Reaction of 3-Substituted and 4-Bromo-3-Substituted Isoquinolin-1-(2*H*)-ones with Propargyl Bromide

Cyril Odianose Usifoh

Department of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Benin, Benin City, Nigeria

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Isoquinolinones were brominated using *N*-bromosuccinimide in dimethylformamide at room temperature to give 4-bromo-3-substituted isoquinolin-1-(2*H*)-ones. The reaction of these isoquinolinones with propargyl bromide in the presence of anhydrous potassium carbonate yielded *N* and *O*-alkylated products.

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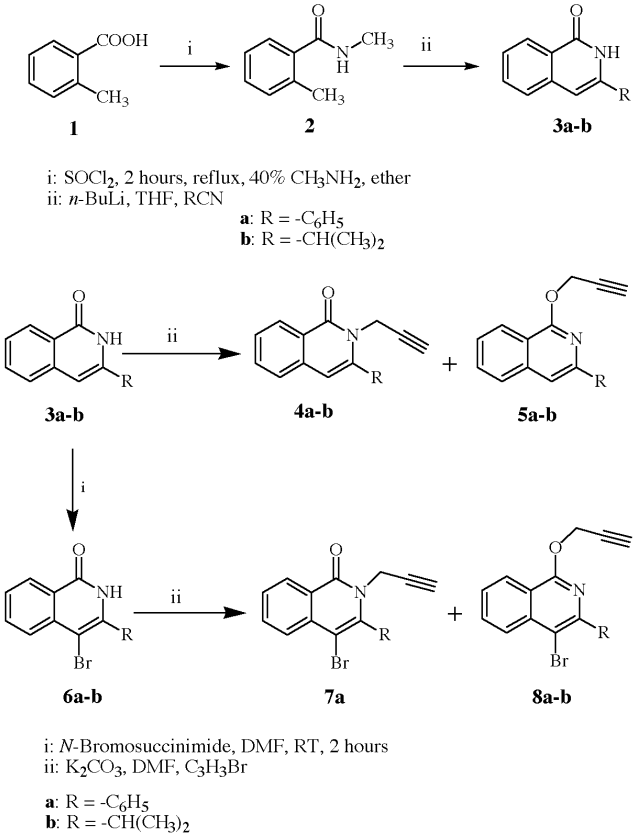
In continuation of the search for interesting heterocyclic compounds with the *N*-prop-2-ynyl moiety, which may have possible biological activity, the isoquinolinones **3** and **6** were synthesized according to literature procedures [1,2,3]. The reactions and formation of heterocycles from processes involving propargyl bromides have continued to receive attention in recent times [4,5,6].

Bromination of the isoquinolinones **3a** and **3b** at position 4 was found to proceed smoothly and optimally in dimethylformamide with *N*-bromosuccinimide at room temperature within 2 hours. The proton nmr clearly shows a singlet at δ 6.67 and δ 6.32 ppm for **3a** and **3b**, respectively corresponding to position 4, and the absence of a singlet in the isoquinolinones **6a** and **6b**. The reaction of propargyl bromide with the isoquinolinone **6a** gave both *N*- and *O*-alkylated products **7a** and **8a**, while the isoquinolinone **6b** gave only *O*-alkylated product **8b** when the substitution at carbon 3 is an isopropyl group.

Scheme



The *O*-alkylation products were obtained when there is steric hindrance or a bulky group at position 3. Bromination at position 4 probably contributed to the steric hindrance such that *O*-alkylation is favored. It is worth mentioning that the phenyl group, though bulky, may also act by stabilizing the isoquinolinone through its aromatic system, which is absent in the isopropyl group.

The nmr spectra show that the prop-2-ynyl moiety of the *O*-alkylated products are shifted downfield compared with that of the *N*-alkylated products. The methylene doublet signal appears at about δ 5.10 ppm for *O*-alkylated products compared to δ 4.20 ppm for the *N*-alkylated products while the triplet of the acetylene proton is situated at about δ 2.40-2.50 ppm for *O*-alkylated and between δ 2.10 and δ 2.30 ppm for *N*-alkylated products. In addition, the infra-red and ^{13}C-nmr spectra confirmed the absence of the carbonyl functional group in *O*-alkylated products, which is present in the *N*-alkylated products. The syntheses of **4a** and **5a** have been previously reported with the only characterization being melting points and elemental analyses [7]. An improved synthetic method and relevant spectroscopic data are presented in this work. All compounds were characterized spectroscopically with support from elemental analyses.

EXPERIMENTAL

Melting points were determined with a Kofler hot stage microscope and are uncorrected. The reactions and purity of the products were monitored by tlc using pre-coated silica gel plates (Merck 60F_{254}). Silica gel Merck 60 (70-230 mesh) was used for column chromatography. The ^{1}H and ^{13}C nmr spectra were recorded on a Varian Gemini 200 with tetramethylsilane as internal standard, infra red spectra were measured on a Perkin-Elmer type 457 and the mass spectra were determined using Varian MAT 44S, EI: 70 eV.

General Synthetic Procedure for Isoquinolines **3a-b**.

N-Methyl-*o*-toluamide (**2**).

To *o*-toluic acid **1** (10.2 g, 0.075 mol) in a 250 ml flask was added thionyl chloride (15.0 g, 0.125 mol) and refluxed for 2

hours. After the excess thionyl chloride was distilled off, 60 ml of diethyl ether was added and the mixture gradually poured into 30 ml of a stirring ice-cooled solution of 40% methylamine. The precipitate formed was filtered and the mother liquor was concentrated *in vacuo* to afford some more of the precipitate. Crystallization of the precipitate from ethanol-water gave 8.5 g (76%) of **2** as a crystalline solid; mp 76-77 °C (Lit. [1] 78-79 °C); ^{1}H nmr (deuterochloroform): δ 2.37 (s, 3H, CH_3), 2.88-2.90 (d, J = 4.8 Hz, 3H, NCH_3), 6.14 (br, 1H, NH), 7.10-7.17 (m, 2H, Ar-H), 7.23-7.28 (m, 2H, Ar-H); ^{13}C nmr (deuterochloroform): δ 20.3, 27.1, 126.2, 127.2, 130.3, 131.5, 136.5, 137.0, 171.5; ms: m/z: 149 [$M^{+\cdot}$].

Synthesis of 3-Phenyl-isoquinolin-1-(2*H*)-one **3a** and 3-Isopropyl-isoquinolin-1-(2*H*)-one **3b**.

To *N*-methyl-*o*-toluamide **2** (7.46 g, 50 mmol) in 300 ml of dry tetrahydrofuran under nitrogen in a 500 ml flask cooled in an ice-salt bath, was added slowly *n*-butyllithium (80 ml, 135 mmol) such that the internal temperature never exceeded 15 °C. The resulting orange-red reaction mixture was stirred at 0 °C for 1.5 hours, cooled to -63 °C and benzonitrile or isobutyronitrile (62 mmol) in 40 ml tetrahydrofuran were added *via* a syringe as quickly as possible. The cooling bath was removed and the reaction mixture allowed to warm up to room temperature. Saturated ammonium chloride solution (150 ml) was carefully added to reaction mixture until the resulting phases separated. The organic phase was washed with water (2 x 30 ml), brine (2 x 30 ml) and dried over anhydrous sodium sulphate. Subsequent filtration and removal of organic solvent *in vacuo* gave a crude product, which was crystallized from ethanol or ethanol-water.

3-Phenyl-isoquinolin-1-(2*H*)-one (**3a**).

This product was obtained by the condensation-hydrolysis-cyclization of dilithiated **2** with benzonitrile. Crystallization from ethanol afforded **3a** as needles; 2.1 g (91%), mp 199-200 °C (Lit. [2] 198-199 °C); ir (potassium bromide): v 3320 (NH), 3000, 2990 (C-H), 1650, 1600, 1140, 770, 700 cm^{-1}; ^{1}H nmr (deuterochloroform): δ 6.77 (s, 1H, 4-H), 7.24-7.48 (m, 4H, Ar-H), 7.49 (d, J = 7.8 Hz, 1H, Ar-H), 7.52-7.54 (t, J = 7.8 Hz, 1H, Ar-H), 7.73-7.78 (m, 2H, Ar-H), 8.38 (d, J = 8.0 Hz, 1H, Ar-H), 11.60 (br, 1H, NH); ^{13}C nmr (deuterochloroform): δ 104.2, 124.9, 126.2, 126.5, 126.6, 127.4, 129.1, 129.5, 132.8, 134.3, 138.3, 139.6, 164.0; ms: m/z 222 (18%) [$M^{+\cdot}$].

3-Isopropyl-isoquinolin-1-(2*H*)-one (**3b**).

This product was crystallized from ethanol-water and gave **3b** as fine needles; 0.99 g (40%) mp 188-189 °C (Lit [2]; 188-189 °C); ir (potassium bromide): v 3325 (NH), 3000, 2990, 1648, 1608, 1556, 1476, 1384, 840, 754 cm^{-1}; ^{1}H nmr (dimethylsulphoxide-d_6): δ 1.21 (d, J = 6.8 Hz, 6H, 2 x CH_3), 2.76 (sept, J = 6.8 Hz, 1H, C*H*$(CH_3)_2$), 6.32 (s, 1H, 4-H), 7.37 (t, J = 8.0 Hz, 1H, Ar-H), 7.55 (d, J = 8.0 Hz, 1H, Ar-H), 7.61 (t, J = 8.0 Hz, 1H, Ar-H), 8.12 (d, J = 8.0 Hz, 1H, Ar-H), 10.82 (br, 1H, NH); ^{13}C nmr (dimethylsulphoxide-d_6): δ 21.3, 31.0 (2 x CH_3), 99.5, 124.4, 125.9, 126.5, 132.3, 138.3, 148.2, 162.6; ms: m/z 188 (16%) [$M^{+\cdot}$], 187 (10) [$M^{+\cdot}$ -1], 172 (67), 159 (20).

Bromination of Isoquinolinones (**3a-b**).

A sample of *N*-bromosuccinimide (4.5 mmol) was added to a stirred solution of isoquinolinone **3a** or **3b** (4.5 mmol) in dimethylformamide (20 ml). The reaction mixture was stirred at room temperature for 2 hours and then poured into cold water (50 ml). The filtration of the solid formed and subsequent crystallization from ethanol afforded needles of **6a** or **6b**.

4-Bromo-3-phenyl-isoquinolin-1-(2*H*)-one (**6a**).

This compound was prepared according to the general procedure to give **6a** as colorless needles, 1.22 g (90%) mp 270-208 °C; ir (potassium bromide): v 3300 (NH), 3005, 2990 (C- H), 1640, 1600, 1590, 1140, 780, 700 cm^{-1}; ^{1}H nmr (dimethylsulphoxide-d_6): δ 7.49 (m, 5H, Ar-H), 7.61-7.68 (t, J = 7.9 Hz, 1H, 6-H), 7.84-7.88 (t, J = 7.9 Hz, 1H, 7-H), 7.93 (d, J = 8.0 Hz, 1H, 5-H), 8.28 (d, J = 8.0 Hz, 1H, 8-H), 11.81 (br, 1H, NH); ^{13}C nmr (dimethylsulphoxide-d_6): δ 97.8 (C-4), 125.5, 126.0, 127.2, 127.4, 128.2, 129.4, 129.6, 133.6, 134.8, 136.2, 140.4, 161.1 (C = 0); ms m/z 301 (100%) [$M^{+\cdot}$ +1], 299 (99) [$M^{+\cdot}$ -1], 255 (12), 220 (69), 193 (80), 177 (5), 165 (78), 150 (4), 114 (6), 96 (7), $C_{15}H_{10}NOBr$ (300.155).

Anal. Calcd. for $C_{15}H_{10}NOBr$: C, 60.02; H, 3.35; N, 4.67. Found: C, 60.00; H, 3.30; N, 4.60.

4-Bromo-3-isopropyl-isoquinolin-1-(2*H*)-one (**6b**).

This compound was prepared according to the general procedure to give **6b** as colorless needles, 1.20 g (80 %) mp: 184-185 °C; ir (potassium bromide): v 3300 (NH), 3000, 2995 (C-H), 1645, 1600, 1590, 1140, 780, 700 cm^{-1}; ^{1}H nmr (deuterochloroform): δ 1.40-1.43 (d, J = 7.2 Hz, 6H, 2 x CH_3), 3.66-3.80 (sept, J = 7.2 Hz, 1H, -C*H*$(CH_3)_2$), 7.47-7.55 (ddd, J = 1.2, 6.9, 8.1 Hz, 1H, 7-H), 7.72-7.79 (ddd, J = 1.2, 7.0, 8.2 Hz, 1H, 6-H), 7.96-8.00 (dd, J = 1.2, 8.0 Hz, 1H, 5-H), 8.40-8.44 (dd, J = 1.3, 8.0 Hz, 1H, 8-H), 10.82 (br, 1H, N-H); ^{13}C nmr (deuterochloroform): δ 20.1 (2 x CH_3), 32.4, 98.9, 125.2, 126.5, 126.8, 127.6, 133.5, 137.3, 144.5, 163.4; ms: m/z 267 (99%) [$M^{+\cdot}$ +1], 266 (18) [$M^{+\cdot}$], 265 (100) [$M^{+\cdot}$ -1], 250 (73), 237 (56), 223 (5), 186 (34) [$M^{+\cdot}$ –Br], 171 (81), 153 (28), 142 (20), 128 (16), 115 (47), 89 (14), 63 (6); $C_{12}H_{12}NOBr$ (266.138).

Anal. Calcd. for $C_{12}H_{12}NOBr$: C, 54.19; H, 4.55; N, 5.26. Found: C, 53.98; H, 4.42; N, 5.06.

General Reaction Procedure of Isoquinolinones **3a-b** and **6a-b** with Propargyl Bromide.

To isoquinolinone (3.03 mmol) either **3a**, **3b**, **6a** or **6b** and potassium carbonate (3.03 mmol) in a 100 ml two-necked flask was added dimethylformamide (30 ml). The solution was stirred at room temperature for 15 minutes. Propargyl bromide 0.12 g (3.03 mmol) was added slowly and the reaction mixture carefully monitored by tlc till the total disappearance of isoquinolinone. The reaction mixture was poured into water (60 ml) and extracted into ethyl acetate (3 x 30 ml). The combined organic phase was washed with brine (2 x 20 ml), dried over anhydrous sodium sulphate and the organic solvent removed *in vacuo* to give a crude product, which was crystallized or subjected to column chromatography for purification and isolation of the product.

Isolation of 3-Phenyl-2-(prop-2-ynyl)-isoquinolin-1-(2*H*)-one **4a** and 3-Phenyl-1-(prop-2-ynyloxy)-isoquinoline **5a**.

The reaction of **3a** with propargyl bromide according to the general procedure yielded a crude product after 72 hours. This was purified by column chromatography (hexane:dichloromethane 1:1 to dichloromethane). 3-Phenyl-1-(prop-2-ynyloxy)-isoquinoline **5a** was isolated first, followed by 3-phenyl-2-(prop-2-ynyl)-isoquinolin-1-(2*H*)-one **4a**. **4a** and **5a** were crystallized

from hexane-dichloromethane to give colorless needles of **4a** and **5a**.

3-Phenyl-2-(prop-2-ynyl)-isoquinolin-1-(2*H*)-one (**4a**).

This compound was prepared according to the general procedure to give **4a** as colorless needles, 0.18 g (23%) mp: 132-133 °C; (Lit [7] 132-133 °C); ir (potassium bromide): v 2990, 2970, 1660, 1620, 1240, 1150, 780, 700 cm^{-1}; ^1H nmr (deuterochloroform): δ 2.22 (t, J = 2.0 Hz, 1H, ≡CH), 4.58 (d, J = 2.0 Hz, 2H, -CH_2-), 6.41 (s, 1H, 4-H), 7.43 (m, 5H, Ar-H), 7.51 (m, 2H, Ar-H), 7.59 (m, 1H, Ar-H), 8.43 (d, J = 8.0 Hz, 1H, Ar-H); ^{13}C nmr (deuterochloroform): δ 35.7 (CH_2), 71.5 (≡CH), 79.3 (C≡), 107.9, 124.7, 125.8, 126.6, 127.9, 128.5, 129.1, 132.5, 135.2, 136.2, 142.9, 162.3; ms: m/z 259 (61%) [$M^{+\cdot}$ +1], 258 (100) [$M^{+\cdot}$], 232 (16), 202 (12), 190 (6), 176 (10), 165 (15), 152 (4), 129 (6), 115 (7), 89 (11); $C_{18}H_{13}NO$ (259.308).

Anal. Calcd. for $C_{18}H_{13}NO$: C, 83.38; H, 5.05; N, 5.40. Found: C, 83.18; H, 5.00; N, 5.30.

3-Phenyl-1-(prop-2-ynyloxy)-isoquinoline (**5a**).

This compound was prepared according to the general procedure to give **5a** as colorless needles, 0.54 g (68 %), mp: 92-93 °C; (Lit [7] 87-88 °C); ir (potassium bromide): v 3000, 2980, 1620, 1600, 1540, 320, 780, 700 cm^{-1}; ^1H nmr (deuterochloroform): δ 2.53 (t, J = 2.4 Hz, 1H, ≡CH), 5.31 (d, J = 2.2 Hz, 2H, -CH_2-), 7.40 (t, J = 8.0 Hz, 1H, Ar-H), 7.70 (s, 1H, 4-H), 7.76 (d, J = 8.0 Hz, 1H, Ar-H), 8.16 (m, 2H, Ar-H), 8.38 (d, J = 8.0 Hz, 1H, Ar-H); ^{13}C nmr (deuterochloroform): δ 53.6 (-CH_2), 74.2 (≡CH), 79.5 (C≡), 111.0, 118.5, 124.1, 126.5, 126.6, 128.4, 128.6, 130.7, 138.9, 139.0, 147.4, 158.5; ms: m/z 260 (4) [$M^{+\cdot}$ +1], 259 (25) [$M^{+\cdot}$], 258 (100) [$M^{+\cdot}$ -1], 229 (8), 202 (6), 190 (4), 165 (11), 129 (7), 115 (3), 89 (11); $C_{18}H_{13}NBrO$ (259.308).

Anal. Calcd. for $C_{18}H_{13}NBrO$: C, 83.38; H, 5.05; N, 5.40. Found: C, 83.32; H, 5.15; N, 5.38.

Isolation of 3-Isopropyl-2-(prop-2-ynyl)-isoquinolin-1-(2*H*)-one **4b** and 3-Isopropyl-1-(prop-2-ynyloxy)-isoquinoline **5b**.

The reaction of **3b** with propargyl bromide according to the general procedure yielded a crude product after 48 hours. This was purified by column chromatography (hexane to hexane-dichloromethane 1:1) to give **5b** as an oil and then closely followed by **4b** which was recrystallised from hexane-dichloromethane.

3-Isopropyl-2-(prop-2-ynyl)-isoquinolin-1-(2*H*)-one (**4b**).

This compound was prepared according to the general procedure to give **4b** as colorless needles, 0.41 g (60 %), mp: 116-117 °C; ir (potassium bromide): v 3000, 2995 (C-H), 1670, 1610, 1595, 1540, 1240, 1140, 780, 700 cm^{-1}; ^1H nmr (deuterochloroform): δ 1.24-1.26 (br, 6H, 2 x CH_3), 2.14 (s, 1H, ≡CH), 3.13-3.16 (m, 1H, C*H*(CH_3)$_2$), 4.89 (s, 2H, -CH_2-), 6.33 (s, 1H, 4-H), 7.23-7.35 (m, 2H, Ar-H), 7.48 (t, J = 8.0 Hz, 1H, Ar-H), 8.27 (d, 1H, J = 8.0 Hz, Ar-H); ^{13}C nmr (deuterochloroform): δ 22.9 (2 x CH_3) 29.7, 32.1, 71.6, 79.2, 102.6, 124.2, 125.5, 126.1, 128.0, 132.4, 136.7, 148.7, 162.8 (C=0); ms: m/z 226 (8%) [$M^{+\cdot}$ + 1], 225 (36) [$M^{+\cdot}$], 210 (100), 195 (27), 182 (17), 167 (18), 154 (6), 128 (15), 115 (18), 89 (11), 77 (4); $C_{15}H_{15}NO$ (225.291).

Anal. Calcd. for $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22. Found: C, 97.96; H, 6.70; N, 6.19.

3-Isopropyl-1-(prop-2-ynyloxy)-isoquinoline (**5b**).

This compound was prepared according to the general procedure to give **5b** as colorless oil, 0.21 g (30%), oil; (sodium chloride): v 3110, 2985, 1620, 1600, 1590, 1140, 770, 700 cm^{-1}; ^1H nmr (deuterochloroform): δ 1.29-1.31 (d, J = 7.1 Hz, 6H, 2 x CH_3), 2.42 (s, 1H, ≡CH), 2.95-3.01 (sept, J = 7.2 Hz, 1H, -C*H*(CH_3)$_2$), 5.15 (s, 2H, CH_2), 7.00 (s, 1H, 4-H), 7.39 (t, J = 8.0 Hz, 1H, Ar-H), 7.53 (t, J = 7.9 Hz, 1H, Ar-H), 7.61 (d, J = 7.9 Hz, 1H, Ar-H), 7.61 (d, J = 7.9 Hz, 1H, Ar-H), 8.17 (d, J = 8.0 Hz, 1H, Ar-H); ^{13}C nmr (deuterochloroform): δ 22.3, 35.6, 53.4, 73.8, 79.7, 110.4, 117.9, 123.9, 125.7, 125.9, 130.3, 138.9, 157.6, 158.3; ms: m/z 225 (26%) [$M^{+\cdot}$], 224 (30) [$M^{+\cdot}$ -1], 210 (100), 195 (27), 182 (22), 167 (21), 154 (10), 141 (5), 128 (8), 115 (10), 89 (7); $C_{15}H_{15}NO$ (225.291).

Anal. Calcd. for $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22. Found: C, 79.94; H, 6.68; N, 6.12.

Isolation of 4-Bromo-3-phenyl-2-(prop-2-ynyl)-isoquinolin-1-(2*H*)-one **7a** and 4-Bromo-3-phenyl-1-(prop-2-ynyloxy)-isoquinoline **8a**.

The reaction of **6a** with propargyl bromide according to the general procedure yielded a crude product after 10 hours which on column chromatography (hexane to hexane:dichloromethane 1:1) gave **8a** and then followed by **7a.** Crystallization from hexane-dichloromethane mixture afforded colorless needles of **8a** and **7a**.

4-Bromo-3-phenyl-2-(prop-2-ynyl)-isoquinolin-1-(2*H*)-one (**7a**).

This compound was prepared according to the general procedure to give **7a** as colorless needles, 0.17 g (15%); mp: 163-164 °C; ir (potassium bromide): v 3210, 2100, 1640 (C=0), 1600, 1560, 760, 700 cm^{-1}. ^1H nmr (deuterochloroform): δ 2.20 (t, J = 2.5 Hz, 1H, 3'-H), 4.55 (d, J = 2.5 Hz, 2H, 1'-H), 7.42-7.51 (m, 2H, Ar-H), 7.53-7.64 (m, 4H, Ar-H), 7.72-7.84 (ddd, J = 1.4, 7.8, 8.0 Hz, 1H, Ar-H), 7.98-8.02 (dd, J = 1.3, 7.8 Hz, 1H, Ar-H), 8.52-8.58 (dd, J = 1.3, 7.9 Hz, 1H, Ar-H); ^{13}C nmr (deuterochloroform): δ 36.9, 71.7, 78.9, 102.9, 123.9, 125.5, 126.7, 128.5, 128.9, 129.6, 129.7, 133.4, 133.6, 135.5, 135.6, 141.5, 161.4; ms: m/z 340 (15%) [$M^{+\cdot}$ +2], 339 (18) [$M^{+\cdot}$ +1], 338 (100) [$M^{+\cdot}$], 337 (85), 336 (88), 310 (11), 292 (13), 257 (55) [$M^{+\cdot}$ -Br], 219 (22), 202 (22), 190 (24), 176 (9), 114 (4), 88 (8), $C_{18}H_{12}NBrO$ (338.204).

Anal. Calcd. for $C_{18}H_{12}NBrO$: C, 63.93; H, 3.58; N, 4.14. Found: C, 64.00; H, 3.60; N, 4.20.

4-Bromo-3-phenyl-1-(prop-2-ynyloxy)-isoquinoline (**8a**).

This compound was prepared according to the general procedure to give **8a** as colorless needles, 0.9 g (80 %); mp: 79-81 °C; ir (potassium bromide): v 3300, 2900, 2885, 2100, 1600, 1560, 1400, 770, 700 cm^{-1}; ^1H nmr (deuterochloroform): δ 2.52 (t, J = 2.5 Hz, 1H, 3'-H), 5.20 (d, J = 2.5 Hz, 2H, 1'-H), 7.42-7.54 (m, 3H, Ar-H), 7.58-7.68 (ddd, J = 1.1, 7.3, 8.1 Hz, 1H, Ar-H), 7.76-7.86 (m, 3H, Ar-H), 8.24-8.38 (t, J = 8.0 Hz, 2H, Ar-H); ^{13}C nmr (deuterochloroform): δ 54.2 (CH_2), 74.6 (C-3'), 79.2 (C-2'), 110.7, 119.7, 124.4, 127.5, 127.8, 128.3, 130.2, 131.7, 132.0, 137.8, 140.6, 158.8; ms: m/z 340 (3) [$M^{+\cdot}$ +2], 339 (20%) [$M^{+\cdot}$ +1], 338 (100) [$M^{+\cdot}$], 337 (22), 336 (96), 310 (3), 292 (26), 257 (32) [$M^{+\cdot}$ -Br], 229 (9), 219 (13), 190 (14), 169 (6), 111 (5), 85 (9), 57 (13); $C_{18}H_{12}NBrO$ (338.204).

Anal. Calcd. for $C_{18}H_{12}NBrO$: C, 63.93; H, 3.58; N, 4.14. Found: C, 63.74; H, 3.52; N, 4.02.

4-Bromo-3-isopropyl-1-(prop-2-ynyloxy)-isoquinoline (**8b**).

The reaction of **6b** with propargyl bromide according to the general procedure yielded a crude product after 12 hours. Subsequent purification of the crude product using column chromatography (hexane) gave colorless oil of **8b**; 0.80 g (90%); ir: (sodium chloride): v = 3205, 2100, 1600, 1520, 760, 700 cm^{-1}; ^1H nmr (deuterochloroform): δ 1.33-1.37 (d, J = 6.7 Hz, 6H, 2 x CH_3), 2.51 (t, J = 2.4 Hz, 1H, 3'-H), 3.70-3.84 (sept, J = 6.7 Hz, 1H, -C*H*$(CH_3)_2$) 5.20 (d, J = 2.4 Hz, 2H, 1'-H), 7.48-7.57 (ddd, J = 1.2, 7.0, 8.2 Hz, 1H, 7-H), 7.68-7.77 (ddd, J = 1.2, 7.1, 8.4 Hz, 1H, 6-H), 8.14 (d, J = 8.6 Hz, 1H, 5-H). 8.21-8.25 (d, J = 8.2 Hz, 1H, 8-H); ^{13}C nmr (deuterochloroform): δ 21.5, 29.8, 34.2, 53.7, 74.2, 79.4, 110.2, 119.3, 124.2, 126.6, 131.5, 137.4, 154.8, 157.7; ms: m/z 305 (25%) [$M^{+\cdot}$ +1], 304 (61) [$M^{+\cdot}$], 303 (25), 302 (57), 288 (32), 275 (6), 224 (5), 209 (100), 88 (5), 184 (3), 170 (12), 115 (11); $C_{15}H_{14}NBrO$ (304.187).

Anal. Calcd. for $C_{15}H_{14}NBrO$: C, 59.23; H, 4.64; N, 4.61. Found: C, 59.10; H, 4.40; N, 4.52.

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REFERENCES AND NOTES

[1] R. L. Vaulx, W. H. Puterbaugh and C. R. Hauser, *J. Org. Chem.*, **29**, 3514 (1964).

[2] G. S Poindexter, *J. Org. Chem.*, **47**, 3787 (1982).

[3] A. A. Patchett, S. E. De Laszlo and W. J. Greenlee, Substituted 1-(2*H*)-Isoquinolinones. European Patent Application, 502 0575 (1992).

[4] H. Liu, S. B. Ko, H. Josien and D. P. Curran, *Tetrahedron. Lett.*, **36**, 8917 (1995).

[5] J. Reisch, A. R. R. Rao and C. O. Usifoh, *Monatsh. Chem.*, **125**, 79 (1994).

[6] J. Reisch, A. R. R. Rao and C. O. Usifoh, *Monatsh. Chem.*, **124**, 1217 (1993).

[7] C. Bogentoft, L. Kronberg and B. Danielsson, *Acta. Pharm. Suecica.*, **6**, 489 (1969).