Light yellow solid, yield: 1.518 g (75%), m.p.: 265–268°C. – ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.20 (br, 2H, –NH · HCl), 10.65 (s, 2H, –OH), 8.94 (s, 2H, –NH–N), 8.54 (s, 2H, –CH=N), 8.18 (d, J = 2.7 Hz, 2H, –C_6H_3), 7.31 (dd, J = 8.8 and 2.7 Hz, 2H, –C_6H_3), 6.99 (d, J = 8.8 Hz, 2H, –C_6H_3) ppm. – ^{13}C NMR (100 MHz, DMSO-d_6): δ = 151.52, 146.54, 142.72, 131.95, 126.88, 124.76, 121.24, 117.21 ppm. – IR (KBr disc, cm^{-1}): 3361, 3104, 2924, 1677, 1629, 1562, 1484, 1426, 1394, 1354, 1265, 1237, 1175, 1097, 960, 917, 880, 823, 725, 703, 651, 589, 480.

2.2.3 1,3-Bis(2-hydroxy-5-nitrophenyl-methylideneamino)guanidine hydrochloride (DG3)

Orange yellow solid, yield: 0.989 g (47%), m.p.: 280–282°C. – ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.60 (br, 2H, –NH · HCl), 10.01 (s, 2H, –OH), 8.89 (s, 2H, –NH–N), 8.67 (s, 2H, –CH=N), 8.34 (d, J = 3.1 Hz, 2H, –C_6H_3), 8.01 (dd, J = 15.0 and 3.0 Hz, 2H, –C_6H_3), 7.05 (d, J = 14.9 Hz, 2H, –C_6H_3) ppm. – ^{13}C NMR (100 MHz, DMSO-d_6): δ = 160.75, 152.09, 144.22, 138.94, 129.06, 124.91, 119.66, 116.89 ppm. – IR (KBr disc, cm^{-1}): 3430, 3285, 1677, 1645, 1615, 1586, 1522, 1488, 1441, 1384, 1345, 1295, 1247, 1178, 1128, 1105, 1079, 956, 828, 748, 640, 506.

2.2.4 1,3-Bis(3,5-dibromo-2-hydroxyphenyl-methylideneamino)guanidine hydrochloride (DG4)

Yellow solid, yield: 1.758 g (54%), m.p.: 277–279°C. – ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.34 (br, 2H, –NH · HCl), 10.31 (s, 2H, –OH), 8.95 (s, 2H, –NH–N), 8.67 (s, 2H, –CH=N), 8.28 (s, 2H, –C_6H_2), 7.86 (s, 2H, –C_6H_2) ppm. – ^{13}C NMR (100 MHz, DMSO-d_6): δ = 156.36, 151.79, 145.02, 136.78, 130.70, 122.15, 118.59, 116.37 ppm. – IR (KBr disc, cm^{-1}): 3440, 3293, 3229, 3133, 3073, 2989, 1676, 1633, 1552, 1459, 1448, 1349, 1312, 1269, 1220, 1145, 958.

2.2.5 1,3-Bis(4-diethylamino-2-hydroxyphenyl-methylideneamino)guanidine hydrochloride (DG5)

Light yellow solid, yield: 1.376 g (58%), m.p.: 224–227°C. – ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.51 (br, 2H, –NH · HCl), 9.72 (s, 2H, –OH), 8.94 (s, 2H, –NH–N), 7.98 (s, 2H, –CH=N), 7.72 (d, J = 8.6 Hz, 2H, –C_6H_3), 6.25 (d, J = 8.1 Hz, 2H, –C_6H_3), 6.14 (s, 2H, –C_6H_3), 3.43 (m, 8H, –CH_2–), 1.10 (t, J = 6.8 Hz, 12H, –CH_3) ppm. – ^{13}C NMR (100 MHz, DMSO-d_6): δ = 158.88, 151.87, 151.13, 142.26, 129.28, 107.34, 104.44, 97.50, 44.32, 13.01 ppm. – IR (KBr disc, cm^{-1}): 3286, 3194, 2967, 1647, 1623, 1546, 1516, 1457, 1401, 1351, 1296, 1244, 1216, 1134, 1075, 1017, 954, 827, 781, 668, 528.

2.2.6 1,3-Bis(3,5-di-*tert*-butyl-2-hydroxyphenyl-methylideneamino)guanidine hydrochloride (DG6)

White solid, yield: 1.516 g (54%), m.p.: 192–194°C. – ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.76 (br, 2H, –NH · HCl), 9.81 (s, 2H, –OH), 8.98 (s, 2H, –NH–N), 8.24 (s, 2H, –CH=N), 7.34 (s, 2H, –C_6H_2), 7.03 (s, 2H, –C_6H_2), 1.27 (s, 18H, –CH_3), 1.23 (s, 18H, –CH_3) ppm. – ^{13}C NMR (100 MHz, DMSO-d_6): δ = 152.35, 144.79, 142.06, 141.02, 139.89, 126.53, 124.62, 121.19, 35.14, 31.25 ppm. – IR (KBr disc, cm^{-1}): 3357, 2959, 1639, 1584, 1472,

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1429, 1391, 1361, 1251, 1235, 1201, 1172, 1079, 1046, 959, 875, 803, 768, 725, 644.

2.2.7 1,3-Bis(4-*iso*-propylphenyl-methylideneamino) guanidine hydrochloride (DG7)

White needle solid, yield: 1.569 g (81%), m.p.: 209–211°C. – ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.21 (br, 2H, –NH · HCl), 8.96 (s, 2H, –NH–N), 8.40 (s, 2H, –CH=N), 7.85 (d, J = 8.3 Hz, 4H, –C_6H_4), 7.35 (d, J = 8.3 Hz, 4H, –C_6H_4), 2.98–2.90 (m, 2H, –CH–), 1.22 (d, J = 6.9 Hz, 12H, –CH_3) ppm. – ^{13}C NMR (100 MHz, DMSO-d_6): δ = 153.79, 151.68, 144.74, 129.22, 127.10, 126.83, 33.90, 24.08 ppm. – IR (KBr disc, cm^{-1}): 3364, 3232, 3133, 2958, 1645, 1511, 1460, 1405, 1345, 1302, 1229, 1182, 1052, 1015, 962, 828, 669, 555.

2.2.8 1,3-Bis(2-nitrophenyl-methylideneamino) guanidine hydrochloride (DG8)

Orange red solid, yield: 1.532 g (78%), m.p.: 240–244°C. – ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.72 (br, 2H, –NH · HCl), 8.97 (s, 2H, –NH–N), 8.77 (s, 2H, –CH=N), 8.49 (d, J = 7.4 Hz, 2H, –C_6H_4), 8.12 (dd, J = 8.2 and 1.0 Hz, 2H, –C_6H_4), 7.86 (t, J = 7.3 Hz, 2H, –C_6H_4), 7.79–7.70 (m, 2H, –C_6H_4) ppm. – ^{13}C NMR (100 MHz, DMSO-d_6): δ = 153.91, 148.20, 145.01, 134.80, 131.97, 129.61, 128.43, 125.56 ppm. – IR (KBr disc, cm^{-1}): 3327, 3029, 1671, 1645, 1598, 1518, 1470, 1440, 1359, 1312, 1218, 1172, 1090, 965, 924, 867, 785, 646, 518, 454.

2.2.9 1,3-Bis(3-hydroxy-phenyl-methylideneamino) guanidine hydrochloride (DG9)

White solid, yield: 1.113 g (67%), m.p.: 165–168°C. – ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.52 (br, 2H, –NH · HCl), 9.83 (s, 2H, –OH), 8.96 (s, 2H, –NH–N), 8.25 (s, 2H, –CH=N), 7.30 (dt, J = 7.6 and 1.5 Hz, 2H, –C_6H_4), 7.21 (t, J = 1.5 Hz, 2H, –C_6H_4), 7.14 (t, J = 7.5 Hz, 2H, –C_6H_4), 6.87 (dt, J = 7.5 and 1.4 Hz, 2H, –C_6H_4) ppm. – ^{13}C NMR (100 MHz, DMSO-d_6): δ = 156.29, 154.44, 145.51, 133.48, 131.37, 128.46, 120.53, 116.84 ppm. – IR (KBr disc, cm^{-1}): 3313, 1643, 1589, 1540, 1454, 1351, 1313, 1269, 1180, 1159, 1048, 970, 948, 872, 686, 552, 458.

2.2.10 1,3-Bis(3-hydroxy-4-methoxyphenyl-methylideneamino)guanidine hydrochloride (DG10)

White solid, yield: 1.534 g (78%), m.p.: 174–176°C. – ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.74 (br, 2H, –NH · HCl), 9.85 (s, 2H, –OH), 8.90 (s, 2H, –NH–N), 8.23 (s, 2H, –CH=N), 7.54 (s, 2H, –C_6H_3), 7.22 (t, J = 2.4 Hz, 2H, –C_6H_3), 6.85 (d, J = 14.7 Hz, 2H, –C_6H_3), 3.62 (s, 6H, –OCH_3) ppm. – ^{13}C NMR (100 MHz, DMSO-d_6): δ = 152.91, 150.08, 148.58, 125.46, 123.36, 115.85, 112.23, 110.68, 65.32 ppm. – IR (KBr disc, cm^{-1}): 3376, 2963, 1656, 1603, 1517, 1450, 1430, 1383, 1283, 1217, 1200, 1170, 1123, 1059, 1034, 948, 858, 784, 761, 668, 613.

2.2.11 1,3-Bis(4-methylsulfonyl-phenyl-methylideneamino)guanidine hydrochloride (DG11)

Light yellow solid, yield: 1.422 g (62%), m.p.: 273–275°C. – ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.63 (br, 2H, –NH · HCl), 8.90 (s, 2H, –NH–N), 8.55 (s, 2H, –CH=N), 8.23 (d, J = 8.5 Hz, 4H, –C_6H_4), 8.02 (d, J = 8.4 Hz, 4H, –C_6H_4), 3.28 (s, 6H, –CH_3) ppm. – ^{13}C NMR (100 MHz, DMSO-d_6): δ = 150.48, 145.12, 144.74, 140.15, 129.04, 127.38, 43.87 ppm. – IR (KBr disc, cm^{-1}): 3345, 3226, 3013, 2926, 1641, 1595, 1525, 1420, 1398, 1306, 1292, 1176, 1141, 1087, 1053, 969, 937, 830, 772, 713, 622, 555, 535, 469.

2.2.12 1,3-Bis(4-dimethylamino-phenylethylideneamino) guanidine hydrochloride (DG12)

Light yellow solid, yield: 1.169 g (60%), m.p.: 183–185°C. – ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.14 (br, 2H, –NH · HCl), 8.96 (s, 2H, –NH–N), 8.13 (s, 2H, –CH=N), 7.44 (d, J = 6.9 Hz, 4H, –C_6H_4), 6.74 (d, J = 7.4 Hz, 4H, –C_6H_4), 2.96 (s, 12H, –$N(CH_3)_2$) ppm. – ^{13}C NMR (100 MHz, DMSO-d_6): δ = 153.78, 152.05, 147.54, 129.86, 121.81, 111.69, 51.82 ppm. – IR (KBr disc, cm^{-1}): 3434, 3309, 3252, 1681, 1609, 1525, 1432, 1360, 1229, 1183, 1167, 1122, 995, 945, 816, 668, 568, 527.

2.2.13 1,3-Bis(4-methoxy-phenylethylideneamino) guanidine hydrochloride (DG13)

White solid, yield: 1.511 g (84%), m.p.: 215–218°C. – ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.04 (br, 2H, –NH · HCl), 8.98 (s, 2H, –NH–N), 8.34 (s, 2H, –CH=N), 7.88 (d, J = 8.8 Hz, 4H, –C_6H_4), 7.03 (d, J = 8.8 Hz, 4H, –C_6H_4), 3.82 (s, 6H, –OCH_3) ppm. – ^{13}C NMR (100 MHz, DMSO-d_6): δ = 161.28, 150.79, 147.94, 131.04, 127. 38, 114.86, 55.94 ppm. – IR (KBr disc, cm^{-1}): 3342, 3165, 2936, 2838, 1650, 1606, 1575, 1514, 1463, 1424, 1346, 1307, 1255, 1178, 1112, 1052, 1027, 954, 831, 779, 635, 582, 530.

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2.2.14 1,3-Bis(4-bromo-phenylethylideneamino) guanidine hydrochloride (DG14)

White solid, yield: 1.274 g (55%), m.p.: 235–239°C. – ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.29 (br, 2H, –NH · HCl), 8.91 (s, 2H, –NH–N), 8.40 (s, 2H, –CH=N), 7.91 (d, J = 8.3 Hz, 4H, –C_6H_4), 7.70 (d, J = 8.3 Hz, 4H, –C_6H_4) ppm. – ^{13}C NMR (100 MHz, DMSO-d_6): δ = 153.69, 144.89, 132.11, 130.01, 119.06 ppm. – IR (KBr disc, cm^{-1}): 3389, 1639, 1609, 1488, 1413, 1396, 1342, 1217, 1068, 1055, 1008, 961, 940, 823, 668, 512, 470.

2.2.15 1,3-Bis(phenylethylideneamino)guanidine hydrochloride (DG15)

White solid, yield: 0.981 g (65%), m.p.: 218–221°C. – ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.45 (br, 2H, –NH · HCl), 8.94 (s, 2H, –NH–N), 8.31 (s, 2H, –CH=N), 7.89 (s, 2H, –C_6H_5), 7.47 (d, J = 3.4 Hz, 4H, –C_6H_5), 7.16 (d, J = 2.8 Hz, 4H, –C_6H_5) ppm. – ^{13}C NMR (100 MHz, DMSO-d_6): δ = 154.80, 144.74, 136.25, 129.95, 128.77, 120.23 ppm. – IR (KBr disc, cm^{-1}): 3437, 3028, 1644, 1597, 1536, 1489, 1448, 1394, 1333, 1226, 1079, 1053, 951, 756, 688, 630, 507, 449.

2.2.16 1,3-Bis(3-phenyl-allylideneamino)guanidine hydrochloride (DG16)

Yellow needle solid, yield: 1.390 g (79%), m.p.: 176–179°C. – ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.94 (br, 2H, –NH · HCl), 8.94 (s, 2H, –NH–N), 8.16 (s, 2H, –CH=N), 7.60 (d, J = 4.1 Hz, 4H, –C_6H_5), 7.40 (m, 6H, –C_6H_5), 7.18 (d, J = 5.6 Hz, 2H, PhC*H*=CH–), 6.98 (d, J = 5.6 Hz, 2H, Ph–CH=C*H*–) ppm. – ^{13}C NMR (100 MHz, DMSO-d_6): δ = 153.89, 149.98, 143.04, 135.74, 135.08, 130.34, 130.11, 127.95, 127.38, 124.88 ppm. – IR (KBr disc, cm^{-1}): 3427, 1645, 1489, 1447, 1405, 1343, 1175, 1050, 977, 749, 688, 668, 507, 461.

2.2.17 1,3-Bis(1-naphthyl-ethylideneamino)guanidine hydrochloride (DG17)

White solid, yield: 1.591 g (79%), m.p.: 227–228°C. – ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.29 (br, 2H, –NH · HCl), 9.37 (s, 2H, –NH–N), 8.63 (s, 2H, –CH=N), 8.42 (dd, J = 7.8 and 4.8 Hz, 4H, Ar–*H*), 8.12 (d, J = 8.2 Hz, 2H, Ar–*H*), 8.06 (d, J = 8.0 Hz, 2H, Ar–*H*), 7.67 (tt, J = 14.3 and 7.3 Hz, 6H, Ar–*H*) ppm. – ^{13}C NMR (100 MHz, DMSO-d_6): δ = 152.94, 147.93, 144.36, 133.82, 131.67, 131.10, 129.38, 129.02, 127.93, 126.81, 126.01, 123.31 ppm. – IR (KBr disc, cm^{-1}): 3447, 3314, 3046, 2871, 1640, 1523, 1423, 1355, 1338, 1245, 1067, 1011, 945, 858, 798, 772, 727, 636, 550, 426.

2.2.18 1,3-Bis(3-pyridinyl-ethylideneamino)guanidine hydrochloride (DG18)

Yellow solid, yield: 1.030 g (68%), m.p.: 182–185°C. – ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.40 (br, 2H, –NH · HCl), 9.08 (d, J = 1.7 Hz, 2H, Py–*H*), 8.90 (s, 2H, –NH–N), 8.65 (d, J = 4.7 Hz, 2H, Py–*H*), 8.47 (s, 2H, –CH=N), 8.40 (d, J = 7.0, 2H, Py–*H*), 7.52 (dd, J = 7.9 and 4.9 Hz, 2H, Py–*H*) ppm. – ^{13}C NMR (100 MHz, DMSO-d_6): δ = 151.79, 149.69, 149.02, 144.65, 136.97, 129.63, 124.02 ppm. – IR (KBr disc, cm^{-1}): 3391, 1679, 1639, 1611, 1547, 1396, 1344, 1235, 1067, 1027, 962, 940, 866, 807, 699, 624, 459.

2.2.19 1,3-Bis(thiophene-2-yl-methylideneamino) guanidine hydrochloride (DG19)

Yellow solid, yield: 0.935 g (60%), m.p.: 208–212°C. – ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.11 (br, 2H, –NH · HCl), 8.93 (s, 2H, –NH–N), 8.24 (s, 2H, –CH=N), 8.08 (dd, J = 2.8 and 1.0 Hz, 2H, –C_4H_3S), 7.81 (dd, J = 5.0 and 2.8 Hz, 2H, –C_4H_3S), 7.67 (dd, J = 5.0 and 2.8 Hz, 2H, –C_4H_3S) ppm. – ^{13}C NMR (100 MHz, DMSO-d_6): δ = 152.56, 144.54, 137.84, 132.73, 130.83, 128.49 ppm. – IR (KBr disc, cm^{-1}): 3397, 3145, 1644, 1426, 1396, 1351, 1317, 1222, 1061, 1041, 940, 858, 832, 709, 645, 574, 504.

2.2.20 1,3-Bis(thiophene-3-yl-methylideneamino) guanidine hydrochloride (DG20)

Yellow solid, yield: 1.025 g (65%), m.p.: 251–253°C. – ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.11 (br, 2H, –NH · HCl), 8.94 (s, 2H, –NH–N), 8.39 (s, 2H, –CH=N), 8.08 (dd, J = 2.8 and 1.0 Hz, 2H, –C_4H_3S), 7.81–7.78 (m, 2H, –C_4H_3S), 7.67 (dd, J = 5.0 and 2.8 Hz, 2H, –C_4H_3S) ppm. – ^{13}C NMR (100 MHz, DMSO-d_6): δ = 150.26, 147.45, 136.58, 129.57, 126.81, 125.82 ppm. – IR (KBr disc, cm^{-1}): 3347, 3242, 3139, 1644, 1501, 1402, 1363, 1328, 1244, 1217, 1168, 1058, 946, 869, 831, 783, 668, 625.

2.2.21 1,3-Bis(5-bromo-thiophene-2-yl-methylideneamino)guanidine hydrochloride (DG21)

Yellow solid, yield: 1.424 g (60%), m.p.: 216–218°C. – ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.25 (br, 2H, –NH · HCl),

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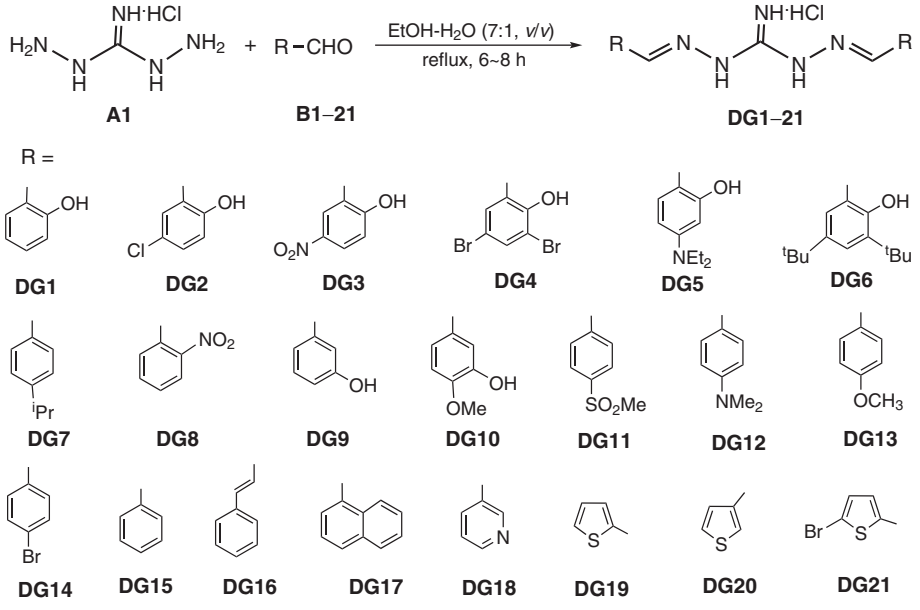
Table 1: Crystallographic data and experimental details for compounds **DG8**, **DG13** · $2H_2O$, **DG20** · $2H_2O$, and **DG21** · H_2O.

	DG8	**DG13 · 2H$_2$O**	**DG20 · 2H$_2$O**	**DG21 · H$_2$O**
Empirical formula	$C_{15}H_{14}ClN_7O_4$	$C_{17}H_{24}ClN_5O_4$	$C_{11}H_{16}ClN_5O_2S_2$	$C_{11}H_{12}Br_2ClN_5OS_2$
Formula weight	391.78	397.86	349.86	489.65
Crystal system	Monoclinic	Triclinic	Orthorhombic	Orthorhombic
Space group	*C*2/*c*	$P\bar{1}$	$Pna2_1$	*Pbca*
a, Å	31.45(2)	7.6663(16)	7.4634(10)	14.723(3)
b, Å	7.159(6)	8.3562(17)	16.630(2)	9.4871(16)
c, Å	15.495(11)	16.329(3)	13.4172(17)	26.049(5)
α, deg	90	90.845(2)	90	90
β, deg	93.366(10)	96.391(2)	90	90
γ, deg	90	100.175(2)	90	90
V, Å^3	3483(5)	1022.6(4)	1665.2(4)	3638.4(11)
Z	8	2	4	8
D_{calcd}, g cm^{-3}	1.49	1.29	1.40	1.79
Temperature, K	296(2)	296(2)	296(2)	296(2)
F(000), *e*	1616	420	728	1920
μ(MoKα), mm^{-1}	0.3	0.2	0.5	4.8
Refl. total	10 085	6303	9790	20 987
Refl. unique	3967	4467	3141	4134
R_{int}	0.0885	0.0156	0.0321	0.0620
Parameters	260	270	214	215
R_1[a]/wR_2[b] ($I > 2\sigma(I)$)	0.1044/0.2704	0.0414/0.0985	0.0426/0.1055	0.0509/0.1163
R_1[a]/wR_2[b] (all data)	0.2206/0.3520	0.0652/0.1132	0.0647/0.1202	0.1197/0.1434
GoF[c]	1.023	1.031	1.032	1.004
Flack (*x*)	–	–	0.0(1)	–
$\Delta\rho_{fin}$ (max/min), *e* Å^{-3}	+0.401/−0.433	+0.178/−0.214	+0.232/−0.210	+0.900/−0.600

[a]$R_1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$. [b]$wR_2 = [\Sigma w(F_o^2 - F_c^2)^2/\Sigma w(F_o^2)^2]^{1/2}$, $w = [\sigma^2(F_o^2) + (AP)^2 + BP]^{-1}$, where $P = (\mathrm{Max}(F_o^2, 0) + 2F_c^2)/3$. [c]$\mathrm{GoF} = S = [\Sigma w(F_o^2 - F_c^2)^2/(n_{obs} - n_{param})]^{1/2}$.



Scheme 1: Synthesis of disubstituted guanidines **DG1–21**.

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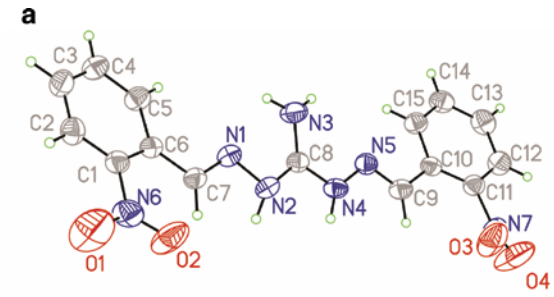
8.94 (s, 2H, –NH–N), 8.33 (s, 2H, –CH=N), 7.44 (d, J = 12.9 Hz, 2H, $-C_4H_2S$), 7.29 (dd, J = 48.6 and 10.1 Hz, 2H, $-C_4H_2S$) ppm. – ^{13}C NMR (100 MHz, DMSO-d_6): δ = 149.55, 146.56, 139.92, 134.15, 131.29, 117.73 ppm. – IR (KBr disc, cm^{-1}): 3335, 3218, 3159, 2850, 1645, 1538, 1426, 1400, 1342, 1298, 1207, 1067, 1051, 969, 940, 792, 759, 669, 636, 552, 506, 463.

2.3 Crystal structure determinations

Crystallographic data and experimental details for **DG8**, **DG13** · $2H_2O$, **DG20** · $2H_2O$, and **DG21** · H_2O are



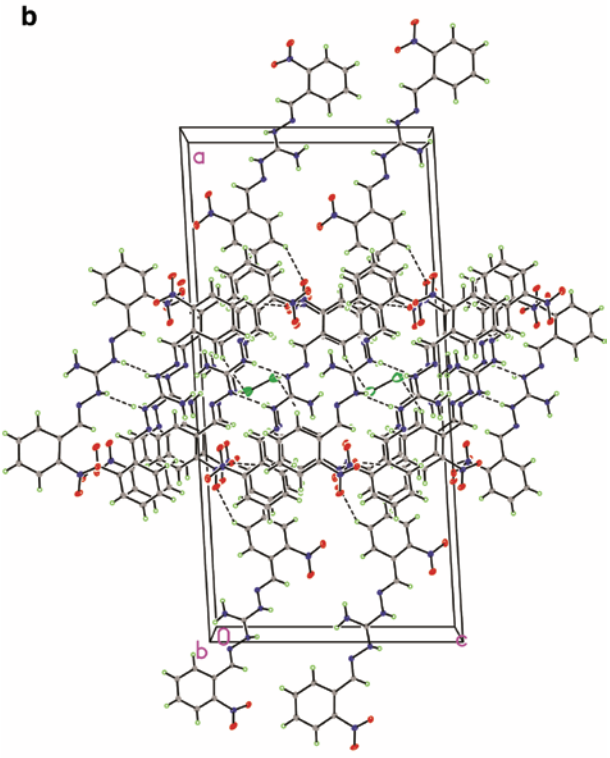


Fig. 1: (a) Molecular structure of **DG8** with the crystallographic numbering. Displacement ellipsoids are shown at the 40% probability level, the Cl^- counterion is omitted. (b) Packing diagram of compound **DG8** in a unit cell, viewed along the crystallographic *ac* plane; hydrogen bonds are shown as dashed lines.

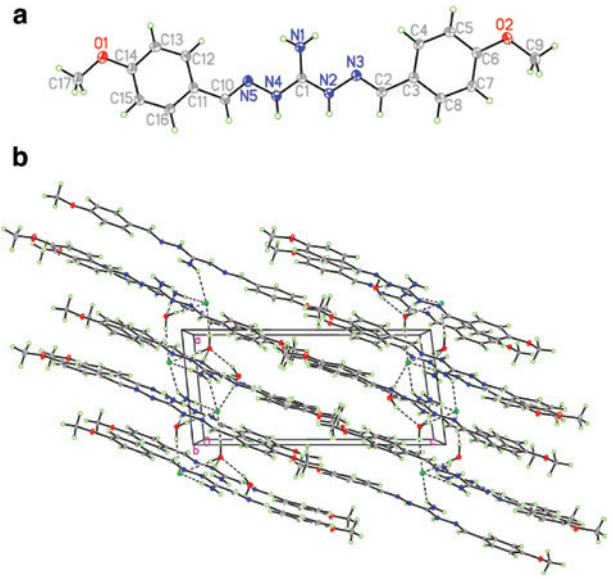


Fig. 2: (a) Molecular structure of **DG13** · $2H_2O$ with the crystallographic numbering. Displacement ellipsoids are shown at the 40% probability level; the Cl^- counterion and the water molecules are omitted. (b) Packing diagram of compound **DG13** · $2H_2O$ in a unit cell, viewed along the crystallographic *ac* plane; hydrogen bonds are shown as dashed lines.

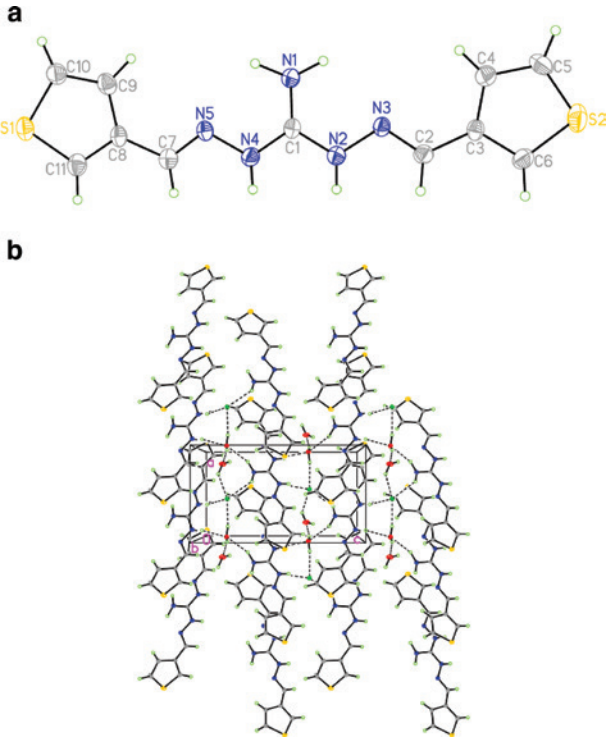


Fig. 3: (a) Molecular structure of **DG20** · $2H_2O$ with the crystallographic numbering. Displacement ellipsoids are shown at the 40% probability level; the Cl^- counterion and the water molecules are omitted. (b) Packing diagram of compound **DG20** · $2H_2O$ in a unit cell, viewed along the crystallographic *ac* plane; hydrogen bonds are shown as dashed lines.

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summarized in Table 1. Intensity data were collected on a Bruker SMART APEX 2 CCD diffractometer using graphite-monochromated MoKα radiation ($\lambda = 0.71073$ Å) at $T = 293(2)$ K. The collected frames were processed with the software SAINT [21]. The data were corrected for absorption using the program SADABS [22]. Structures were solved by the Direct Methods and refined by full-matrix least squares on F^2 using the SHELXTL software package [23, 24]. All non-hydrogen atoms except for the solvate molecules were refined anisotropically. The positions of all hydrogen atoms were generated geometrically (C_{sp3}–H = 0.96 and C_{sp2}–H = 0.93 Å), assigned isotropic thermal parameters, and allowed to ride on their respective parent carbon or nitrogen atoms in the final of least-squares refinement cycles. DFIX commands are used for compounds **DG20** · $2H_2O$ and **DG21** · H_2O to restrain the bond lengths of N–H and O–H due to disorder. OMIT commands are used to delete the most disagreeable reflections.

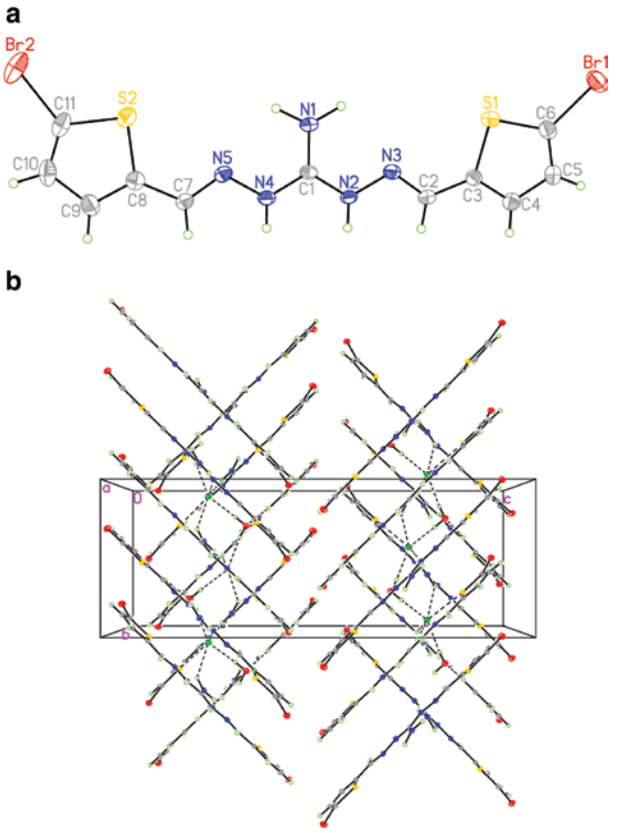

Fig. 4: (a) Molecular structure of **DG21** · H_2O with the crystallographic numbering. Displacement ellipsoids are shown at the 40% probability level; the Cl^- counterion and the water molecule are omitted. (b) Packing diagram of compound **DG21** · H_2O in a unit cell, viewed along the crystallographic *bc* plane; hydrogen bonds are shown as dashed lines.

CCDC 1585065, 1585066, 1585067, and 1585068 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

3 Results and discussion

Previously, Sondhi et al. synthesized a number of biologically active disubstituted guanidine derivatives by condensation of 1,3-diaminoguanidine monohydrochloride with various aldehydes and ketones [25]. To enrich this group of compounds, a series of new guanidine derivatives, 1,3-bis(aryl- and heteroaryl-methyleneamino)guanidine hydrochlorides **DG1–21**, have been synthesized by a similar procedure (Scheme 1). Fourier transform infrared spectroscopy analyses of **DG1–21** clearly show absorption bands at around 3300 and 3200 cm^{-1} for ν(NH) and at ~1640 cm^{-1} for ν(C=N) groups. In the ^1H NMR spectra, characteristic –C=NH_2 protons appeared at around 12.0 ppm as a broad singlet. Only one singlet signal was assigned to the –C*H*=N (~8.4 ppm) or –N–N*H* (~9.0 ppm), indicating their symmetrical structures in the solution state [20]. The ^{13}C NMR spectra exhibit the –*C*=NH_2 signal at around 150 ppm, comparable with that in some similar compounds [20]. The molecular structures of compounds **DG8**, **DG13** · $2H_2O$, **DG20** · $2H_2O$, and **DG21** · H_2O were established by single-crystal X-ray diffraction. The results clearly show their existence as ionic species with the Cl^- ion as the counter anion (Figs. 1–4). Limited reported structures of related compounds, the bis-guanidinium derivatives 1,3-bis(1-naphthethylideneamino) guanidine benzoic acid and 1,3-bis(1-pentafluorophenylideneamino)guanidine benzoic acid, showed the C=N_{NH2} bond lengths of 1.300 and 1.311 Å and the C–N_{NH} bond lengths of 1.331–1.350 Å [20]. In compounds **DG13** · $2H_2O$, **DG20** · $2H_2O$, and **DG21** · H_2O, the C=N_{NH2} bond lengths are in the range of 1.293(6)–1.317(6) Å, which agree well with that of the known compounds [20]. Similarly, the corresponding C–N_{NH} bond lengths (1.330(2)–1.350(6) Å) in the present compounds are comparable with those in related compounds (1.331–1.350 Å) [20]. As expected, N–H···Cl, C–H···Cl, and O–H···Cl hydrogen bonding interactions exist in the crystals of **DG8**, **DG13** · $2H_2O$, **DG20** · $2H_2O$, and **DG21** · H_2O, as shown in Figs. 1–4b.

The optical properties of **DG1** and **DG2** in the presence of tetrabutylammonium (n-Bu_4N)$^+$ salts of different anions (F^-, Cl^-, and Br^-) were studied in detail because of the potential N–H···X hydrogen bonding. Only in the

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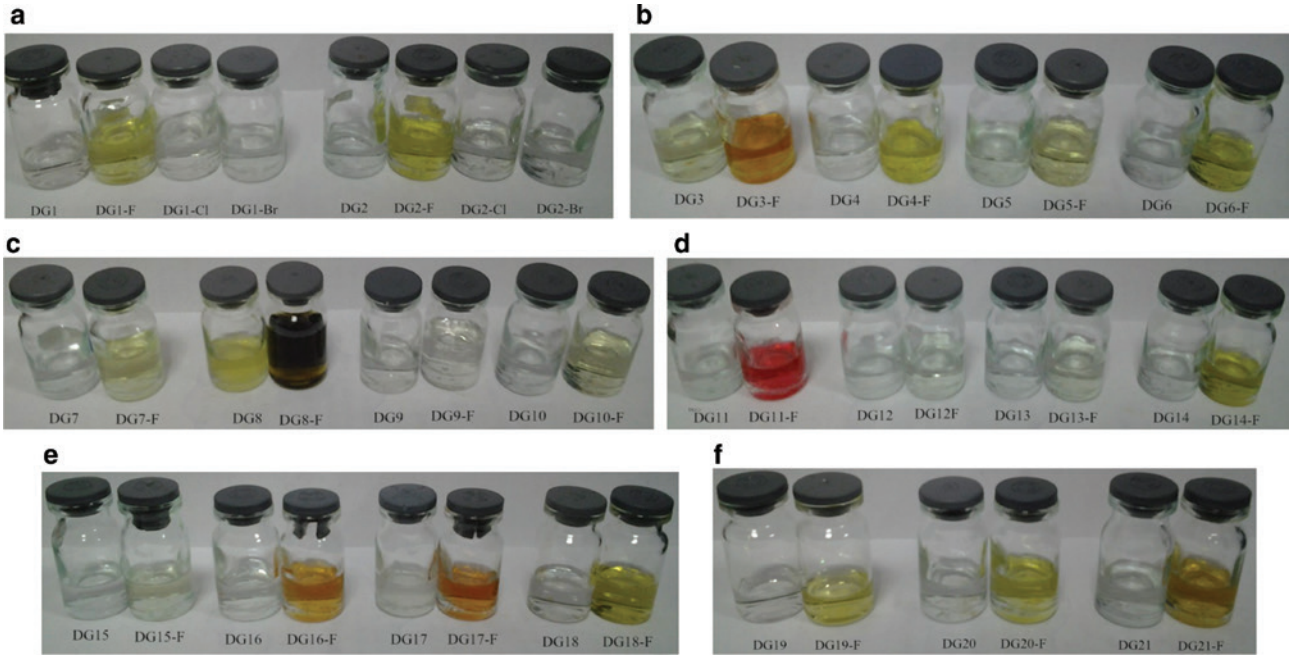

Fig. 5: Color change experiment of **DG1–21** in the presence of halide. (a) **DG1,2** for F^-, Cl^-, and Br^-, (b) **DG3–6** for F^-, (c) **DG7–10** for F^-, (d) **DG11–14** for F^-, (e) **DG15–18** for F^-, (f) **DG19–21** for F^-.

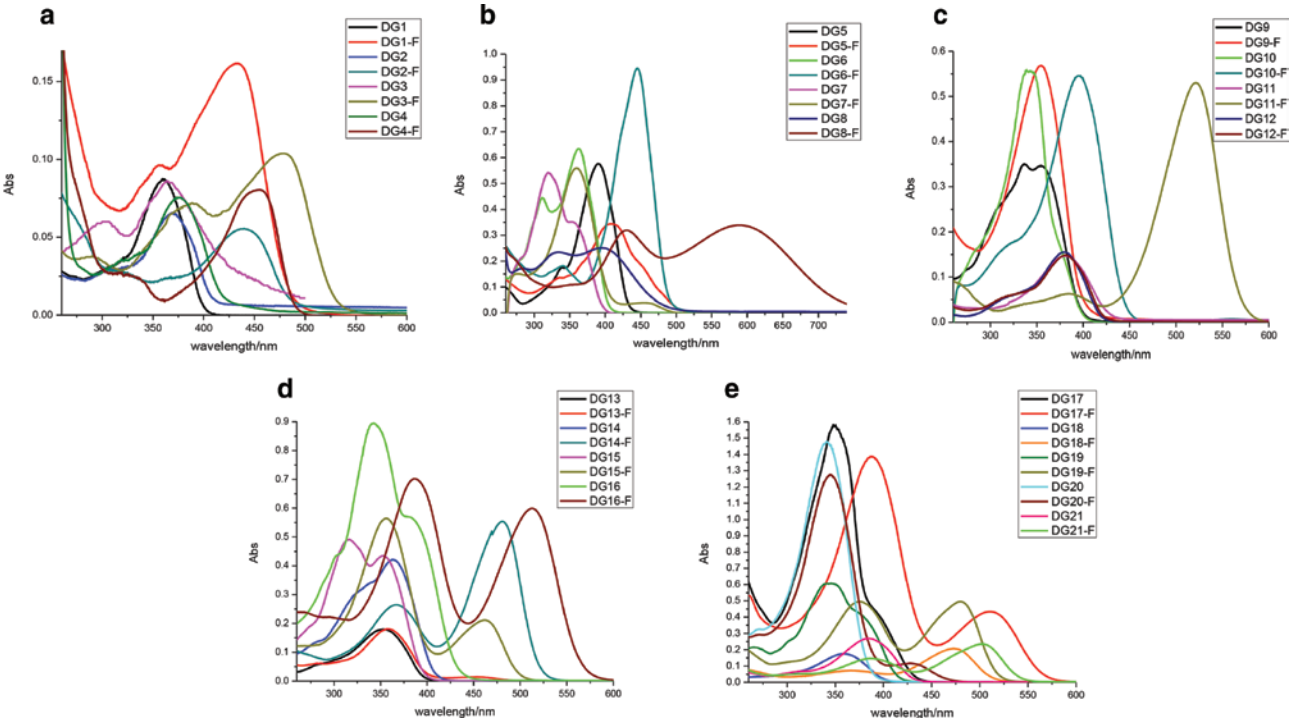

Fig. 6: Changes in the UV/Vis absorption spectra of **DG1–21** in the presence of F^-. (a) **DG1–4**, (b) **DG5–8**, (c) **DG9–12**, (d) **DG13–16**, (e) **DG17–21**.

presence of F^- anion that a change from colorless to yellow is observed (Fig. 5a), which showed that **DG1** and **DG2** could detect F^- anion selectively. As a result, the optical properties of compounds **DG3–21** were investigated only in the presence of F^- anions. Figure 5c–f show that most of the new functionalized bis-guanidinium derivatives change color in the presence of F^- anion. Compounds **DG3** and **DG8** bearing the strongly electron-withdrawing

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group $-NO_2$ resulted even in an obvious color change from light yellow to orange and from yellow to purple, respectively. Compound **DG11** with the strong electron-withdrawing group $-SO_2Me$ led to a clear color change from colorless to red. Compounds **DG16** and **DG17** with a bigger π-electron delocalized system are also sensitive to F^- anion, while the $-NMe_2$ and −OMe groups in compounds **DG12** and **DG13** seem to be unfavorable to detect F^- anion.

The ultraviolet/visible (UV/Vis) spectra of **DG1–21** with and without the presence of F^- anion were studied, and the corresponding changes are shown in Fig. 6. The absorption peak at 359 nm of **DG1** is mainly due to the Ar–CH=N–NH conjugation framework [20]. In the presence of F^-, the above peak diminished, with the appearance of a new intense absorption peak at approximately 400–500 nm (Fig. 6a). For compounds **DG2–11** and **DG14–16**, the characteristic absorption peaks are also red-shifted because of the basic nature of the aryl guanidinium moiety. However, the absorption peaks of compounds **DG12** and **DG13** did not show a red shift (Fig. 6c, d), which was identical with the aforementioned phenomenon. Upon the changes from phenyl in **DG15** to styryl in **DG16**, naphthyl in **DG17**, and heteroaryls in **DG18–21**, the aromaticity increases to some extent, and as a result, new absorption peaks appear at approximately 400–600 nm in the presence of F^- (Fig. 6e). Conversely, color changes from colorless to yellow or orange were also observed for compounds **DG16–21** (Fig. 5e, f).

In summary, we have synthesized a series of new disubstituted guanidinium chlorides bearing two Schiff base functions **DG1–21**. Single crystal X-ray crystallography on four typical compounds has established their ionic form. Most of these guanidinium chloride derivatives, especially compounds with strong electron-withdrawing groups or with a large π-electron delocalized systems, show selective color changes with F^- anion because of a red shift of the bands in their UV/Vis absorption spectra.

Acknowledgments: This project was supported by the National Natural Science Foundation of China (21372007).

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