Application of Ring-Closing Metathesis for the Synthesis of Benzo[3,4]azepino[1,2-*b*]isoquinolin-9-ones

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Cycloaddition reaction between toluamides and benzonitriles was applied to prepare the 3-arylisoquinolines, and their chemical transformation to the dienes 4 was performed. The ring-closing metathesis (RCM) reaction afforded the desired heterocyclic compounds, benzo[3,4]azepino[1,2-*b*]isoquinolinones 5 in good yield.

Key words ring-closing metathesis; benzo[3,4]azepino[1,2-*b*]isoquinolinone; 3-arylisoquinoline; chemical shift difference

In order to heal cancer, chemotherapeutic treatments have been investigated over the last several decades.[1,2] Conformation studies and synthesis of medium-sized heterocyclic compounds, which have been investigated as the scaffolds of many biologically interesting structures, have received more attention.[3—5] Recently, we studied the synthesis of 3-arylisoquinoline derivatives such as indeno[1,2-*c*]isoquinolines,[6,7] isoindolo[2,1-*b*]isoquinolines,[8] benz[*b*]oxepines[9] and benzo[*c*]phenanthridinones[10] as constrained structures through molecular modeling to find plausible antitumor agents. The diversely rigidified 3-arylisoquinoline analogs exhibited promising cytotoxicities and topoisomerase I inhibitory activities.[11] We also reported the convenient synthesis of protoberberines using ring-closing metathesis (RCM) as shown in Fig. 1.[12]

Seven-membered heterocyclic rings are considered attractive molecules due to the points of structural determination of natural products as well as their interesting pharmacological actions.[3—5]

In this paper we applied RCM[13—26] for the formation of seven-membered benzo[3,4]azepino[1,2-*b*]isoquinolinone **5**, and the retrosynthetic pathway of benzo[3,4]azepino[1,2-*b*]isoquinolinone **5** is depicted in Chart 1. The coupling reaction of toluamide **7** with benzonitrile **8** afforded the 3-arylisoquinolinone **6**, which could be modified to diene **4** as a key intermediate for the RCM reaction.

The synthetic approach of using the RCM reaction to prepare the seven-membered ring was based on the synthesis of 3-arylisoquinolines **4** that contain olefins at the appropriate positions. To synthesize the 3-arylisoquinoline **6a**, a coupling reaction between *N*,*N*-diethyl-*o*-toluamide **7a** and benzonitrile **8a** was performed (Chart 2).[10] Generally, the chemical yield of this reaction is low (33 to 49%) due to the unknown side product and it is quite dependent on the substitution pattern of aromatic rings of the starting materials.[10] As a part of our continuous research on natural alkaloids synthesis, including biological evaluation of 3-arylisoquinolines, the coupling reaction of *o*-toluamides with benzonitriles was utilized to provide the desired molecules.[27] Significant increases in the topoisomerase I inhibitory activities of these compounds were observed through conversion of flexible 3-aryl rings to rigid forms such as isoindolo[2,1-*b*]isoquinolinones, benz[*b*]oxepines, 12-oxobenzo[*c*]phenanthridinones and indeno[1,2-*c*]isoquinolines, and molecular docking studies were used to explain the potency of these compounds.[11] The above coupling reaction has advantages as a synthetic tool for the construction of 3-arylisoquinolines because it is easily adaptable to starting materials with diverse aromatic ring substitutions and it is a one-pot procedure for the construction of all essential carbon atoms in the desired molecules.

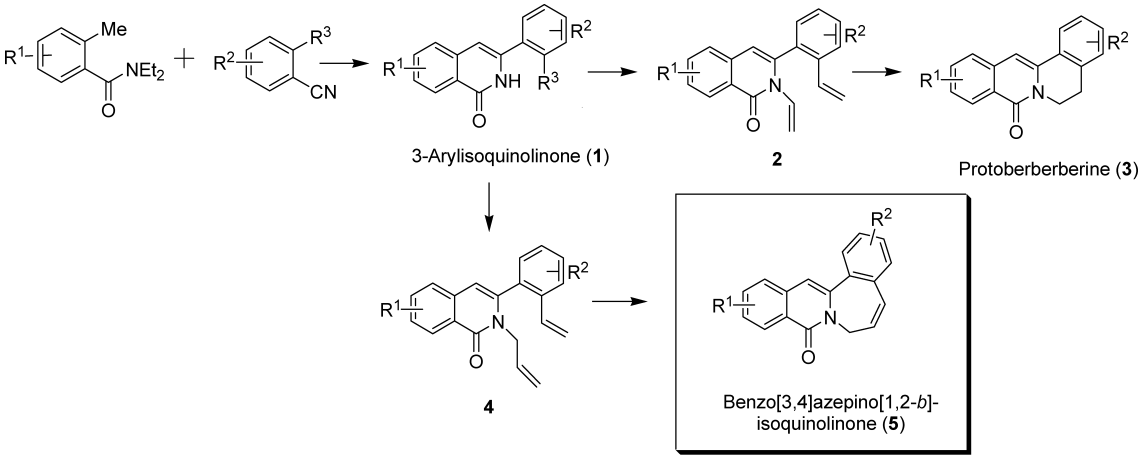

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Fig. 1. Structural Modification of 3-Arylisoquinolinone to Protoberberine **3** and Benzo[3,4]azepino[1,2-*b*]isoquinolinone **5** *via* Ring-Closing Metathesis

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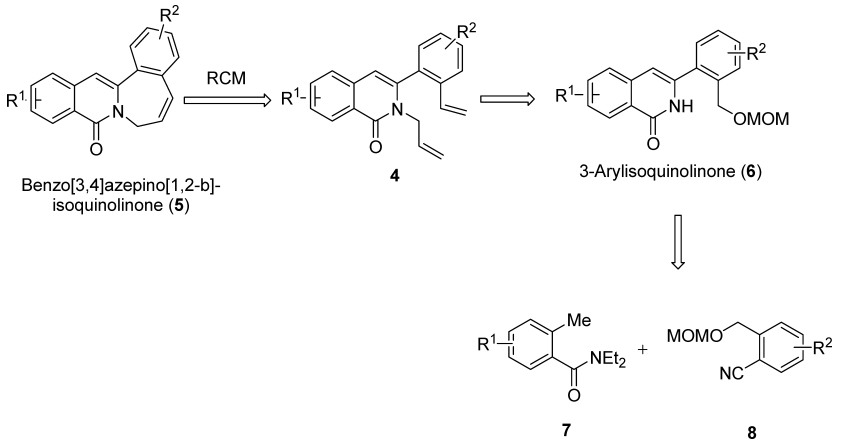

Chart 1. Retrosynthetic Pathway of Benzo[3,4]azepino[1,2-*b*]isoquinolinone **5**

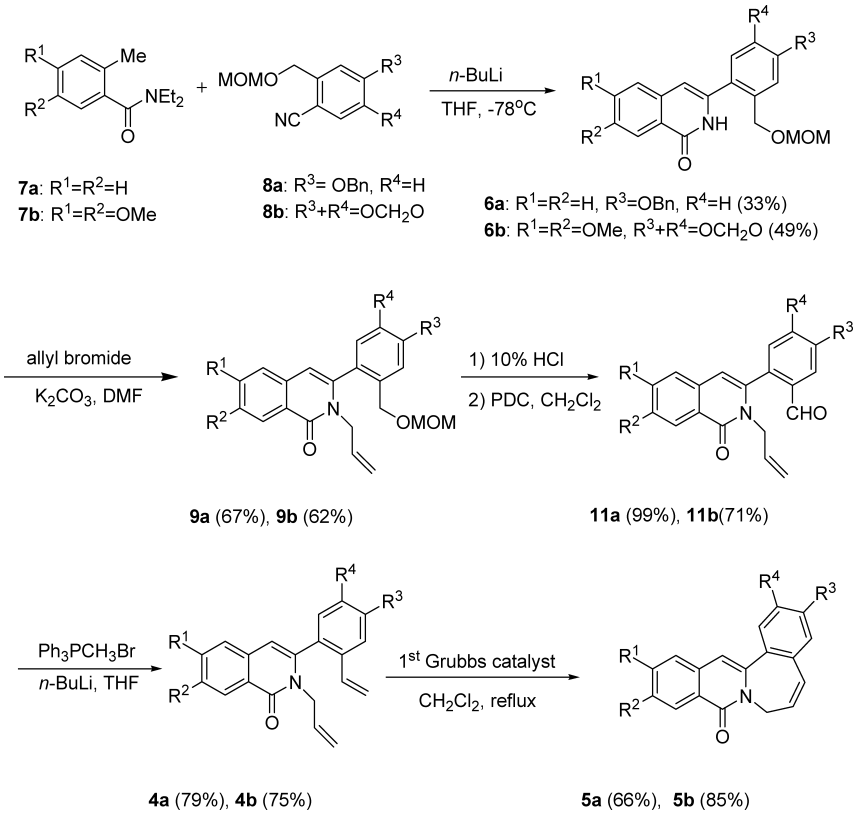

Chart 2. Synthesis of Benzo[3,4]azepino[1,2-*b*]isoquinolinone **5**

Next, the amide **6a** was reacted with allyl bromide and K_2CO_3 in *N*,*N*-dimethylformamide (DMF) to provide the *N*-allyl compound **9a** in 67% yield without giving an *O*-allyl product. When we tried to get an alkyl group such as methyl or PMB, only *N*-alkylated compounds were obtained. Methoxymethyl (MOM) was removed from **9a** with 10% HCl to afford the alcohol **10a**, which was then reacted with PDC in CH_2Cl_2 to furnish the aldehyde **11a** in 99% yield. Wittig reactions of the aldehyde **11a** with Ph_3PCH_3Br and *n*-BuLi in tetrahydrofuran (THF) gave the desired olefin **4a** in 79% yield. Finally, RCM reaction of **4a** with 1st generation Grubbs catalyst in CH_2Cl_2 furnished the desired cyclized product **5a** in 66% yield. When we carried out this reaction using 2nd generation catalyst, the similar result was obtained. 4,5-Dimethoxy toluamides **7b** and benzonitriles **8b** also provided the corresponding coupling products **6b** in 49% yield. The reactions for the preparation of **9b**, **10b**, **11b**, **4b**, and **5b** were also conducted following similar procedures applied for **5a**.

The structures of benzoazepinoisoquinolones were determined by 1D ^{1}H-, ^{13}C-NMR and 2D ^{1}H–^{1}H correlation spectroscopy (COSY), ^{1}H–^{13}C heteronuclear single quantum coherence (HSQC), heteronuclear multiple bond coherence (HMBC) spectra (spectral data of **5a** is compiled in Table 1). ^{1}H-NMR spectrum of **5a** revealed H10 proton signaled at δ 8.42 (d, J=8 Hz, 1H) and rest of aromatic protons between 7.67—6.89 ppm. H14 and benzylic protons appeared as singlet at 6.54 and 5.14 ppm respectively. Ethylene protons H5

Table 1. ^{1}H- and ^{13}C-NMR Data and HMBC Correlations of **5a**

Carbon No.	δ_C	δ_H	HMBC H→C
1	131.21	7.67 (d, J=8.5)	3, 4a, 14a
2	114.90	7.03 (dd, J=3, 8.7)	3, 4, 14b
3	159.22		
4	114.36	6.89 (d, J=3)	2, 3, 5, 14b
4a	137.45		
5	134.46	6.82 (d, J=10)	4, 4a, 7, 14b
6	129.99	6.49—6.44 (m)	4a, 7
7	39.53	α: 5.74 (dd, J=8, 13.5)	5, 6, 9, 14a
		β: 3.53 (dd, J=6.5, 13.5)	5, 6, 9, 14a
9	161.27		
9a	124.03		
10	127.91	8.42 (d, J=8)	9, 12, 13a
11	126.25	7.50—7.34 (m)	9a, 13
12	132.11	7.61 (t, J=7.5)	10, 13a
13	125.92	7.50—7.34 (m)	9a, 11, 14
13a	136.57		
14	107.48	6.54 (s)	9a, 13, 13a, 14a, 14b
14a	142.67		
14b	128.87		
1′	136.36		
2′	127.91	7.50—7.34 (m)	1′, 3′, 6′
3′	128.67	7.50—7.34 (m)	2′
4′	128.18	7.50—7.34 (m)	2′, 6′
5′	128.67	7.50—7.34 (m)	6′
6′	127.91	7.50—7.34 (m)	1′, 2′, 5′
7′	70.14	5.14 (s)	3, 1′, 2′, 6′

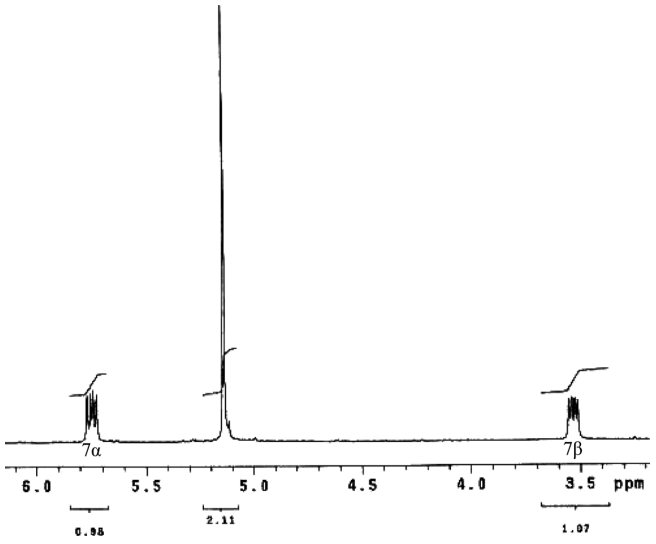

Fig. 2. A Portion of ^{1}H-NMR Spectrum of **5a** Showing Nonequivalence of Geminal Protons H7α and H7β

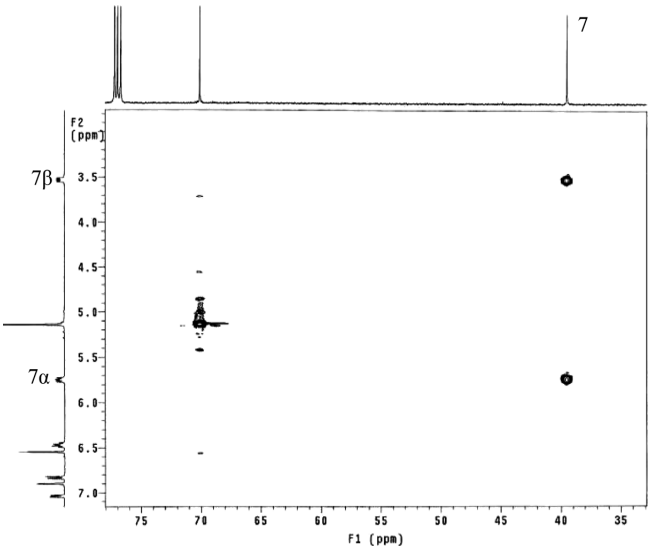

Fig. 3. HSQC Spectrum of **5a** Showing Correlations between Geminal Protons H7α and H7β with C7

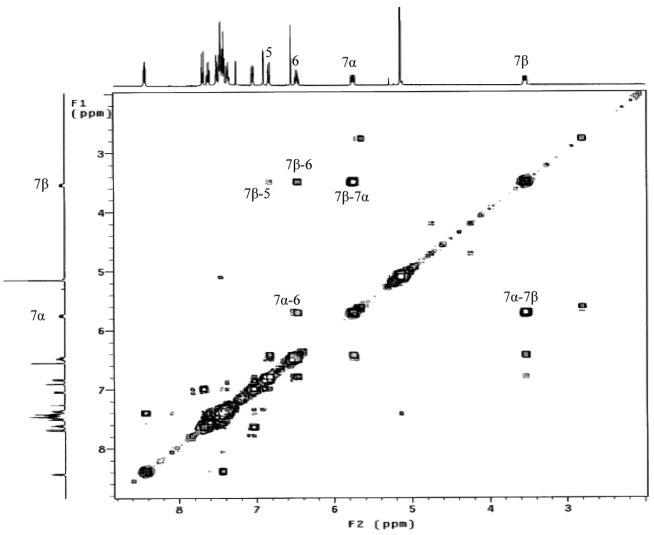

Fig. 4. A Portion of ^{1}H–^{1}H COSY Spectrum of **5a** Showing Correlations between Nonequivalent Geminal Protons H7α and H7β

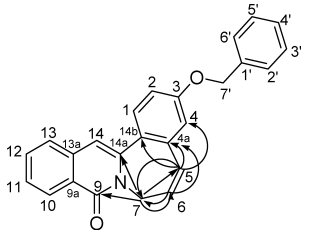

Fig. 5. Selected HMBC Correlations of **5a**

and H6 of the azepine ring, showed up at δ 6.82 (d, J=10 Hz, 1H) and at δ 6.49—6.44 (m, 1H). Interestingly, methylene protons labeled as H7α and H7β signaled as doublets of doublets centered at δ 5.74 (J=8, 13.5 Hz, 1H) and 3.53 (J=6.5, 13.5 Hz, 1H) respectively (Fig. 2). HSQC cross peaks of H7α/C7 and H7β/C7 corroborated that the protons are attached to the same carbon C7 (Fig. 3). Furthermore, ^{1}H–^{1}H COSY correlation peaks of H7α/H7β and H7β/H7α enforced that the geminal protons lie in different magnetic environment (Fig. 4). Difference in chemical shifts of geminal, methylene protons of azepine ring adjoined to naphthoquinone and of azocine ring bridging biphenyl group have also been reported.[28,29]

In addition, formation of azepine ring by RCM of olefin **4** was established by HMBC analysis (Fig. 5). HMBC correlation peaks, H5/C7, H6/C4a and H7α,β/C5, clearly indicated that seven membered ring was formed by intramolecular olefin metathesis. In the similar manner, the spectral data of

azepine derivatives **5b** were in total agreement with the proposed structure.

In conclusion, cycloaddition reaction between toluamides **7a**, **b** and benzonitriles **8a**, **b** was utilized to prepare the 3-arylisoquinolines **6a**, **b**, which retain the main template for the RCM reaction, to construct the seven-membered heterocyclic compounds, benzo[3,4]azepino[1,2-*b*]isoquinolinones **5a**, **b**. The conventional transformation of 3-arylisoquinolines **6a**, **b** to dienes **4a**, **b** was carried out and the subsequent RCM reaction furnished the desired benzo[3,4]azepino[1,2-*b*]isoquinolinones **5a**, **b** in 66% and 85% yield, respectively. We believe that the RCM reaction could be an efficient method for the preparation of heterocyclic medium-sized rings.

Experimental

Melting points were determined by the capillary method on an Electrothermal IA9200 digital melting point apparatus and were uncorrected. ^{1}H-NMR spectra were obtained at 300 or 500 MHz, using Varian 300 or Kjui 500-Inova 500 FT spectrometer at the Korea Basic Science Institute and were reported in ppm, downfield from the peak of the internal standard, tetramethylsilane. The data are reported as follows: chemical shift, number of protons, multiplicity (s: singlet, d: doublet, t: triplet, q: quartet, m: multiplet, b: broadened). ^{1}H–^{1}H COSY, HSQC and HMBC spectra were obtained using Kjui 500-Inova 500 FT spectrometer. IR spectra were recorded on a JASCO-FT IR spectrometer using $CHCl_3$ or KBr pellets. Mass spectra were obtained on JEOL JNS-DX 303 using the electron-impact (EI) method. Column chromatography was performed on Merck silica gel 60 (70—230 mesh). TLC was performed using plates coated with silica gel 60 F254 that were purchased from Merck.

3-(4-Benzyloxy-2-methoxymethoxymethyl-phenyl)-2*H*-isoquinolin-1-one (6a) A solution of *N*,*N*-diethylbenzamide **7a** (1.6 g, 8.0 mmol) and benzonitrile **8a** (3.4 g, 12 mmol) in dry THF (20 ml) were added drop wise to a solution of *n*-butyllithium (5 ml of 2.5 M in hexane, 12.5 mmol) in THF (20 ml) at −70 °C, and then the reaction mixture was stirred at the same temperature for 6 h. The reaction was quenched with water, extracted with ethyl acetate and dried over sodium sulfate. After removal of the solvent, the residue was purified by column chromatography with *n*-hexane–ethyl acetate (1 : 1) to afford compound **6a** as pale yellow needles (1.04 g, 33%). mp: 130—131 °C (Et_2O). IR (cm^{-1}): 3400 (NH), 1657 (C=O). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 9.74 (s, 1H), 8.40 (m, 1H), 7.67 (m, 1H), 7.58—7.36 (m, 8H), 7.12 (d, 1H), 7.02 (m, 1H), 6.51 (s, 1H), 5.13 (s, 2H), 4.78 (s, 2H), 4.55 (s, 2H), 3.41 (s, 3H). EI-MS: *m/z* 401 (M^+, 86). High resolution (HR)-MS-EI (Calcd for $C_{25}H_{23}NO_4$): 401.1627, Found 401.1623.

6,7-Dimethoxy-3-(6-methoxymethoxymethylbenzo[1,3]dioxol-5-yl)-2*H*-isoquinolin-1-one (6b) The procedure described for compound **6a** was used with *N*,*N*-diethyl-4,5-dimethoxy-2-methylbenzamide **7b** (1.51 g, 6 mmol) and benzonitrile **8b** (11.66 g, 7.5 mmol) in the presence of *n*-BuLi (6 ml of 2.5 M in hexane, 15 mmol) to give compound **6b** as bright yellow solid (1.2 g, 49%). mp 151.0—154.2 °C (Et_2O). IR (cm^{-1}): 3400 (NH), 1657 (C=O). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 9.62 (s, 1H), 7.78 (s, 1H), 6.97 (s, 1H), 6.95 (s,1H), 6.92 (s, 1H), 6.44 (s, 1H), 6.06 (s, 2H), 4.80 (s, 2H), 4.46 (s, 2H), 4.02 (s, 3H), 4.01 (s, 3H), 3.44 (s, 3H). EI-MS, *m/z* (%): 399 (M^+, 75). HR-MS-EI (Calcd for $C_{21}H_{21}NO_7$): 399.1318, Found 399.1312.

2-Allyl-3-(4-benzyloxy-2-methoxymethoxymethylphenyl)-2*H*-isoquinolin-1-one (9a) To a solution of 3-arylisoquinoline **6a** (1.0 g, 2.5 mmol) and K_2CO_3 (1.05 g, 7.5 mmol) in DMF (20 ml) was added allyl bromide (600 mg, 5 mmol). The mixture was stirred at room temperature for 12 h, quenched with water, and extracted with ethyl acetate. The combined ethyl acetate extracts were washed with water and brine and dried over anhydrous sodium sulfate. After removing the solvent *in vacuo*, the residue was purified by column chromatography on silica gel with *n*-hexane–ethyl acetate (2 : 1) to give compound **9a** as yellow oil (735 mg, 67%). IR (cm^{-1}): 1650 (CO). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 8.46 (d, 1H), 7.64 (m, 1H), 7.51—7.37 (m, 8H), 7.21 (m, 2H), 6.95 (dd, 1H), 6.39 (s, 1H), 5.80 (m, 1H), 5.14 (s, 2H), 5.05 (dd, 1H), 4.80 (dd, 1H), 4.74 (m, 1H), 4.58 (m, 2H), 4.39 (s, 2H), 4.18 (m, 1H), 3.27 (s, 3H). EI-MS, *m/z* (%): 441 (M^+, 65). HR-MS-EI (Calcd for $C_{28}H_{27}NO_4$): 441.1940, Found 441.1941.

2-Allyl-6,7-dimethoxy-3-(6-methoxymethoxymethylbenzo[1,3]dioxol-5-yl)-2*H*-isoquinolin-1-one (9b) The procedure described for compound **9a** was used with 3-arylisoquinoline **6b** (373 mg, 0.93 mmol) and K_2CO_3 (400 mg, 3 mmol) in DMF (20 ml) and allyl bromide (240 mg, 2 mmol) to give compound **9b** as yellow oil (252 mg, 62%). IR (cm^{-1}): 1650 (C=O). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.84 (s, 1H), 7.02 (s, 1H), 6.82 (s, 1H), 6.74 (s, 1 H), 6.32 (s, 1H), 6.04 (d, 2H), 5.82 (m, 1H), 5.08 (dd, 1H), 4.80 (dd, 1H), 4.69 (m, 1H), 4.59 (d, 2H), 4.29 (s, 2H), 4.24 (m, 1H), 4.02 (s, 3H), 3.98 (s, 3H), 3.25 (s, 3H). EI-MS, *m/z* (%): 439 (M^+, 76). HR-MS-EI (Calcd for $C_{24}H_{25}NO_7$): 439.1631, Found 439.1633.

2-Allyl-3-(4-benzyloxy-2-hydroxymethylphenyl)-2*H*-isoquinolin-1-one (10a) To a solution of compound **9a** (700 mg, 0.84 mmol) in THF (15 ml) was added 10% HCl (10 ml), and the reaction was refluxed for 2 h. After cooling to room temperature, the reaction mixture was poured into water and extracted with ethyl acetate. The ethyl acetate extracts were washed with water and brine and dried over anhydrous sodium sulfate. After removal of the solvent *in vacuo* the residue was purified by column chromatography on silica gel with *n*-hexane–ethyl acetate (1 : 2) to produce the alcohol **10a** as yellow oil (421 mg, 67%). IR (cm^{-1}): 3300 (OH), 1641 (C=O). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 8.41 (d, 1H), 7.62 (m, 1H), 7.49—7.37 (m, 8H), 7.18 (d, 1H), 6.93 (dd, 1H), 6.39 (s, 1H), 5.77 (m, 1H), 5.14 (s, 2H), 5.02 (dd, 1H), 4.76 (dd, 1H), 4.63 (m, 1H), 4.51 (d, 2H), 4.22 (m, 1H). EI-MS, *m/z* (%): 397 (M^+, 100). HR-MS-EI (Calcd for $C_{26}H_{23}NO_3$): 397.1678, Found 397.1677.

2-Allyl-3-(6-hydroxymethylbenzo[1,3]dioxol-5-yl)-6,7-dimethoxyisoquinolin-1(2*H*)-one (10b) The procedure described for compound **10a** was used with compound **9b** (230 mg, 0.52 mmol) in THF (15 ml) and 10% HCl (10 ml) to give the alcohol **10b** as colorless needles (145 mg, 70%). mp 185—189 °C (Et_2O). IR (cm^{-1}): 3300 (OH), 1641 (C=O). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.80 (s, 1H), 7.08 (s, 1H), 6.81 (s, 1H), 6.72 (s, 1H), 6.32 (s, 1H), 6.04 (d, 2H), 5.80 (m, 1H), 5.06 (dd, 1H), 4.78 (dd, 1H), 4.57 (m, 1H), 4.40 (s, 2H), 4.31 (m, 1H), 4.00 (s, 3H), 3.97 (s, 3H). EI-MS, *m/z* (%): 395 (M^+, 100). HR-MS-EI (Calcd for $C_{22}H_{21}NO_6$): 395.1369, Found 395.1366.

2-(2-Allyl-1-oxo-1,2-dihydroisoquinolin-3-yl)-5-benzyloxybenzaldehyde (11a) To a solution of alcohol **10a** (400 mg, 1.0 mmol) in methylene chloride (30 ml) was added PDC (760 mg, 2 mmol), and the mixture was stirred for 2 h at room temperature. The reaction mixture was filtered off and the filtrate was washed with CH_2Cl_2. The solvent was evaporated off, and the residue was purified by column chromatography on silica gel with *n*-hexane–ethyl acetate (2 : 1) to afford the aldehyde **11a** as a brown oil (390 mg, 99%). IR (cm^{-1}): 1700, 1640 (C=O). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 9.89 (s, 1H), 8.47 (d, 1H), 7.67—7.30 (m, 11H), 6.42 (s, 1H), 5.78 (m, 1H), 5.19 (s, 2H), 5.03 (dd, 1H), 4.73 (dd, 1H), 4.50 (m, 2H). EI-MS, *m/z* (%): 395 (M^+, 23). HR-MS-EI (Calcd for $C_{26}H_{21}NO_3$): 395.1521, Found 395.1524.

6-(2-Allyl-1,2-dihydro-6,7-dimethoxy-1-oxoisoquinolin-3-yl)benzo[*d*][1,3]dioxole-5-carbaldehyde (11b) The procedure described for compound **11a** was used with alcohol **10b** (125 mg, 0.32 mmol) and PDC (240 mg, 0.65 mmol) in CH_2Cl_2 (20 ml) to give the aldehyde **11b** as colorless needles (88 mg, 71%). IR (cm^{-1}): 1700, 1640 (C=O). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 9.78 (s, 1H), 7.80 (s, 1H), 7.44 (s, 1H), 7.08 (s, 1H), 6.84 (s, 1H), 6.32 (s, 1H), 6.14 (d, 2H), 5.82 (m, 1H), 5.06 (dd, 1H), 4.79 (dd, 1H), 4.51—4.44 (m, 2H), 4.00 (s, 3H), 3.97 (s, 3H). EI-MS, *m/z* (%): 393(M^+, 46). HR-MS-EI (Calcd for $C_{22}H_{19}NO_6$): 393.1212, Found 393.1215.

2-Allyl-3-(4-benzyloxy-2-vinylphenyl)-2*H*-isoquinolin-1-one (4a) To a solution of methyltriphenylphosphonium bromide (1.6 g, 4.5 mmol) in dry THF (30 ml) was added *n*-butyllithium (1.8 ml of 2.5 M in hexane, 4.5 mmol) at 0 °C, and the solution was stirred at 0 °C for 1 h. To this mixture was added the aldehyde **11a** (350 mg, 0.9 mmol) in THF (10 ml); the resulting mixture was stirred at room temperature for 1 h, quenched with water, and extracted with ethyl acetate. The combined organic layers were washed with water and brine and dried over sodium sulfate. After removing the solvent, the residue was purified by column chromatography with *n*-hexane–ethyl acetate (3 : 1) to afford the olefin **4a** as a brown oil (281 mg, 79%). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 8.47 (d, 1H), 7.64 (m, 1H), 7.50—7.25 (m, 8H), 7.19 (d, 1H), 6.94 (dd, 1H), 6.50 (dd, J=17.0, 10.0 Hz, 1H), 6.39 (s, 1H), 5.72 (m, 1H), 5.68 (d, J=17.0 Hz, 1H), 5.22 (d, J=10.0 Hz, 1H), 5.14 (s, 2H), 5.01 (m, 1H), 4.81 (m, 2H), 4.08 (m, 1H). EI-MS, *m/z* (%): 393 (M^+, 86). HR-MS-EI (Calcd for $C_{27}H_{23}NO_2$): 393.1729, Found 393.1726.

2-Allyl-6,7-dimethoxy-3-(6-vinylbenzo[1,3]dioxol-5-yl)-2*H*-isoquinolin-1-one (4b) The procedure described for compound **4a** was used with the aldehyde **11b** (88 mg, 0.224 mmol) and methyltriphenylphosphonium bromide (430 mg, 1.12 mmol) and *n*-butyllithium (0.5 ml of 2.5 M in hexane, 1.25 mmol) in dry THF (30 ml) to afford the olefin **4b** as yellow oil (56 mg, 75%). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.80 (s, 1H), 7.11 (s, 1H), 7.08 (s,

1H), 6.71 (s, 1H), 6.43 (dd, J=17.0, 10.0 Hz, 1H), 6.23 (s, 1H), 6.04 (d, 2H), 5.79 (m, 1H), 5.58 (d, J=17.0 Hz, 1H), 5.12 (d, J=10.0 Hz, 1H), 5.01 (d, 1H), 4.84—4.74 (m, 2H), 4.10 (m,1H), 4.01 (s, 3H). 3.95 (s, 3H). EI-MS, m/z (%): 391 (M^+, 88). HR-MS-EI (Calcd for $C_{23}H_{21}NO_5$): 391.1420, Found 391.1422.

3-Benzyloxy-7*H*-benzo[3,4]azepino[1,2-*b*]isoquinolin-9-one (5a) The reaction mixture of compound **4a** (170 mg, 0.43 mmol) and 1st generation Grubbs catalyst (70 mg, 20%) in CH_2Cl_2 (15 ml) was stirred for 2 h at room temperature and filtered off. The filtrate was washed with CH_2Cl_2. The solvent was evaporated off, and the residue was purified by column chromatography on silica gel with *n*-hexane–ethyl acetate (2 : 1) to afford the azepine **5a** as brown needles (104 mg, 66%). mp 187—189 °C (Et_2O). IR (cm^{-1}): 1640 (C=O). ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 8.42 (d, J=8 Hz, 1H), 7.67 (d, J=8.5 Hz, 1H), 761 (t, J=7.5 Hz, 1H), 7.50—7.34 (m, 7H), 7.03 (dd, J=3, 8.7 Hz, 1H), 6.89 (d, J=3 Hz, 1H), 6.82 (d, J=10 Hz, 1H), 6.54 (s, 1H), 6.49—6.44 (m, 1H), 5.74 (dd, J=8, 13.5 Hz, 1H), 5.14 (s, 2H), 3.53 (dd, J=6.5, 13.5 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 161.2, 159.2, 142.6, 137.4, 136.5, 136.3, 134.4, 132.1, 131.2, 129.9, 128.6, 128.1, 127.9, 127.4, 126.2, 125.9, 124.0, 114.9, 114.3, 107.4, 70.1, 39.5. EI-MS, m/z (%): 365 (M^+, 56). HR-MS-EI (Calcd for $C_{25}H_{19}NO_2$): 365.1416, Found 365.1416.

11,12-Dimethoxy-2,3-[1,3-dioxol])-7*H*-benzo[3,4]azepino[1,2-*b*]isoquinolin-9-one (5b) The procedure described for compound **5a** was used with the olefin **4b** (55 mg, 0.14 mmol) and 1st generation Grubbs catalyst (23 mg, 20%) in CH_2Cl_2 (15 ml) to produce the azepine **5b** as brown needles (43 mg, 85%). mp 128—132 °C (Et_2O). ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.79 (s 1H), 7.19 (s, 1H), 6.86 (s, 1H), 6.76 (s, 1H), 6.75 (d, J=9.6 Hz, 1H), 6.48 (s, 1H), 6.44—6.36 (m, 1H), 6.07 (d, J=5.5 Hz, 2H), 5.75 (dd, J=7.5, 13.3 Hz, 1H), 4.02 (s, 3H), 3.98 (s, 3H), 3.49 (dd, J=6.6, 13.2 Hz, 1H). ^{13}C-NMR ($CDCl_3$) δ: 160.3, 153.4, 148.9, 148.2, 147.2, 134.0, 132.1, 130.9, 128.5, 128.5, 128.3, 118.2, 109.3, 108.4, 107.5, 107.0, 105.8, 101.7, 56.1, 56.0, 39.6. EI-MS, m/z (%): 363 (M^+, 69). HR-MS-EI (Calcd for $C_{21}H_{17}NO_5$): 363.1107, Found 363.1105.

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