Alkylation of Quinazoline-2,4(1*H*,3*H*)-diones with 1,4-Dibromo-2-methylbut-2-ene under Phase-Transfer-Catalysis

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Quinazoline-2,4(1*H*,3*H*)-dione (**1**) was reacted with 1,4-dibromo-2-methylbut-2-ene (**2**) to give two dialkylated products and two monoalkylated products. The reaction of 6,7-dimethoxyquinazoline-2,4(1*H*,3*H*)-dione (**8**) with 1,4-dibromo-2-methylbut-2-ene (**2**) resulted in the formation of three dialkylated products.

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Quinazoline alkaloids and its synthetic analogues have been found to exhibit interesting biological activities [2]. Some of these activities include antimicrobial [3], antimalarial [4], anticonvulsive [5] *etc.* The unique biological activities and characteristic chemical structures have made quinazoline synthetic studies over the years very attractive.

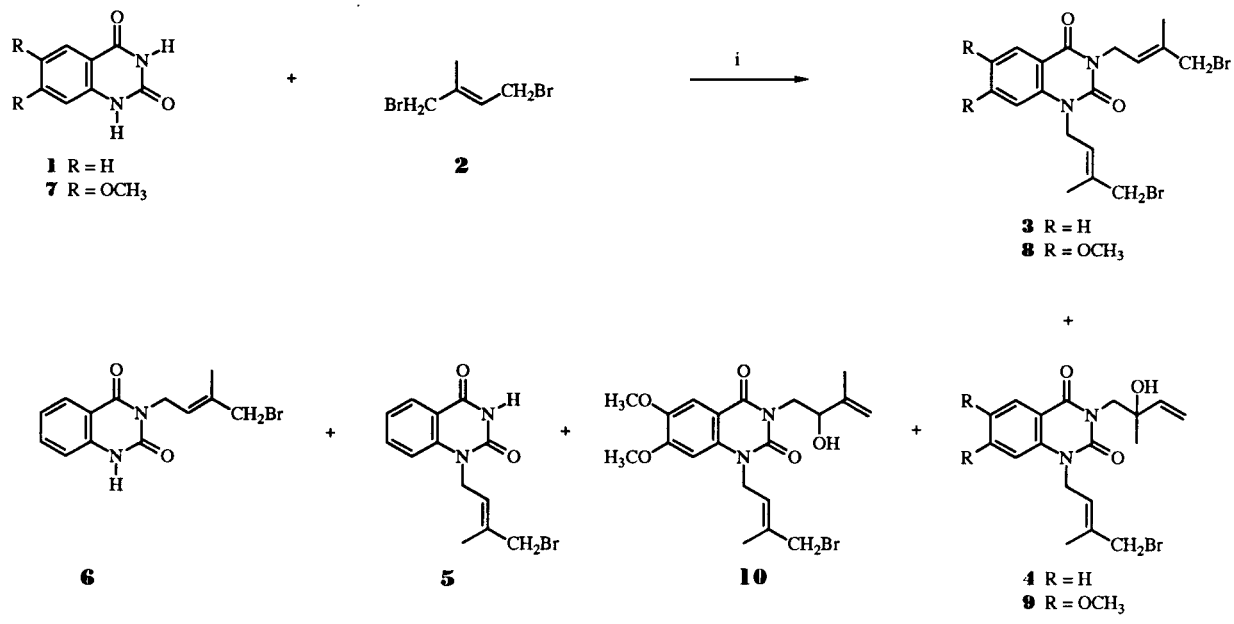
In the present study, the alkylation of quinazoline-2,4-(1*H*,3*H*)-dione (**1**) and 6,7-dimethoxyquinazoline-2,4(1*H*, 3*H*)-dione (**8**) with 1,4-dibromo-2-methylbut-2-ene (**2**) was carried out to give *N*-prenylated derivatives. These derivatives, biosynthetically related to quinoline [6], could be intermediates for potential natural products.

The addition of 1,4-dibromo-2-methylbut-2-ene (**2**) to quinazoline-2,4(1*H*,3*H*)-dione (**1**) in a sodium hydroxide/-methanol/water mixture [7] yielded negligible alkylated products.

Under phase transfer conditions [8] using dichloromethane as the organic phase, four alkylated products were produced. The chromatographic separation of the reaction mixture afforded the main product (*E,E*)-1,3-bis(4-bromo-3-methylbut-2-enyl)quinazoline-2,4-(1*H*,3*H*)-dione (**3**) with the least polarity, together with **4**, **5** and **6**.

Treatment of **8** with 1,4-dibromo-2-methylbut-2-ene (**2**) under the same conditions afforded (*E,E*)-1,3-bis(4-bromo-3-methylbut-2-enyl)-6,7-dimethoxyquinazoline-2,4(1*H*,3*H*)-

Scheme



i: sodium hydroxide/dichloromethane, TBABr, room temperature.

dione (**9**), as main product as well as **10** and **11**.

The dialkylated products have lower melting points compared to the monoalkylated ones probably because of the absence of an NH group. All compounds were characterised by their spectroscopic data. The instability of the compounds with the elimination of a bromine radical ultimately required the use of chemical ionisation (ci) for the mass spectra determination. The bromine isotopic peaks were identified in all cases. The ir spectra indicated the presence of two strong absorptions for the products **3, 4, 5** and **6** at about 1715 and 1650 cm^{-1} and for the 6,7-dimethoxy derivatives at about 1690 and 1640 cm^{-1} which are diagnostic for the carbonyl functional group of quinazoline-2,4(1*H*,3*H*)-diones [9].

EXPERIMENTAL

Melting points were determined on a Kofler hot stage apparatus and were uncorrected. The uv spectra were measured with a Shimadzu UV-160 A spectrophotometer. The ir spectra were taken on a Shimadzu IR-470 spectrophotometer. The ^1H nmr and ^{13}C nmr spectra were recorded in deuteriochloroform with tetramethylsilane as the internal reference on a Varian Gemini 200 spectrometer. Mass spectra were obtained on a Varian MAT 44S instrument at 70 eV and high resolution mass spectra on a Finnigan MAT 312 or in the case of chemical ionisation on a Finnigan MAT 8230. Silica gel 60 F_{254} (precoated, aluminium sheets, 0.2 mm thickness, Merck 5549) was used for analytical tlc and 60 F_{254} (glass plates, 0.25 mm thickness, Merck 5715) for preparative work. Column chromatography was carried out on silica gel 60 (particle size 0.063-0.200 mm, Merck 7734). The synthesized compounds must be protected against light and moisture.

Reaction of Quinazoline-2,4(1*H*,3*H*)-dione (**1**) with 1,4-Dibromo-2-methylbut-2-ene (**2**) under PTC Conditions.

To a suspension of 500 mg (3 mmoles) quinazoline-2,4(1*H*,3*H*)-dione (**1**) in 20 ml of dichloromethane was added a solution of 246 mg (6 mmoles) of sodium hydroxide in 20 ml of water. The reaction mixture was then stirred for 1 hour at room temperature, after which 92 mg (0.3 mmole) of tertiary butyl ammonium bromide (TBABr) was added and followed by dropwise addition of 2.1 g (9 mmoles) of 1,4-dibromo-2-methylbut-2-ene (**2**) within 15 minutes. Further stirring was continued for 3 hours. The phases were separated and the aqueous phase was extracted several times with dichloromethane. The combined organic phase was filtered, dried over sodium sulfate and concentrated under reduced pressure by a rotary evaporator. Column chromatography separation using dichloromethane gave 505.6 mg of **3** as the main product. Preparative tlc using diethyl ether:ethyl acetate (95:5) further yielded 22.1 mg of (*E*)-1-(bromo-3-methylbut-2-enyl)-3-(2-methylbut-3-en-2-olyl)quinazoline-2,4(1*H*,3*H*)-dione (**4**), 27.5 mg of (*E*)-1-(4-bromo-3-methylbut-2-enyl)quinazoline-2,4(1*H*,3*H*)-dione (**5**) and 32.4 mg of (*E*)-3-(4-bromo-3-methylbut-2-enyl)quinazoline-2,4-(1*H*,3*H*)-dione (**6**).

(*E,E*)-1,3-bis(4-Bromo-3-methylbut-2-enyl)quinazoline-2,4-(1*H*,3*H*)-dione (**3**).

The first eluate of the column (dichloromethane) afforded compound **3**, which was isolated from *n*-pentane as colourless needles, 505.6 mg (36%), mp 91-94°; uv (methanol): λ max (log ε) 311.4 (3.02), 272.0 (2.32), 222.0 (4.13) nm; ir (potassium bromide): ν 2950, 1695 (C=O), 1650 (C=O), 1600, 1480, 1400, 1230, 758, 610 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.99 (2 s, 6H, H-5', H-5''), 3.92 (s, 2H, H-4'), 3.94 (s, 2H, H-4''), 4.69 (d, J = 6.92 Hz, 2H, H-1'), 4.79 (d, J = 5.9 Hz, 2H, H-1''), 5.60 (dt, J = 0.8, 5.9 Hz, 1H, H-2''), 5.70 (dt, J = 1.3, 6.9 Hz, 1H, H-2'), 7.08 (d, J = 8.3 Hz, 1H, H-8), 7.25 (t, J = 7.9 Hz, 1H, H-6), 7.66 (m, 1H, H-7), 8.18 (dd, J = 1.6, 7.9 Hz, 1H, H-5); ^{13}C nmr (deuteriochloroform): δ 15.08 (C-5'), 15.36 (C-5''), 39.36 (C-4''), 39.78 (C-1'), 40.15 (C-4'), 42.02 (C-1''), 113.63 (C-8), 115.60 (C-4a), 123.01 (C-6), 124.47 (C-2', C-2''), 128.97 (C-5), 135.10 (C-7), 136.25 (C-3', C-3''), 139.54 (C-8a), 150.41 (C-2), 161.19 (C-4); ms: m/z 377 (M^+ (^{81}Br) -Br, 42), 375 (M^+ (^{79}Br) -Br, 42), 331 (8), 295 (M^+ -2 Br, 5), 230 (15), 229 (377 $-C_5H_8Br$, 375 $-C_5H_8Br$, 100), 228 (20), 211 (4), 199 (3), 186 (26), 163 (27), 158 (8), 156 (6), 146 (729), 132 (19), 119 (12), 110 (9), 90 (23), 77 (12), 67 (69), 55 (19), 53 (20); ms: (ci, NH_3) m/z 477 (M^+ (^{81}Br) + NH_4 + H, 10), 476 (M^+ (^{81}Br) + NH_4, 44), 475 (M^+ ($^{79}Br/^{81}Br$) + NH_4 + H, 23), 474 (M^+ ($^{79}Br/^{81}Br$) + NH_4, 100), 473 (M^+ (^{81}Br) + NH_3, 13), 472 (M^+, (^{79}Br) + NH_4, 17), 459 (M^+ (^{81}Br) + H, 5), 457 (M^+ ($^{79}Br/^{81}Br$) + H, 10), 455 (M^+ (^{79}Br) + H, 6), 430 (10), 428 (8), 412 (12), 410 (13), 395 (16), 393 (16), 377 (M^+ (^{81}Br) -Br, 31), 375 (M^+ (^{79}Br) -Br, 30), 331 (6), 313 (22), 252 (7), 229 (19), 214 (8), 170 (11), 152 (8), 142 (69), 134 (8), 128 (59), 116 (34), 102 (11), 99 (21), 84 (5); hrms: (ci, NH_3) Calcd. for $C_{18}H_{20}N_2O_2$: $^{79}Br_2$ + NH_4 472.023521. Found: 472.024139.

(*E*)-1-(4-Bromo-3-methylbut-2-enyl)-3-(2-methylbut-3-en-2-olyl)-quinazoline-2,4(1*H*,3*H*)-dione (**4**).

Compound **4** was separated from reaction mixture by preparative tlc (diethyl ether:ethyl acetate, 95:5), which was isolated as colourless needles from dichloromethane/methanol, 22.1 mg (0.16%), mp 98-100°; uv (methanol): λ max (log ε) 309.2 (3.59), 248.9 (3.89, shoulder), 219.8 (4.22), 210.0 (4.24) nm; ir (potassium bromide): ν 2920, 2350, 1700 (C=O), 1650 (C=O), 1606, 1480, 1398, 755 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.34 (s, 3H, H-5'), 2.02 (d, J = 1.1 Hz, 3H, H-5'), 3.94 (d, J = 0.4, 3H, H-4'), 4.30 (q, J_{AB} = 14.0 Hz, 2H, H-1'), 5.05 (dd, J = 10.5 Hz, J_{AB} = 1.8 Hz, 1H, H_B-4''), 5.37 (dd, J = 17.1 Hz, J_{AB} = 1.8 Hz, 1H, H_A-4''), 5.58 (t, br, J = 6.2 Hz, H-2'), 5.95 (dd, J = 10.5, 17.1 Hz, 1H, H-3''), 7.12 (d, J = 8.5 Hz, 1H, H-8), 7.30 (t, J = 7.3 Hz, 1H, H-6), 7.71 (m, 1H, H-7), 8.24 (dd, J = 1.4, 7.9 Hz, 1H, H-5); ^{13}C nmr (deuteriochloroform): δ 15.51 (C-5'), 26.66 (C-5''), 39.23 (C-1'), 42.43 (C-4'), 51.37 (C-1''), 74.53 (C-2''), 113.45 (C-8), 113.84 (C-4'), 115.58 (C-4a), 123.54 (C-6), 124.09 (C-2'), 129.58 (C-5), 135.62 (C-7), 136.93 (C-3'), 139.52 (C-8a), 142.29 (C-3''), 152.27 (C-2), 163.09 (C-4); ms: m/z 295 (M^+ -Br $-H_2O$, 5), 243 (19), 229 (12), 186 (26), 175 (16), 163 (9), 146 (100), 132 (18), 119 (19), 110 (10), 90 (31), 77 (15), 71 (31), 67 (68), 55 (25), 53 (27); ms: (ci, NH_3) m/z 426 (6), 424 (6), 395 (M^+ (^{81}Br) + H, 30), 393 (M^+ (^{79}Br) + H, 31), 377 (395 $-H_2O$, 97), 375 (393 $-H_2O$, 100), 349 (3), 331 (15), 313 (15), 229 (5), 186 (2); hrms: (ci, NH_3) Calcd. for $C_{18}H_{21}{}^{79}BrN_2O_3$ + H: 393.081378. Found: 393.072449.

(*E*)-1-(4-Bromo-3-methylbut-2-enyl)quinazoline-2,4(1*H*,3*H*)-dione (**5**).

Preparative tlc (diethyl ether:ethyl acetate, 95:5) afforded further the monoalkylated **5**, which crystallised from dichloromethane/*n*-pentane as colourless needles, 27.5 mg (2.9%), mp 177-179°; uv (methanol): λ max (log ε) 310.6 (3.13), 240.1 (3.60,

shoulder), 219.8 (4.23) nm; ir (potassium bromide): ν 3200 (NH), 3060 (NH), 2910, 1715 (C=O), 1650 (C=O), 1600, 1488, 1450, 1275, 760 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.70 (s, 3H, H-5'), 3.95 (s, 2H, H-4'), 4.74 (d, J = 7.0 Hz, 2H, H-1'), 5.74 (t, J = 7.0 Hz, 1H, H-2'), 7.14 (d, J = 8.1 Hz, 1H, H-8), 7.26 (m, 1H, H-6), 7.65 (m, 1H, H-7), 8.14 (dd, J = 1.1, 8.0 Hz, 1H, H-5), 10.54 (s, br, 1H, NH); ^{13}C nmr (deuteriochloroform): δ 15.16 (C-5'), 38.99 (C-1'), 40.02 (C-4'), 115.08 (C-8), 116.09 (C-4a), 123.54 (C-6), 124.33 (C-2'), 128.41 (C-5), 135.16 (C-7), 138.55 (C-3'), 141.94 (C-8a), 151.98 (C-2), 162.10 (C-4); ms: m/z 229 (M^+ -Br, 100), 175 (8), 163 (47), 146 (89), 119 (16), 90 (18), 67 (23), 53 (7); ms: (ci, NH_3) m/z 328 (M^+ (^{81}Br) + NH_4, 4), 326 (M^+ (^{79}Br) + NH_4, 3), 278 (3), 229 (M^+ -Br, 100), 102 (12); hrms: Calcd. for $C_{13}H_{13}N_2O_2$ (M^+ -Br): 229.097703. Found: 229.097307.

(*E*)-3-(4-Bromo-2-methylbut-2-enyl)quinazoline-2,4(1*H*,3*H*)-dione (**6**).

Compound **6** was isolated also by preparative tlc (diethyl ether:ethyl acetate, 95:5). Compound **6** could be obtained from dichloromethane/*n*-pentane as colourless needles, 32.4 mg (3.4%), mp 181-184°; uv (methanol): λ max (log ε) 312.6 (3.10), 242.0 (3.22, shoulder), 218.7 (4.25) nm; ir (potassium bromide): ν 3200 (NH), 3060 (NH), 2920, 1715 (C=O), 1650 (C=O), 1600, 1488, 1450, 1275, 1200, 760 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.63 (s, 3H, H-5'), 3.94 (s, 2H, H-4'), 4.73 (d, J = 7.0 Hz, 2H, H-1'), 5.73 (t, br, J = 7.0 Hz, 1H, H-2'), 7.11 (d, J = 8.2 Hz, 1H, H-8), 7.25 (t, J = 7.6 Hz, 1H, H-6), 7.64 (m, 1H, H-7), 8.14 (dd, J = 0.9, 7.6 Hz, 1H, H-5), 10.05 (s, br, 1H, NH); ^{13}C nmr (deuteriochloroform): δ 15.43 (C-5'), 39.26 (C-1'), 40.28 (C-4'), 114.91 (C-4a), 115.19 (C-8), 123.80 (C-6), 124.59 (C-2'), 128.75 (C-5), 135.41 (C-7), 136.84 (C-3'), 138.73 (C-8a), 151.89 (C-2), 162.34 (C-4); ms: (ci, NH_3) m/z 328 (M^+ (^{81}Br) + NH_4, 8), 326 (M^+ (^{79}Br) + NH_4, 8), 278 (29), 247 (11), 229 (M^+ -Br, 100), 102 (16); hrms: Calcd. for $C_{13}H_{13}N_2O_2$ (M^+ -Br); 229.097703. Found: 229.097307.

Reaction of 6,7-Dimethoxyquinazoline-2,4(1*H*,3*H*)-dione (**8**) with 1,4-Dibromo-2-methylbut-2-ene (**2**) under PTC Conditions.

6,7-Dimethoxyquinazoline-2,4(1*H*,3*H*)-dione (**8**) (570 mg, 3 mmoles) was reacted with 1,4-dibromo-2-methylbut-2-ene (**2**) under the same conditions described for quinazoline-2,4(1*H*,3*H*)-dione (**1**). After stirring for 1 hour the phases were separated and aqueous phase was extracted several times with dichloromethane. The combined organic phase was filtered, dried over sodium sulfate and concentrated under reduced pressure. Column chromatography separation using dichloromethane gave 768 mg of **9** as the main product. Preparative tlc using diethyl ether:ethyl acetate (9:1) yielded 45.8 mg of (*E*)-1-(4-bromo-3-methylbut-2-enyl)-3-(2-methylbut-3-en-2-olyl)-6,7-dimethoxyquinazoline-2,4-(1*H*,3*H*)-dione (**10**) and 235.3 mg of (*E*)-1-(4-bromo-3-methylbut-2-enyl)-3-(3-methyl-3-en-2-olyl)-6,7-dimethoxyquinazoline-2,4-(1*H*,3*H*)-dione (**11**).

(*E*,*E*)-1,3-bis(4-Bromo-3-methylbut-2-enyl)-6,7-dimethoxyquinazoline-2,4(1*H*,3*H*)-dione (**9**).

The first eluate of the column afforded compound **3**, which crystallized as colourless needles from diethyl ether/petroleum ether, 768 mg (50%), mp 110-114°; uv (methanol): λ max (log ε) 324 (3.07), 259.8 (3.02), 238.8 (3.91), 211.0 (3.66) nm; ir (potassium bromide): ν 2950, 2250, 2050, 1690 (C=O), 1648 (C=O), 1615, 1514, 1483, 1400, 1358, 1012, 610 cm^{-1}; ^1H nmr (deuteriochloroform): δ 2.00 (s, 3H, H-5'), 2.03 (s, 3H, H-5''), 3.93 (s, 6H, 2 x OCH_3), 3.98 (m, 4H, H-4', H-4''), 4.70 (d, J = 6.9 Hz, 2H, H-1'), 4.81 (d, J = 5.9 Hz, 2H, H-1''), 5.61 (t, J = 5.9 Hz, 1H, H-2''), 5.70 (t, J = 6.9 Hz, 1H, H-2'), 6.49 (s, 1H, H-8), 7.57 (s, 1H, H-5); ^{13}C nmr (deuteriochloroform): δ 15.09 and 15.32 (2 x CCH_3), 39.36, 39.88, 40.23, 42.41 (C-1', C-1'', C-4', C-4''), 56.30 (2 x OCH_3), 96.76 (C-8), 108.00 (C-4a), 109.05 (C-5), 124.71, 125.42 (C-2', C-2''), 135.44, 135.99 (C-3', C-3''), 136.18 (C-6), 145.72 (C-8a), 150.75 (C-7), 155.19 (C-2), 160.94 (C-4); ms: m/z 437 (M^+ -Br, 25), 435 (M^+ -Br, 24), 355 (437 -HBr, 435 -HBr, 8), 289 (31), 246 (19), 223 (7), 206 (52), 192 (15), 150 (15), 135 (8), 110 (19), 82 (15), 67 (100), 53 (38); ms: (ci, NH_3) m/z 536 (M^+ (^{81}Br) + NH_4, 3), 534 (M^+ ($^{79}Br/^{81}Br$) + NH_4, 6), 532 (M^+ (^{79}Br) + NH_4, 3), 520 (M^+ (^{81}Br) + 2 H, 3), 519 (M^+ (^{81}Br) + H, 11), 518 (M^+ (^{81}Br), 6), 517 (M^+ ($^{79}Br/^{81}Br$) + H, 21), 516 (M^+ ($^{79}Br/^{81}Br$), 3), 515 (M^+ (^{79}Br) + H, 11), 455 (536 -^{81}Br, 534 -^{79}Br, 17), 453 (534 -^{81}Br, 532 -^{79}Br, 16), 437 (M^+ -Br, 20), 435 (M^+ -Br, 16), 373 (7), 355 (437 -HBr, 435 -HBr, 5), 289 (373 -OC_5H_8, 51), 90 (100), 84 ($OC_5H_8^+$, 18).

Anal. Calcd. for $C_{20}H_{24}Br_2N_2O_4$: C, 46.53; H, 4.69; Br, 30.96; N, 5.43. Found: C, 46.68; H, 4.67; Br, 30.98; N, 5.54.

(*E*)-1-(4-Bromo-3-methylbut-2-enyl)-3-(2-methylbut-3-en-2-olyl)-6,7-dimethoxyquinazoline-2,4(1*H*,3*H*)-dione (**10**).

Compound **10** was obtained by preparative tlc using diethyl ether:ethyl acetate (9:1) and was isolated as colourless needles from diethyl ether/ethyl acetate, 45.8 mg (3.5%), mp 102-104°; uv (methanol): λ max (log ε) 323.8 (3.15), 260.6 (3.13), 238.8 (3.97), 212.5 (3.51, shoulder) nm; ir (potassium bromide): ν 3520 (OH), 2963, 2258, 1695 (C=O), 1648 (C=O), 1600, 1484, 1398, 1210, 756 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.34 (s, 3H, H-5'), 2.03 (d, J = 1.0 Hz, 3H, H-5''), 3.41 (s, br, 1H, OH), 3.95 (s, 5H, H-4', OCH_3), 3.99 (s, 3H, OCH_3), 4.31 (dd, J = 14.0, H-1''), 4.84 (dd, J = 0.5, 6.3 Hz, 2H, H-1'), 5.05 (dd, J_{AB} = 1.7 Hz, J_B = 10.5 Hz, 1H, H_B-4''), 5.37 (dd, J_{AB} = 1.7 Hz, J_A = 17.0 Hz, 1H, H_A-4''), 5.58 (m, 1H, H-2'), 5.94 (dd, J_{BX} = 10.5 Hz, J_{AX} = 17.0 Hz, 1H, H-3''), 6.51 (s, 1H, H-8), 7.58 (s, 1H, H-5); ^{13}C nmr (deuteriochloroform): δ 15.38 (C-5'), 26.59 (C-5''), 39.18 (C-1'), 42.73 (C-4'), 51.37 (C-1''), 56.36 (2 x OCH_3), 74.49 (C-2''), 96.83 (C-8), 107.82 (C-4a), 109.35 (C-5), 113.32 (C-4''), 124.94 (C-2'), 135.35 (C-6), 136.40 (C-3'), 142.34 (C-3''), 146.06 (C-8a), 152.41 (C-7), 155.64 (C-2), 162.41 (C-4); ms: m/z 373 (M^+ -Br, 28), 355 (373 -H_2O, 6), 303 (35), 289 (13), 246 (43), 235 (20), 223 (11), 206 (100), 192 (26), 150 (21), 135 (12), 110 (23), 94 (26), 67 (45), 55 (21); ms: (ci, NH_3) m/z 456 (M^+ (^{81}Br) + 2 H, 22), 455 (M^+ (^{81}Br) + H, 91), 454 (M^+ (^{81}Br), 27), 453 (M^+ (^{79}Br) + H, 100), 375 (456 -Br, 81), 374 (455 -HBr, 16), 373 (M^+ -Br, 29).

Anal. Calcd. for $C_{20}H_{25}BrN_2O_5$: C, 52.99; H, 5.56; Br, 17.63; N, 6.18. Found: C, 53.06; H, 5.56; Br, 17.50; N, 6.12.

(*E*)-1-(4-Bromo-3-methylbut-2-enyl)-3-(3-methylbut-3-en-2-olyl)-quinazoline-2,4(1*H*,3*H*)-dione (**11**).

Further preparative tlc using diethyl ether:ethyl acetate (9:1) afforded compound **11**, which was obtained as colourless needles from diethyl ether/ethyl acetate, 325.6 mg (17%), mp 118-121°; uv (methanol): λ max (log ε) 323.4 (3.23), 260.6 (3.23), 238.8 (4.00), 210.0 (3.62, shoulder) nm; ir (potassium bromide): ν 3515 (OH), 2970 (CH), 2260, 1692 (C=O), 1636 (C=O), 1598, 1513, 1486, 1256, 1027, 747 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.88 (s, 3H, H-5''), 2.03 (s, 3H, H-5'), 3.41 (m, br, 1H, OH), 3.94 (s, 3H, OCH_3), 3.96 (s, 2H, H-4'), 3.99 (s, 3H, OCH_3), 4.30 (dd, J_{BM} = 8.1 Hz, J_{AM} = 10.0 Hz, 2H, H-1''), 4.40 (m, 1H, H-2''), 4.82 (d, J = 6.0 Hz, 2H, H-1'), 4.94 (s, br, 1H, H_A-4''), 5.13 (s, br, 1H, H_B-4''), 5.60 (m, 1H,

H-2'), 6.51 (s, 1H, H-8), 7.58 (s, 1H, H-5); ^{13}C nmr (deuteriochloroform): δ 15.39 (C-5'), 18.52 (C-5''), 39.27 (C-1'), 42.64 (C-4'), 46.85 (C-1''), 56.38 (2 x OCH_3), 74.78 (C-2''), 96.86 (C-8), 108.00 (C-4a), 109.19 (C-5), 111.69 (C-4''), 125.12 (C-2'), 135.54 (C-3'), 136.28 (C-6), 145.17 (C-3''), 145.99 (C-8a), 152.01 (C-7), 152.53 (C-2), 162.22 (C-4); ms: m/z 373 (M^+ -Br, 53), 303 (373 -C_4H_6O, 14), 289 (373 -C_5H_8O, 26), 246 (46), 235 (289 -C_4H_6, 14), 223 (21), 206 (100), 192 (42), 164 (9), 150 (19), 135 (8), 110 (32), 67 (47), 55 (17), 53 (14); ms: (ci, NH_3) m/z 456 (M^+(^{81}Br) + 2 H, 12), 455 (M^+(^{81}Br) + H, 49), 454 (M^+(^{79}Br) + 2 H, 13), 453 (M^+(^{79}Br) + H, 46), 375 (456 -Br, 76), 374 (456 -HBr, 29), 373 (453 -HBr, 100), 359 (9), 332 (4), 307 (13), 237 (9).

Anal. Calcd. for $C_{20}H_{25}BrN_2O_5$: C, 52.99; H, 5.56; Br, 17.63; N, 6.18. Found: C, 53.14; H, 5.52; Br, 17.68; N, 6.12.

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