JOC The Journal of Organic Chemistry

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Iodocyclization of *o*-Alkynylbenzamides Revisited: Formation of Isobenzofuran-1(3*H*)-imines and 1*H*-Isochromen-1-imines Instead of Lactams

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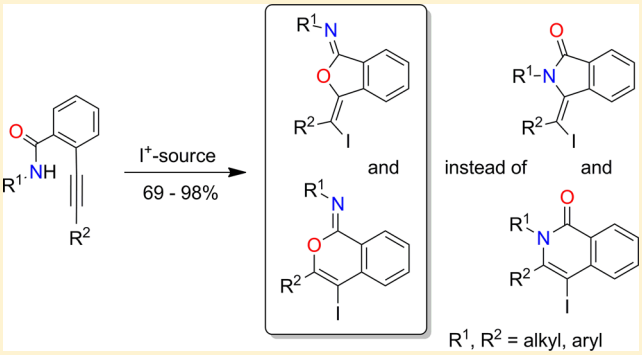
Supporting Information

ABSTRACT: The iodocyclization of *o*-alkynylbenzamides with various electrophiles has been reported to yield five- or six-membered lactams by nucleophilic attack of the amide nitrogen onto the triple bond. While the formation of an isobenzofuran-1(3*H*)-imine with two bulky substituents under Larock conditions was initially attributed to steric hindrance, we found out that cyclization via the amide oxygen is the rule rather than the exception. Thus, the structures of the products reported in the literature need to be revised.



INTRODUCTION

Intramolecular attack of nucleophiles onto triple bonds activated by carbophilic electrophiles such as iodine,[1] interhalogens,[2] arylselenium halides,[3] mercury ions,[4] or gold complexes[5,6] is a powerful and frequently used tool for the construction of five- and six-membered heterocycles.[7−18] As an example, the cyclization of *o*-alkynylbenzamides with iodine or other soft electrophiles published by Larock and co-workers[3] has been reported to furnish either 2-substituted 3-(1-iodoalkylidene)-2,3-dihydro-1*H*-isoindolin-1-ones or 2,3-disubstituted 4-iodoisoquinolin-1(2*H*)-ones. The ratio of the products of a 5-*exo*-dig or a 6-*endo*-dig cyclization strongly depends on the substituents and the reaction conditions.

In a project on the synthesis of metabolically stable glycomimetics, we chose an iodocyclization[19,20] according to Larock[3] as the key step for the rapid construction of diglycosylated heterocycles.[21] More specifically, glycosylacetylenes such as **4** were reacted with *N*-galactosyl-2-iodobenzamides such as **5** in a Sonogashira[22] coupling to furnish the cyclization precursors **1** and **6** (Scheme 1).

Reaction with iodine in MeCN in the presence of $NaHCO_3$ smoothly yielded compounds **3** and **8**, which were initially thought to be the corresponding isoindolinones[21] **2** and **7** as judged by 2D NMR spectroscopy and comparison with literature data.[3] While **3** was an oil, its nitro-substituted derivative **8** gave crystals suitable for X-ray crystallography, and we were surprised to identify the product as an isobenzofuran instead (Figure 1). Highly similar ^{15}N chemical shifts for **3** and **8** (215.1 and 220.2 ppm) inconsistent with a lactam structure indicated that this behavior is not due to the presence of the nitro substituent.

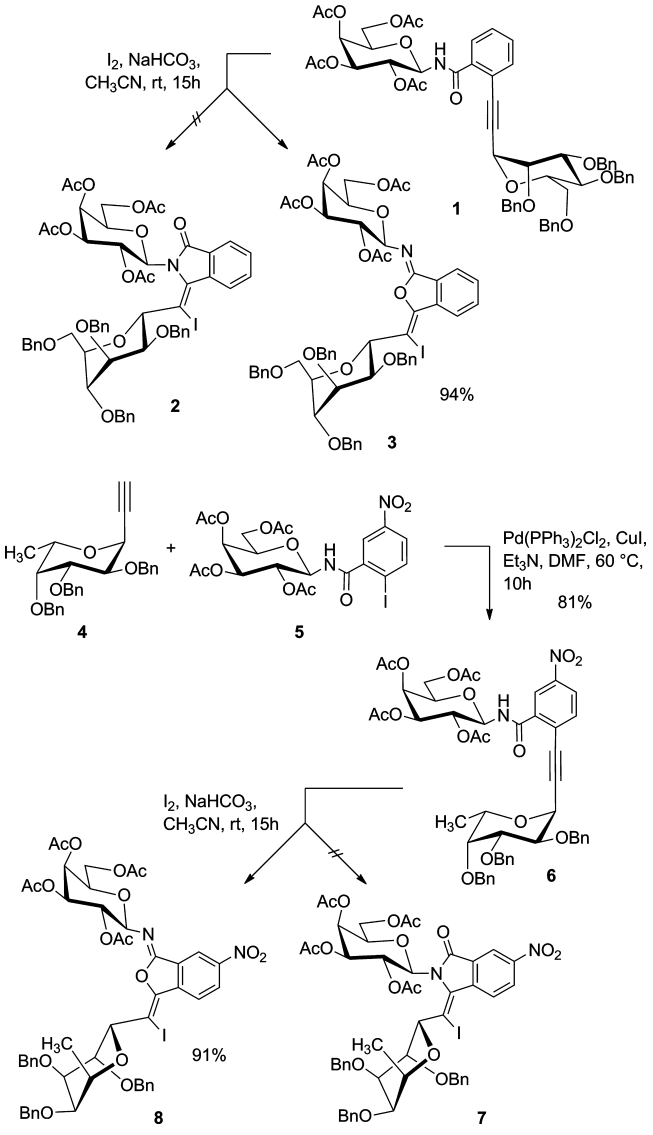
A literature search on products of halocyclizations of alkynes onto amides revealed N-attack to be broadly accepted. However, in the case of bulky backbone substituents[10] or iodocyclizations on olefinic double bonds within conjugated dienoic amides,[23] O-attack was reported. Studies on iodocyclization[24] and Pd-catalyzed cyclization[25] of allenoic amides by Ma and co-workers also showed that sterically demanding groups may favor O- over N-attack. To rule out the two bulky glycosyl residues as the cause for the deviant reactivity of compounds **1** and **6**, we decided to resynthesize one of Larock's isoindolinones for comparison of the characteristic ^{15}N chemical shifts.

RESULTS AND DISCUSSION

(3*E*)-3-[Iodo(phenyl)methylidene]-2-phenyl-2,3-dihydro-1*H*-isoindolin-1-one (**10a**) was prepared according to the published procedure,[3] and crystals were grown for X-ray structural analysis. Again, the compound was found to be an O-cyclized product instead, i.e., (1*Z*,3*E*)-3-[iodo(phenyl)methylidene]-*N*-phenyl-2-benzofuran-1(3*H*)-imine (**11a**; Scheme 2, Figure 2). This was repeated with an identical result for the cyclization of *N*-methyl-2-(phenylethynyl)benzamide (**12**; Scheme 3), in which the small *N*-methyl group was chosen to exclude steric effects as the cause for the observed O/N-selectivity.

Received: August 16, 2012
Published: October 22, 2012

Scheme 1. Attempted Preparation of Diglycosylisoindolinones



To check the identity of the corresponding six-membered products, 2-(cyclohex-1-en-1-ylethynyl)-*N*-phenylbenzamide (**14**) was used as the substrate as a preference for the 6-*endo*-dig cyclization has been observed by Larock and Yao.[3] Both cyclization products **15a** and **15b** could be readily separated by HPLC but were obtained as liquids (Scheme 4).

^{15}N HMBC spectra showed similar chemical shifts for both compounds which were in the same range as those of **8** and **11a** (**11a**, 223.8 ppm; **11b**, 230.0 ppm; **13a**, 209.7 ppm; **15a**, 226.5 ppm; **15b**, 229.1 ppm). NOESY data of **15b** showed only weak contacts between the phenyl and the cyclohexenyl residues, which supports the presence of an isochromene core in this product. The preferential O-attack also in the six-membered series could be unequivocally proven by crystallographic analysis of **11b** and **13b** (Figure 3, Supporting Information).

While the former compound was prepared by the action of ICl on precursor **9** (97% yield, **11a**:**11b** = 56:44), the latter material crystallized as its hydrotriiodide salt. As the spectroscopic data of compounds **11a**, **11b**, **13a**, **15a**, and **15b** match those reported in the literature,[3] the structural

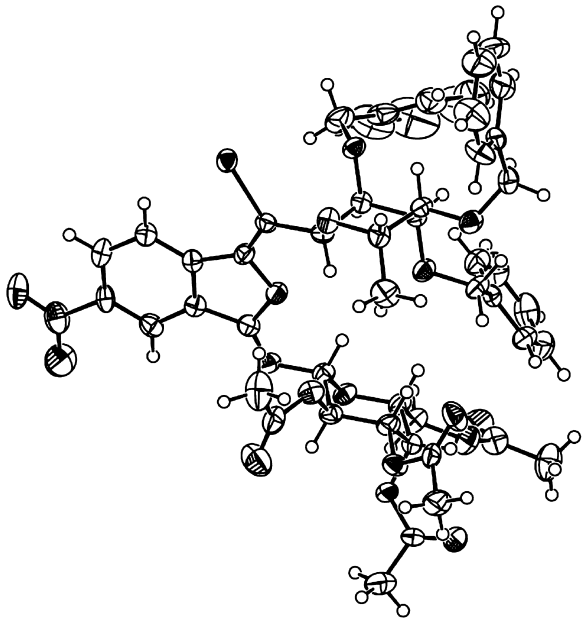
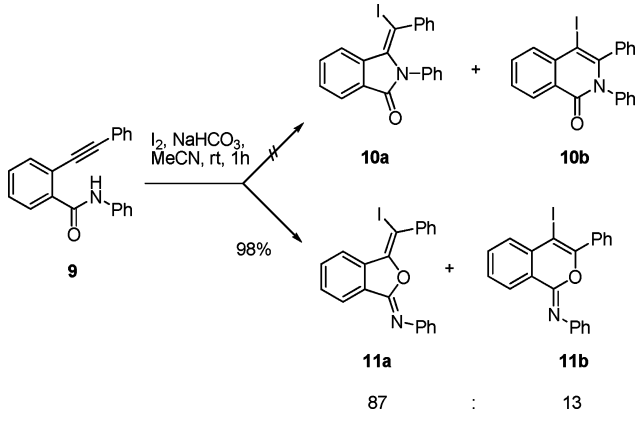


Figure 1. Crystal structure of compound **8** (ORTEP plot).

Scheme 2. Iodocyclization of Compound 9



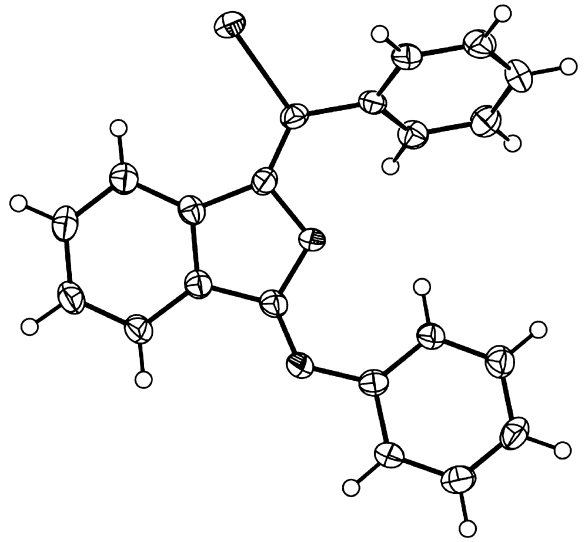
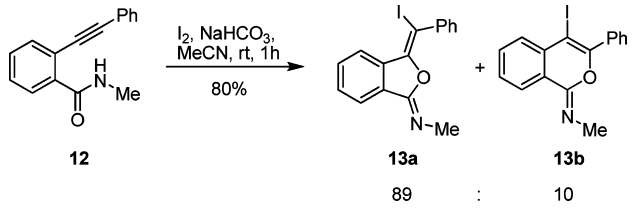


Figure 2. Crystal structure of compound **11a** (ORTEP plot).

dx.doi.org/10.1021/jo3017378 | J. Org. Chem. 2012, 77, 10118−10124

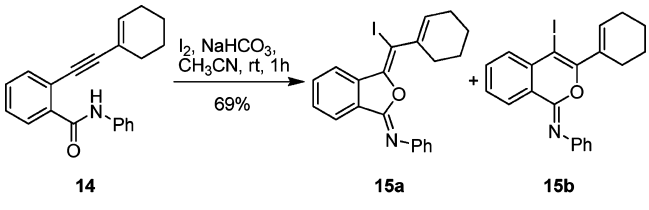
Scheme 3. Iodocyclization of Compound 12



12 13a : 13b

89 : 10

Scheme 4. Iodocyclization of Compound 14



14 15a : 15b

23 : 77

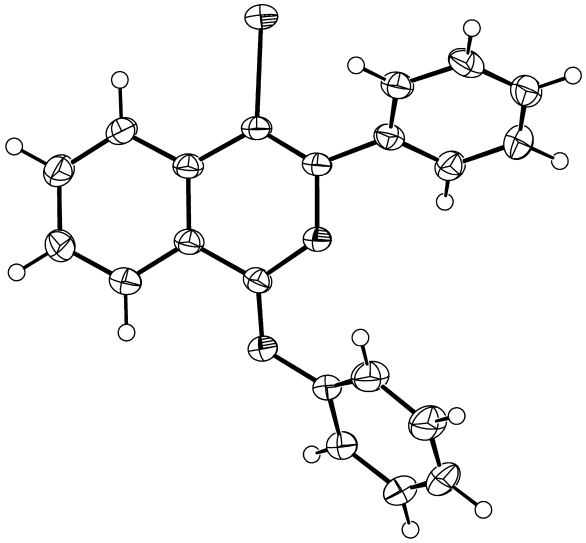


Figure 3. Crystal structure of compound **11b** (ORTEP plot).

revision of similar products, including the glycomimetics published earlier by us, will be necessary.[21]

Since O- and N-attacks have been observed in transition-metal-catalyzed cyclizations of *o*-alkynylbenzamides,[13,18] we became interested in energetic aspects of Larock's iodocyclization. As a system suitable for DFT calculations, we chose bis(collidine)iodonium hexafluorophosphate[26,27] in combination with compound **9** as an electrophile and starting material. The cyclization was performed in CH_2Cl_2 as well as in MeCN to give the two products **11a** and **11b** along with unreacted alkyne. The conversion and the ratio of the five- versus the six-membered ring were determined by ^1H NMR spectroscopy. In the former case, a conversion of 33% (reflux conditions, 16 h) and a ratio of **11a** to **11b** of 10:1 were observed. In the latter case (MeCN), the conversion amounted to 40% and the ratio of the two products was 15:1.

The structure optimizations were performed at the PBE-D3/LACV3P**++ level of theory in the Jaguar 7.9 program package.[28−35] Tolane derivative **9** was used as a model substrate, enabling a direct comparison with experimental results. The use of the cationic iodine source avoids charge separation as would be the case in a neutral substrate−reagent adduct. In the reaction, the iodonium center transfers a positive formal charge to the substrate's carboxamide fragment.

A Curtin−Hammett scenario emerged.[36] The preferred substrate conformation comprises a more favorable interaction of the NH fragment with the alkyne's π-system (Figure 4). The weak interaction of the negatively polarized carbonyl oxygen with the positively polarized aniline *ortho* hydrogen is also energetically more beneficial than the repulsions of the oxygen's lone pair and the alkyne's π-system and of the NH and the *ortho* proton in the alternative conformer.

The exchange of collidine versus alkyne at the iodine cation, presumably being the rate-determining step, leads to a low concentration of an iodine π-complex. The nucleophilic attack of the carbonyl's oxygen and the concerted C−I single bond formation proceed in a remarkably shallow energy hypersurface. The transition states are characterized by C−O distances of 260 ± 15 pm (five-membered cycle) and 298 ± 5 pm (six-membered cycle) with their kinetically controlled C−O bond formation being irreversible. These 5-*exo*-dig and the 6-*endo*-dig processes are both favorable according to Baldwin's rules.[37] The activation energies are equal within the accuracy of the computed scan of C−O distances. As a consequence, the observed product ratios can significantly depend on the solvent and counterion. The nucleophilic attack of an electron lone pair of the carbonyl group features lower barriers than the C−N bond formation pathways, which would lead to thermodynamically more stable isomeric products after eventual deprotonation (Figure 5).

The isoindolone formation is more disfavored than the isoquinolone pathway. The loss of resonance energy renders the C−N formation transition states noncompetitive. Remarkably, considering the transformation of the high-energy alkyne fragment, the respective *N*-acylammonium intermediates plus collidine are thermodynamically less stable than substrate **9** and the iodonium cation. Thus, the hypothetical ammonium intermediates would be extremely strong acids.

CONCLUSION

The iodocyclization of *o*-alkynylbenzamides leads to five-membered and six-membered oxacycles instead of the reported C−N bond formation. Previous investigations on other electrophilic cyclizations of the same reactants revealed the formation of lactones.[4,9] Lactones could also be obtained from the cyclic imidates described herein by acid hydrolysis of the exocyclic C=N bond, while the exergonic rearrangement of the iodocyclization products to the corresponding lactams was observed neither under acidic nor under basic conditions. DFT model calculations find a Curtin−Hammett scenario of a more stable, yet unreactive, conformer with an NH fragment oriented toward the alkyne. Favored C−O bond formation pathways are also predicted computationally, featuring a concerted formation of a C−I single bond.

EXPERIMENTAL SECTION

General Procedure for Preparation of the *o*-(1-Alkynyl)-benzamides.[3] To a solution of the corresponding organic iodide (1.0 mmol) and the terminal alkyne (1.2 mmol, 1.2 equiv) in Et_3N (4.00 mL) were added $PdCl_2(PPh_3)_2$ (1.40 mg, 2 mol %) and CuI (2.00 mg, 1 mol %). The resulting mixture was then heated under an argon atmosphere at 55 °C. The reaction was monitored by TLC to establish completion. When the reaction was complete, the mixture was allowed to cool to room temperature, and the reaction mixture was diluted with ethyl acetate (20.0 mL) and water (10.0 mL). The organic phase was washed twice with water (10.0 mL), dried over Na_2SO_4, and

dx.doi.org/10.1021/jo3017378 | J. Org. Chem. 2012, 77, 10118−10124

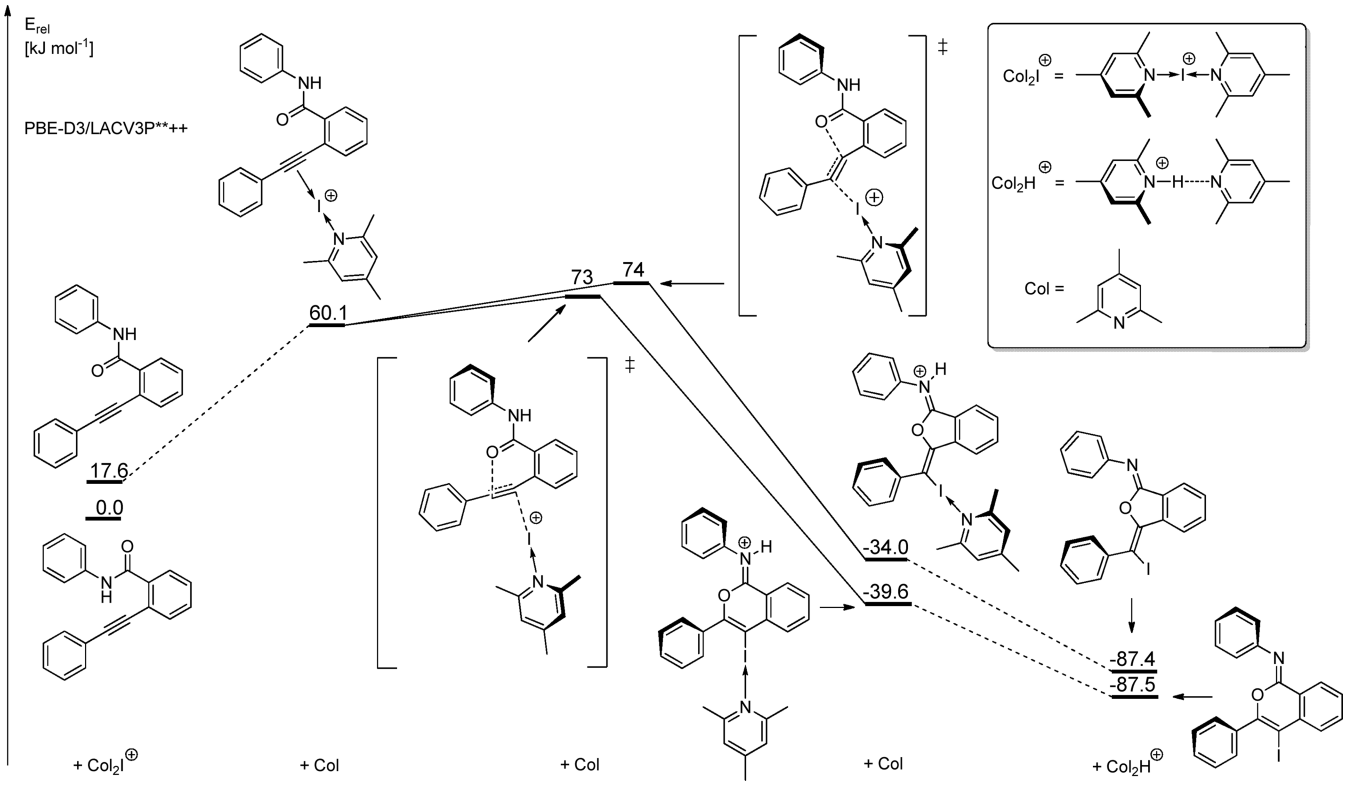


Figure 4. DFT energies for the iodocyclization onto amide oxygen.

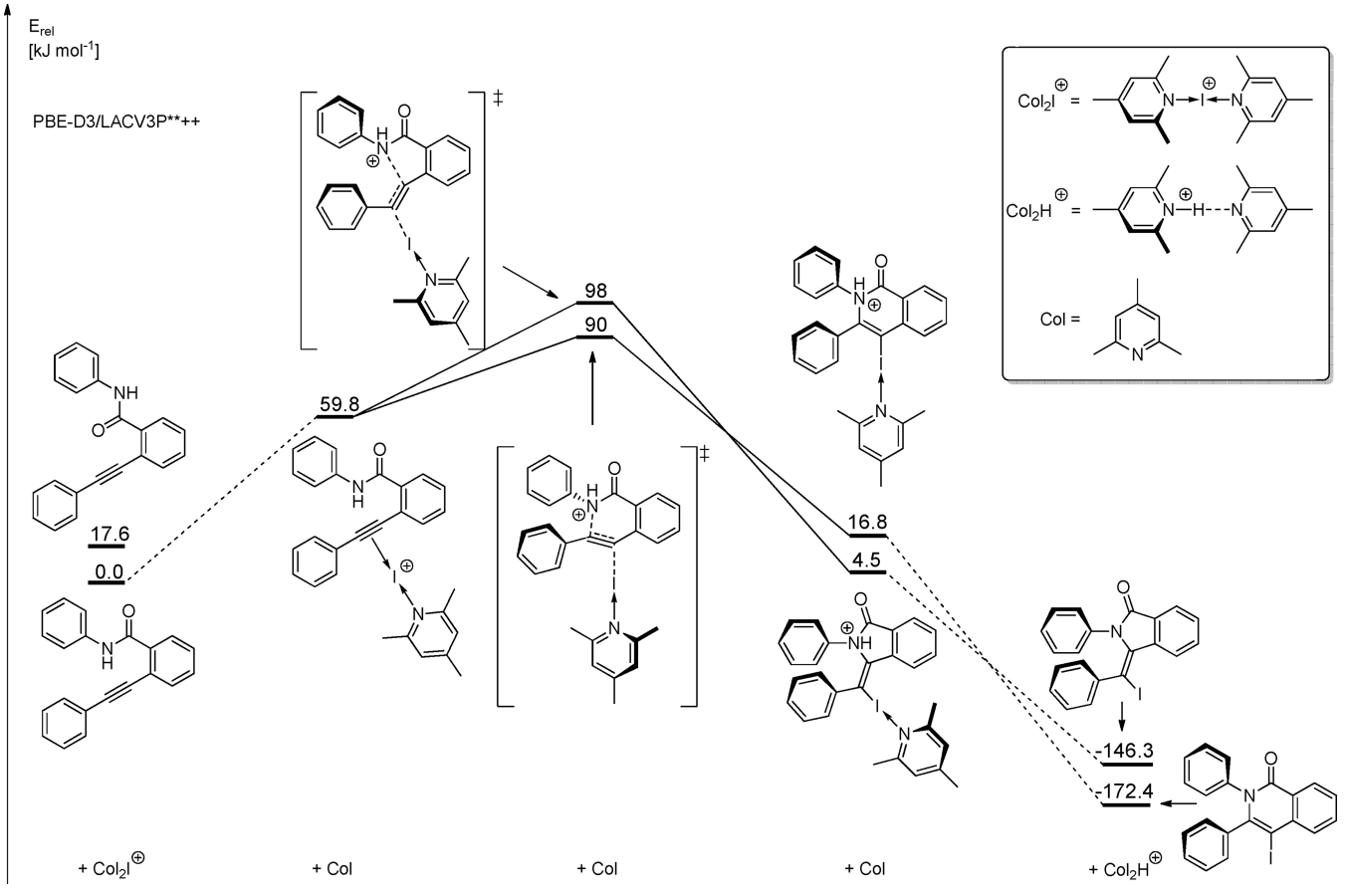


Figure 5. DFT energies for the (hypothetical) iodocyclization onto amide nitrogen.

dx.doi.org/10.1021/jo3017378 | J. Org. Chem. 2012, 77, 10118−10124

filtered, the solvent was removed under reduced pressure, and the residue was purified by flash column chromatography on silica gel to afford the corresponding *o*-(1-alkynyl)benzamide.

General Procedure for Electrophilic Cyclization of the *o*-(1-Alkynyl)benzamides by I_2.[3] The alkynylarenecarboxamide (0.30 mmol), I_2 (3.0 equiv), $NaHCO_3$ (3.0 equiv), and CH_3CN (3.00 mL) were placed in a Schlenk flask and flushed with argon. The reaction mixture was stirred at room temperature for 1 h unless otherwise indicated. The reaction mixture was then diluted with ether (50.0 mL), washed with satd aq $Na_2S_2O_3$ (25.0 mL), dried over Na_2SO_4, and filtered. The solvent was evaporated under reduced pressure, and the product was isolated by chromatography on a silica gel column or HPLC.

General Procedure for Electrophilic Cyclization of the *o*-(1-Alkynyl)benzamides by ICl.[3] The alkynylarenecarboxamide (0.30 mmol) was placed into a Schlenk flask and dissolved in CH_2Cl_2 (3.00 mL) in an argon atmosphere. A solution of ICl (1.2 equiv) in CH_2Cl_2 (0.50 mL) was added dropwise to the flask by a syringe. The reaction was stirred at room temperature for 30 min unless otherwise indicated. The reaction mixture was then diluted with ether (50.0 mL), washed with satd aq $Na_2S_2O_3$ (25.0 mL), dried over Na_2SO_4, and filtered. The solvent was evaporated under reduced pressure, and the product was isolated by chromatography on a silica gel column.

***N*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-2-ethynyl-*C*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)benzamide (1).**[21] Purification by flash chromatography (eluent cyclohexane/EtOAc, 2:1) afforded the title compound (199 mg, 76%) as a colorless oil: $[\alpha]_D^{22}$ = +15.7 (*c* = 1.00, $CHCl_3$); ^{1}H NMR, COSY (400 MHz, $CDCl_3$) δ = 7.44−7.20 (m, 24H, Ph, H-3^{ar}, H-4^{ar}, H-5^{ar}, H-6^{ar}), 7.17−7.19 (m, 1H, NH), 5.37 (pseudo-t, 1H, ^3J = 9.2 Hz, H-1^{gal}), 5.31 (dd, 1H, $^3J_{3,4}$ = 3.4 Hz, $^3J_{4,5}$ = 0.8 Hz, H-4^{gal}), 5.18 (dd, 1H, $^3J_{1,2}$ = 9.2 Hz, $^3J_{2,3}$ = 10.3 Hz, H-2^{gal}), 5.15 (d, 1H, $^3J_{1,2}$ = 2.1 Hz, H-1^{man}), 5.09 (dd, 1H, $^3J_{2,3}$ = 10.3 Hz, $^3J_{3,4}$ = 3.4 Hz, H-3^{gal}), 4.92 (d, 1H, ^2J = 10.6 Hz, CH_2Ph), 4.81 (d, 1H, ^2J = 12.6 Hz, CH_2Ph), 4.77−4.71 (m, 3H, CH_2Ph), 4.68 (d, 1H, ^2J = 12.0 Hz, CH_2Ph), 4.58 (d, 1H, ^2J = 10.6 Hz, CH_2Ph), 4.56 (d, 1H, ^2J = 12.0 Hz, CH_2Ph), 4.26 (dd, 1H, $^3J_{3,4}$ = 9.3 Hz, $^3J_{2,3}$ = 2.9 Hz, H-3^{man}), 4.11 (pseudo-t, 1H, $^3J_{3,4}$ = 9.3 Hz, $^3J_{4,5}$ = 9.6 Hz, H-4^{man}), 4.05−4.01 (m, 4H, H-6a^{gal}, H-6b^{gal}, H-5-^{man}, H-2-^{man}), 3.88 (dd, 1H, $^3J_{5,6}$ = 4.4 Hz, ^3J = 10.9 Hz, H-6a^{man}), 3.78 (dd, 1H, $^3J_{5,6}$ = 1.3 Hz, ^2J = 10.9 Hz, H-6b^{man}), 3.69 (dt, 1H, $^3J_{4,5}$ = 0.8 Hz, H-5^{gal}), 2.06, 2.01, 2.00, 1.98 (4 × s, 4 × 3H, CH_3^{acetyl}) ppm; ^{13}C NMR, HSQC (101 MHz, $CDCl_3$) δ = 171.3, 170.4, 170.1, 169.8 (4 × C=O^{acetyl}), 169.6 (C=O^{amide}), 138.7, 138.6, 138.5, 138.2 (4 × C_qPh), 134.2 (C-1), 129.1 (C-2), 128.4, 128.3, 128.2, 128.1, 128.0, 127.8, 127.7, 127.6, 127.5, 127.4 (C-3^{ar}, C-4^{ar}, C-5^{ar}, C-6^{ar}, CPh), 90.3 (C^{alkyne}-man), 83.2 (C^{alkyne}-ar), 80.6 (C-3^{man}), 79.2 (C-1^{gal}), 77.4 (C-5^{man}), 75.5 (CH_2Ph), 75.4 (C-2^{man}), 75.1 (C-4^{man}), 73.6 (CH_2Ph), 72.5 (C-5^{gal}), 72.2 (CH_2Ph), 71.9 (CH_2Ph), 71.1 (C-3^{gal}), 69.7 (C-6^{man}), 68.7 (C-2^{gal}), 67.4 (C-4^{gal}), 67.0 (C-1^{man}), 61.2 (C-6^{gal}), 20.7, 20.6, 20.5, 20.4 (4 × CH_3^{acetyl}) ppm; ESI-HRMS *m*/*z* calcd for $C_{57}H_{60}NO_{15}$ 998.3963, found 998.3965.

(1*Z*,3*E*)-3-[Iodo(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)methylidene]-*N*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-2-benzofuran-1(3*H*)-imine (3).[21] After flash chromatography (eluent cyclohexane/EtOAc, 2:1) the title compound (202 mg, 94%) was isolated as a colorless oil: $[\alpha]_D^{22}$ = +32.1 (*c* = 1.00, $CHCl_3$); ^{1}H NMR, COSY, NOESY (400 MHz, $CDCl_3$) δ = 8.79 (d, 1H, $^3J_{3,4}$ = 8.1 Hz, H-3), 7.99 (d, 1H, $^3J_{5,6}$ = 7.7 Hz, H-6), 7.67 (pseudo-t, 1H, $^3J_{4,3}$ = 8.1 Hz, $^3J_{4,5}$ = 7.4 Hz, H-4), 7.58 (pseudo-t, 1H, $^3J_{4,5}$ = 7.4 Hz, $^3J_{5,6}$ = 7.7 Hz, H-5), 7.36−7.09 (m, 20H, Ph), 5.34−5.28 (m, 2H, H-2^{gal}, H-4^{gal}), 5.27 (d, 1H, $^3J_{1,2}$ = 8.5 Hz, H-1^{gal}), 5.09 (d, 1H, $^3J_{1,2}$ = 9.1 Hz, H-1^{man}), 5.05 (dd, 1H, $^3J_{2,3}$ = 9.4 Hz, $^3J_{3,4}$ = 3.3 Hz, H-3^{gal}), 4.66−4.58 (m, 4H, CH_2Ph), 4.54 (d, 1H, ^2J = 12.5 Hz, CH_2Ph), 4.45−4.32 (m, 4H, 3 × CH_2Ph, H-5 ^{man}), 4.12−4.08 (m, 2H, H-6a^{gal}, H-6a^{man}), 4.05−3.99 (m, 3H, H-2^{man}, H-3^{man}, H-6b^{man}), 3.97 (dd, 1H, $^3J_{6b,5}$ = 6.8 Hz, ^2J = 10.3 Hz, H-6b^{gal}), 3.83 (dd, 1H, $^3J_{3,4}$ = 2.9 Hz, $^3J_{4,5}$ = 1.8 Hz, H-4^{man}), 3.57 (t, 1H, $^3J_{5,6}$ = 6.5 Hz, H-5^{gal}), 2.14, 1.99, 1.91, 1.58 (4 × s, 4 × 3H, CH_3^{acetyl}) ppm; ^{13}C NMR, HSQC, HMBC (101 MHz, $CDCl_3$) δ = 170.4, 170.3, 169.9, 169.8 (4 × C=O^{acetyl}), 155.9 (C-1), 150.2 (C-3), 138.4, 138.3, 138.2, 138.0 (4 × C_qPh), 135.7 (C-3a), 132.5 (C-5), 131.5 (C-7a), 131.2 (C-6), 128.5, 128.4, 128.4, 128.2, 127.9, 127.9, 127.8, 127.8, 127.7, 127.6, 127.4 (CPh), 124.9 (C-4), 124.7 (C-7), 85.7 (C-I), 81.7 (C-1^{gal}), 77.1 (C-2^{man}), 75.0 (C-5^{man}), 74.7 (C-4^{man}), 73.1 (C-3^{man}), 72.9 (CH_2Ph), 72.4 (C-5^{gal}), 71.9 (CH_2Ph), 71.7 (CH_2Ph), 71.6 (C-3^{gal}), 69.9 (C-2^{gal}), 68.8 (C-6^{man}), 68.4 (C-1^{man}), 67.6 (C-4^{gal}), 61.9 (C-6^{gal}), 20.9, 20.8, 20.7, 20.4 (4 × s, 4 × 3H, CH_3^{acetyl}) ppm; ^{15}N HMBC (600/61 MHz, $CDCl_3$) δ = 215.1 (C=N) ppm; ESI-HRMS *m*/*z* calcd for $C_{57}H_{58}INO_{15}Na$ 1146.2749, found 1146.2758

(2,3,4-Tri-*O*-benzyl-α-L-fucopyranosyl)acetylene (4).[21] Purification by flash chromatography (eluent toluene/EtOAc, 30:1) afforded the title compound (3.72 g, 91%) as a colorless oil: $[\alpha]_D^{20}$ = −129.3 (*c* = 1.00, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.24−7.39 (m, 15H, Ph), 4.96 (d, 1H, ^2J = 11.5 Hz, CH_2Ph), 4.87 (d, 1H, ^2J = 11.8 Hz, CH_2Ph), 4.69−4.79 (m, 4H, H-1, 3 × CH_2Ph), 4.63 (d, 1H, ^2J = 11.5 Hz, CH_2Ph), 4.07 (dd, 1H $^3J_{2,1}$ = 5.8 Hz, $^3J_{2,3}$ = 9.9 Hz, H-2), 4.02 (qd, 1H, $^3J_{5,4}$ = 1.2 Hz, $^3J_{5,6}$ = 6.4 Hz, H-5), 3.87 (dd, 1H, $^3J_{3,4}$ = 2.8 Hz, $^3J_{3,2}$ = 9.9 Hz, H-3), 3.64 (dd, 1H, $^3J_{4,5}$ = 1.2 Hz, $^3J_{4,3}$ = 2.8 Hz, H-4), 2.47 (d, 1H, $^4J_{C\equiv CH,1}$ = 2.3 Hz, C≡CH), 1.13 (d, 3H, $^3J_{6,5}$ = 6.4 Hz, H-6) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ = 139.1, 138.8, 138.5 (3 × C_qPh), 128.7, 128.6, 128.4, 128.2, 127.9, 127.8, 127.73, 127.70 (CPh), 80.8 (C-3), 79.6 (C≡CH), 77.8 (C-4), 76.0 (C≡CH), 75.3 (C-2), 75.2, 73.6, 73.4 (CH_2Ph), 70.0 (C-5), 67.3 (C-1), 17.1 (C-6) ppm; IR (ATR) ν (cm^{-1}) = 3287, 2924, 1652, 1454, 1073; ESI-HRMS *m*/*z* calcd for $C_{29}H_{30}O_4Na$ 465.2036, found 465.2036.

2-Iodo-5-nitro-*N*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)benzamide (5). 2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosylamine (1.01 g, 2.91 mmol) was dissolved in anhydrous THF (20.0 mL). To this solution was added *N*-ethylmorpholine (0.46 mL, 1.05 equiv), and the resulting mixture was stirred for 10 min. 2-Iodo-5-nitrobenzoic acid chloride (1.18 g, 1.03 equiv)[38] was dissolved in anhydrous THF (10.0 mL) and precooled to 0 °C before addition of the above mixture. After complete addition the reaction was stirred for an additional 30 min. The hydrochloride was filtered off and washed with THF. The resulting solution was concentrated under reduced pressure, and the crude product was purified by flash chromatography (eluent EtOAc/cylohexane, 3:1) to give the product (1.58 g, 87%) as a yellow foam: $[\alpha]_D^{22}$ = +16.3 (*c* = 1.00, $CHCl_3$); ^{1}H NMR, COSY (400 MHz, $CDCl_3$) δ = 8.15 (d, 1H, $^4J_{4,6}$ = 2.6 Hz, H-6), 8.11 (d, 1H, $^3J_{3,4}$ = 8.7 Hz, H-3), 7.96 (dd, 1H, $^3J_{3,4}$ = 8.7 Hz, $^4J_{4,6}$ = 2.6 Hz, H-4), 6.76 (d, 1H, $^3J_{NH,1}$ = 9.0 Hz, NH), 5.48 (d, 1H, $^3J_{3,4}$ = 2.3 Hz, H-4^{gal}), 5.41 (pseudo-t, 1H, $^3J_{1,2}$ = $^3J_{1,NH}$ = 9.0 Hz, H-1^{gal}), 5.22−5.15 (m, 2H, H-2^{gal}, H-3^{gal}), 4.19−4.10 (m, 3H, H-6$_{a/b}$^{gal}, H-5^{gal}), 2.15, 2.14, 2.06, 2.01 (4 × s, 4 × 3H, CH_3^{acetyl}) ppm; ^{13}C NMR, HSQC (101 MHz, $CDCl_3$) δ = 171.7, 170.5, 170.1, 169.9 (4 × C=O^{acetyl}), 167.2 (C=O^{amide}), 147.9 (C-5), 142.1 (C-1), 141.8 (C-3), 125.8 (C-4), 122.5 (C-6), 100.9 (C-2), 78.9 (C-1^{gal}), 72.7 (C-5^{gal}), 70.8 (C-3^{gal}), 68.5 (C-2^{gal}), 67.1 (C-4^{gal}), 61.1 (C-6^{gal}), 21.3, 20.8, 20.7, 20.6 (4 × CH_3^{acetyl}) ppm; IR (ATR) ν (cm^{-1}) = 3021, 1747, 1694, 1526, 1368, 1351, 1214, 1053, 745; ESI-HRMS *m*/*z* calcd for $C_{21}H_{23}IN_2O_{12}Na$ 645.0193, found 645.0204.

***N*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-2-ethynyl-*C*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-5-nitrobenzamide (6).** 2-Iodo-5-nitro-*N*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-benzamide (1.17 g, 1.88 mmol) was dissolved in anhydrous DMF (33.0 mL) together with bis(triphenylphosphine)palladium(II) chloride (3.8 mol %) and copper(I) iodide (7.2 mol %). To this solution as added dropwise anhydrous Et_3N (1.83 mL), and the reaction mixture was stirred for 1 h at room temperature. Then 2-*C*-(2,3,4,6-tetra-*O*-benzyl-α-L-fucopyranosyl)acetylene (1.2 equiv) dissolved in anhydrous DMF (33.0 mL) was added, and the solution was warmed to 60 °C and stirred at this temperature overnight.[39] The resulting dark brown mixture was coevaporated twice with toluene (30.0 mL). The crude product was redissolved in $CHCl_3$, washed with water (3 × 30.0 mL), dried over anhydrous Na_2SO_4, and concentrated in vacuo. The residue was purified by flash chromatography (eluent cylohexane/EtOAc, 3:1) to afford the product (1.43 g, 81%) as a green oil: $[\alpha]_D^{22}$ = −105.1 (*c* = 1.00, $CHCl_3$); ^{1}H NMR, COSY, NOESY (500 MHz, $CDCl_3$) δ = 8.79 (d, 1H, $^4J_{2,4}$ = 2.4 Hz, H-2), 8.25 (dd, 1H, $^3J_{4,5}$ = 8.5 Hz, $^4J_{2,4}$ = 2.4 Hz, H-4), 7.98 (d, 1H, $^3J_{NH,1}$ = 8.9 Hz, NH), 7.60

dx.doi.org/10.1021/jo3017378 | J. Org. Chem. 2012, 77, 10118−10124

(d, 1H, $^3J_{4,5}$ = 8.5 Hz, H-5), 7.41−7.39 (m, 3H, Ph), 7.36−7.28 (m, 12H, Ph), 5.44 (d, 1H, $^3J_{3,4}$ = 3.3 Hz, H-4^{gal}), 5.43 (pseudo-t, 1H, $^3J_{1,NH}$ = $^3J_{1,2}$ = 9.3 Hz, H-1^{gal}), 5.23 (pseudo-t, 1H, $^3J_{1,2}$ = $^3J_{2,3}$ = 9.8 Hz, H-2^{gal}), 5.21 (d, 1H, $^3J_{1,2}$ = 5.9 Hz, H-1^{fuc}), 5.15 (dd, 1H, $^3J_{2,3}$ = 10.1 Hz, $^3J_{3,4}$ = 3.3 Hz, H-3^{gal}), 4.99 (d, 1H, ^2J = 11.5 Hz, CH_2Ph), 4.88 (d, 1H, ^2J = 12.0 Hz, CH_2Ph), 4.85 (d, 1H, ^2J = 11.9 Hz, CH_2Ph), 4.82 (d, 1H, ^2J = 12.0 Hz, CH_2Ph), 4.78 (d, 1H, ^2J = 11.9 Hz, CH_2Ph), 4.66 (d, 1H, ^2J = 11.5 Hz, CH_2Ph), 4.22, (dd, 1H, $^3J_{1,2}$ = 5.9 Hz, $^3J_{2,3}$ = 9.8 Hz, H-2^{fuc}), 4.14−4.02 (m, 4H, H-5^{fuc}, H-5^{gal}, 2 × H-6^{gal}), 3.97 (dd, 1H, $^3J_{2,3}$ = 9.8 Hz, $^3J_{3,4}$ = 2.7 Hz, H-3^{fuc}), 3.75 (d, 1H, $^3J_{3,4}$ = 2.7 Hz, H-4^{fuc}), 2.06, 2.02, 1.99, 1.96 (4 × s, 4 × 3H, CH_3^{acetyl}), 1.23 (d, 3H, $^3J_{5,CH3}$ = 6.4 Hz, CH_3^{fuc}) ppm; ^{13}C NMR, HSQC, HMBC (126 MHz, $CDCl_3$) δ = 171.0, 170.5, 170.3, 169.9 (4 × C=O^{acetyl}), 164.3 (C=O^{amide}), 147.3 (C-3), 138.8, 138.5, 138.4 (3 × C_qPh), 135.9 (C-1), 135.7 (C-5), 128.6, 128.5, 128.4, 128.0, 127.9, 127.8, 127.7, 127.6 (CPh), 126.6 (C-6), 125.6 (C-4), 124.9 (C-2), 98.8 (C^{alkyne}-fuc), 83.8 (C^{alkyne}-ar), 80.5 (C-3^{fuc}), 79.5 (C-1^{gal}), 77.4 (C-4^{fuc}), 75.3 (C-2^{fuc}), 75.1, 73.2, 73.0 (3 × CH_2Ph), 72.9 (C-5^{fuc}), 71.0 (C-5^{gal}), 70.8 (C-3^{gal}), 68.4 (C-2^{gal}), 68.0 (C-1^{fuc}), 67.2 (C-4^{gal}), 61.2 (C-6^{gal}), 20.8, 20.7, 20.7, 20.6 (4 × CH_3^{acetyl}), 17.1 (CH_3^{fuc}) ppm; IR (ATR) ν (cm^{-1}) = 3400, 3019, 2360, 1748, 1682, 1523, 1368, 1345, 1216, 746; ESI-HRMS m/z calcd for $C_{50}H_{52}N_2O_{16}Na$ 959.3215, found 959.3223.

(1*Z*,3*E*)-3-[Iodo(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-methylidene]-*N*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-6-nitro-2-benzofuran-1(3*H*)-imine (8). Purification of the product by flash chromatography (eluent cyclohexane/EtOAc, 3:1) afforded the title compound (508 mg, 91%) as yellow crystals: mp 160.5−162.7 °C; $[\alpha]_D^{22}$ = +70.8 (c = 1.00, $CHCl_3$); ^{1}H NMR, COSY, NOESY (400 MHz, $CDCl_3$) δ = 8.95 (d, 1H, $^3J_{4,5}$ = 8.8 Hz, H-4), 8.79, (d, 1H, $^4J_{5,7}$ = 1.9 Hz, H-7), 8.48 (dd, 1H, $^3J_{4,5}$ = 8.8 Hz, $^4J_{5,7}$ = 1.9 Hz, H-5), 7.44−7.29 (m, 10H, Ph), 7.22−7.19 (m, 2H, *o*-Ph(C-3^{fuc})), 7.09−7.06 (m, 2H, *m*-Ph(C-3^{fuc})), 7.02−6.98 (m, 1H, *p*-Ph(C-3^{fuc})), 5.21 (dd, 1H, $^3J_{1,2}$ = 8.6 Hz, $^3J_{2,3}$ = 10.1 Hz, H-2^{gal}), 5.15 (d, 1H, $^3J_{1,2}$ = 2.0 Hz, H-1^{fuc}), 5.09−5.08 (m, 1H, H-4^{gal}), 4.99 (d, 1H, $^3J_{1,2}$ = 8.6 Hz, H-1^{gal}), 4.92 (d, 1H, ^2J = 12.9 Hz, CH_2Ph), 4.78 (d, 1H, ^2J = 12.9 Hz, CH_2Ph), 4.76 (dd, 1H, $^3J_{2,3}$ = 10.1 Hz, $^3J_{3,4}$ = 3.4 Hz, H-3^{gal}), 4.66 (d, 1H, ^2J = 11.9 Hz, CH_2Ph), 4.59 (d, 1H, ^2J = 11.9 Hz, CH_2Ph), 4.55 (d, 1H, ^2J = 12.2 Hz, CH_2Ph), 4.50 (m, 1H, H-5^{fuc}), 4.39 (d, 1H, ^2J = 12.2 Hz, CH_2Ph), 4.11 (dd, 1H, $^3J_{3,4}$ = 3.1 Hz, $^3J_{4,5}$ = 5.9 Hz, H-4^{fuc}), 4.08−4.03 (m, 2H, H-6a/b^{gal}), 4.00 (pseudo-t, 1H , $^3J_{2,3}$ = $^3J_{3,4}$ = 3.3 Hz, H-3^{fuc}), 3.89 (dd, 1H, $^3J_{1,2}$ = 2.0 Hz, $^3J_{2,3}$ = 3.4 Hz, H-2^{fuc}), 3.02−2.98 (m, 1H, H-5^{gal}), 2.14, 2.08, 1.97, 1.79 (4 × s, 4 × 3H, CH_3^{acetyl}), 1.64 (d, 3H, $^3J_{5,6}$ = 6.8 Hz, H-6^{fuc}) ppm; ^{13}C NMR, HSQC, HMBC (101 MHz, $CDCl_3$) δ = 170.4, 170.2, 169.9, 169.3 (4 × C=O^{acetyl}), 153.5 (C-1), 149.2 (C-3),145.0 (C-6) 139.9 (C-3a), 139.1, 138.4, 137.1 (3 × C_qPh), 132.2 (C-7a), 128.9, 128.8, 128.6, 128.3, 128.0, 127.9, 127.8, 127.5, 127.1 (CPh), 127.2 (C-5) 125.5 (C-4), 119.9 (C-7), 87.8 (C-I), 86.0 (C-1^{gal}), 78.0 (C-2^{fuc}), 75.6 (C-3^{fuc}), 74.6 (C-4^{fuc}), 73.4 (CH_2Ph), 73.3 (CH_2Ph), 72.0 (CH_2Ph), 71.9 (C-5^{gal}), 71.8 (C-5^{fuc}), 70.9 (C-3^{gal}), 70.3 (C-2^{gal}), 67.3 (C-4^{gal}), 64.4 (C-1^{fuc}), 61.8 (C-6^{gal}), 20.9, 20.8, 20.7, 20.6 (4 × s, 4 × 3H, CH_3^{acetyl}), 13.8 (C-6^{fuc}) ppm; ^{15}N HMBC (600/61 MHz, $CDCl_3$) δ = 220.2 (C=N), 363.7 (NO_2) ppm; IR (ATR) ν (cm^{-1}) = 1747, 1710, 1615, 1216, 747; ESI-HRMS m/z calcd for $C_{50}H_{51}IN_2O_{16}Na$ 1085.2181, found 1085.2220.

***N*-Phenyl-2-(phenylethynyl)benzamide (9).** Recrystallization from ethyl acetate gave 3.22 g (69%) of the product as colorless crystals with spectral properties identical to those previously reported: mp 154.4−156.6 °C (lit.[39] mp 151.0−153.0 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.21 (br s, 1H, NH), 8.16−8.13 (m, 1H), 7.68−7.64 (m, 3H), 7.52−7.47 (m, 4H), 7.41−7.32 (m, 5H), 7.14 (t, 1H, J = 7.4 Hz).

(1*Z*,3*E*)-3-[Iodo(phenyl)methylidene]-*N*-phenyl-2-benzofuran-1(3*H*)-imine (11a). Purification by flash chromatography (eluent petroleum ether/EtOAc, 30:1) afforded 1.19 g (54%) of the product as yellow crystals with spectral properties identical to those previously reported (additionally, we assigned the ^{13}C shift of 75.1 ppm to the quaternary carbon connected to the double bond, originally reported as missing): mp 96.0−97.0 °C (lit.[3] mp 97.0−99.0 °C); ^{1}H NMR, COSY (600 MHz, $CDCl_3$) δ = 8.89 (d, 1H, $^3J_{4,5}$ = 7.8 Hz, H-4), 8.08 (d, 1H, $^3J_{6,7}$ = 7.7 Hz, H-7), 7.73 (t, 1H, $^3J_{4,5}$ = $^3J_{5,6}$ = 7.8 Hz, H-5), 7.68−7.62 (m, 3H, H-6, 2 × *o*-Ph), 7.40−7.38 (m, 4H, 2 × *m*-Ph, 2 × *o*-Anil), 7.32 (t, 1H, $^3J_{m,p}$ = 7.3 Hz, *p*-Ph), 7.29−7.26 (m, 2H, 2 × *m*-Anil), 7.13 (t, 1H, $^3J_{m,p}$ = 7.3 Hz, *p*-Anil) ppm; ^{13}C NMR, HSQC, HMBC (151 MHz, $CDCl_3$) δ = 151.9 (C-1), 147.6 (C-3), 144.8 (C-1^{Anil}), 140.4 (C-1^{Ph}), 135.6 (C-3a), 132.5 (C-7a), 131.9 (C-5), 130.7 (C-6), 130.3 (C-2^{Ph}), 128.6 (C-3^{Anil}), 128.5 (C-4^{Ph}), 127.9 (C-3^{Ph}), 125.3 (C-4^{Anil}), 125.0 (C-4), 124.9 (C-2^{Anil}), 123.9 (C-7), 75.1 (C-I) ppm; ^{15}N HMBC (600/61 MHz, $CDCl_3$) δ = 223.8 ppm; IR (ATR) ν (cm^{-1}) = 1681, 1589, 1007, 745; ESI-HRMS m/z calcd for $C_{21}H_{15}INO$ 424.0198, found 424.0205.

(1*Z*)-4-Iodo-*N*,3-diphenyl-1*H*-isochromen-1-imine (11b). After purification by flash chromatography (eluent petroleum ether/EtOAC, 30:1) 948 mg (43%) of the product was obtained as yellow crystals with spectral properties identical to those reported previously (additionally, we assigned the ^{13}C shift of 75.8 ppm to the quaternary carbon connected to the double bond, originally reported as missing): mp 132.8−134.2 °C (lit.[3] mp 131.0−132.0 °C); ^{1}H NMR, COSY (600 MHz, $CDCl_3$) δ = 8.40 (dd, 1H, $^3J_{7,8}$ = 7.9 Hz, $^4J_{6,8}$ = 1.0 Hz, H-8), 7.76 (dd. 1H, $^3J_{5,6}$ = 7.9 Hz, $^4J_{5,7}$ = 0.7 Hz, H-5), 7.64 (td, 1H, $^3J_{5,6}$ = $^3J_{6,7}$ = 7.9 Hz, $^4J_{6,8}$ = 1.0 Hz, H-6), 7.61−7.60 (m, 2H, 2 × *o*-Ph), 7.49 (td, 1H, $^3J_{6,7}$ = $^3J_{7,8}$ = 7.9 Hz, $^4J_{5,7}$ = 0.7 Hz, H-7), 7.42−7.38 (m, 3H, 2 × *m*-Ph, *o*-Ph), 7.32−7.29 (m, 2H, 2 × *m*-Anil), 7.23−7.22 (m, 2H, *o*-Anil), 7.07 (t, 1H, $^3J_{m,p}$ = 7.4 Hz, *p*-Anil) ppm; ^{13}C NMR, HSQC, HMBC (151 MHz, $CDCl_3$) δ = 153.2 (C-3), 148.6 (C-1), 145.9 (C-1^{Anil}), 135.4 (C-1^{Ph}), 134.8 (C-4a), 133.1 (C-6), 131.1 (C-5), 130.0 (C-2^{Ph}), 130.0 (C-4^{Ph}), 129.3 (C-7), 128.7 (C-3^{Anil}), 128.0 (C-3^{Ph}), 127.5 (C-8), 123.9 (C-4^{Anil}), 123.8 (C-8a), 122.9 (C-2^{Anil}), 75.8 (C-I) ppm; ^{15}N HMBC (600/61 MHz, $CDCl_3$) δ = 230.0 ppm; IR (ATR) ν (cm^{-1}) = 1655, 1590, 1085, 693.

***N*-Methyl-2-(phenylethynyl)benzamide (12).** After flash chromatography (eluent cyclohexane/EtOAc, 2:1) the product (439 mg, 97%) could be obtained as colorless crystals with spectral properties identical to those previously reported: mp 106.9−107.6 °C (lit.[40] mp 105.0−107.0 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.04−7.99 (m, 1H), 7.59−7.55 (m, 1H), 7.53−7.49 (m, 2H), 7.44−7.40 (m, 2H), 7.39−7.37 (m, 3H), 7.33 (br s, 1H, NH), 3.06 (d, 3H, $^3J_{CH_3,NH}$ = 4.9 Hz) ppm.

(1*Z*,3*E*)-3-[Iodo(phenyl)methylidene]-*N*-methyl-2-benzofuran-1(3*H*)-imine (13a). Purification by flash chromatography (eluent petroleum ether/EtOAc, 7:1) afforded the product (220 mg, 72%) as light yellow crystals with spectral properties identical to those reported previously: mp 126.5−129.3 °C (lit.[3] mp 122.0−125.0 °C); ^{1}H NMR, COSY, NOESY (600 MHz, $CDCl_3$) δ = 8.82 (d, 1H, $^3J_{4,5}$ = 7.9 Hz, H-4), 7.85 (d, 1H, $^3J_{6,7}$ = 7.6 Hz, H-7), 7.64−7.62 (m, 3H, H-5, 2 × *o*-Ph), 7.54 (td, 1H, $^3J_{5,6}$ = $^3J_{6,7}$ = 7.6 Hz, $^4J_{4,6}$ = 0.5 Hz, H-6), 7.40−7.37 (m, 2H, 2 × *m*-Ph), 7.28 (t, 1H, $^3J_{m,p}$ = 7.4 Hz, *p*-Ph), 3.16 (s, 3H, CH_3) ppm; ^{13}C NMR, HSQC, HMBC (151 MHz, $CDCl_3$) δ = 154.6 (C-1), 147.2 (C-3), 140.6 (C-1^{Ph}), 135.9 (C-3a), 131.8 (C-7a), 131.2 (C-5), 130.6 (C-6), 130.2 (C-2^{Ph}), 128.3 (C-4^{Ph}), 127.9 (C-3^{Ph}), 124.9 (C-4), 122.9 (C-7), 73.4 (C-I), 35.1 (CH_3) ppm; ^{15}N HMBC (600/61 MHz) δ = 209.7 ppm; IR (ATR) ν (cm^{-1}) = 1708, 1613, 1020, 759; ESI-HRMS m/z calcd for $C_{16}H_{13}INO$ 362.0042, found 362.0056.

(1*Z*)-4-Iodo-*N*-methyl-3-phenyl-1*H*-isochromen-1-imine (13b).[3] Purification by flash chromatography (eluent petroleum ether/EtOAc, 7:1) afforded the product (26.0 mg, 8%) as a yellow solid. Crystals suitable for X-ray formed with I_3^- as the counterion: ^{1}H NMR, COSY, NOESY (600 MHz, $CDCl_3$) δ = 8.12 (d, 1H, $^3J_{8,7}$ = 8.9 Hz, H-8), 7.69−7.68 (m, 3H, H-5, 2 × *o*-Ph), 7.56 (t, 1H, $^3J_{5,6}$ = $^3J_{6,7}$ = 8.9 Hz, H-6), 7.49−7.45 (m, 3H, 2 × *m*-Ph, *p*-Ph), 7.40 (t, 1H, $^3J_{6,7}$ = $^3J_{7,8}$ = 8.9 Hz, H-7), 3.17 (s, 3H, CH_3) ppm; ^{13}C NMR, HSQC, HMBC (151 MHz, $CDCl_3$) δ = 153.4 (C-3), 150.8 (C-1), 136.2 (C-1^{Ph}), 133.9 (C-4a), 132.4 (C-6), 131.2 (C-5), 129.9 (C-4^{Ph}), 129.9 (C-2^{Ph}), 129.1 (C-7), 128.2 (C-3^{Ph}), 126.3 (C-8), 123.9 (C-8a), 75.5 (C-I), 33.8 (CH_3) ppm; ^{15}N HMBC (600/61 MHz) δ = 282.6 ppm; IR (ATR) ν (cm^{-1}) = 1662, 1602, 1078, 754.

2-(Cyclohex-1-en-1-ylethynyl)-*N*-phenylbenzamide (14). Purification by HPLC (eluent isocratic MeCN/H_2O, 95:5) afforded the product (189 mg, 41%) as yellow crystals with spectral properties identical to those previously reported: mp 97.0−98.3 °C (lit.[3] mp 99.0−100.0 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.33 (br s, 1H,

dx.doi.org/10.1021/jo3017378 | J. Org. Chem. 2012, 77, 10118−10124

NH), 8.17−8.14 (m, 1H), 7.69−7.67 (m, 2H), 7.55−7.52 (m, 1H), 7.47−7.42 (m, 2H), 7.39−7.35 (m, 2H), 7.16−7.12 (m, 1H), 6.29−6.28 (m, 1H), 2.21−2.14 (m, 4H), 1.70−1.58 (m, 4H) ppm.

(1*Z*,3*E*)-3-[Cyclohex-1-en-1-yl(iodo)methylidene]-*N*-phenyl-2-benzofuran-1(3*H*)-imine (15a). Purification by HPLC (eluent MeCN/H_2O, 90:10, to 100% MeCN) afforded the product (32.5 mg, 16%) as a yellow oil with spectral properties identical to those previously reported:[3] ^{1}H NMR, COSY, NOESY (600 MHz, $CDCl_3$) δ = 7.97−7.95 (m, 1H, H-7), 7.79−7.77 (m, 1H, H-4), 7.67−7.65 (m, 2H), 7.51−7.49 (m, 2H, H-5, H-6), 7.42−7.39 (m, 2H, *m*-Ph) 7.19 (t, 1H, $^3J_{m,p}$ = 7.3 Hz, *p*-Ph), 6.11−6.10 (m, 1H, H-2^{CyH}), 2.33−2.26 (m, 2H, H-6^{CyH}), 2.18−2.17 (m, 2H, H-3^{CyH}), 1.86−1.82 (m, 2H, H-5^{CyH}), 1.75−1.71 (m, 2H, H-4^{CyH}) ppm; ^{13}C NMR, HSQC, HMBC (151 MHz, $CDCl_3$) δ = 152.2 (C-1), 149.6 (C-3), 144.9 (C-1^{Anil}), 136.7 (C-1^{CyH}), 133.8 (C-3a), 132.7 (C-7a), 132.1 (C-5), 130.7 (C-2^{CyH}), 129.8 (C-6), 128.9 (C-3^{Anil}), 125.4 (C-4^{Anil}), 125.2 (C-2^{Anil}); 124.0 (C-7), 122.5 (C-4), 81.7 (C-I), 27.9 (C-6^{CyH}), 25.9 (C-3^{CyH}), 22.7 (C-5^{CyH}), 21.9 (C-4^{CyH}) ppm; ^{15}N HMBC (600/61 MHz) δ = 226.5 ppm; IR (ATR) ν (cm^{-1}) = 1687, 1651, 1006, 749; ESI-HRMS *m*/*z* calcd for $C_{21}H_{19}INO$ 428.0511, found 428.0505.

(1*Z*)-3-(Cyclohex-1-en-1-yl)-4-iodo-*N*-phenyl-1*H*-isochromen-1-imine (15b). Purification by HPLC (eluent MeCN/H_2O, 90:10, to 100% MeCN) afforded the product (115 mg, 53%) as a yellow oil with spectral properties identical to those previously reported:[3] ^{1}H NMR, COSY, NOESY (600 MHz, $CDCl_3$) δ = 8.33 (dd, 1H, $^3J_{7,8}$ = 7.9 Hz, $^4J_{6,8}$ = 0.8 Hz, H-8), 7.66 (d, 1H, $^3J_{5,6}$ = 7.9 Hz, H-5), 7.58 (td, 1H, $^3J_{5,6}$ = $^3J_{6,7}$ = 7.9 Hz, $^4J_{6,8}$ = 0.8 Hz, H-6), 7.43 (td, 1H, $^3J_{6,7}$ = $^3J_{7,8}$ = 7.9 Hz, $^4J_{5,7}$ = 0.5 Hz, H-7), 7.37−7.35 (m, 2H, 2 × *m*-Ph), 7.21−7.20 (m, 2H, 2 × *o*-Ph), 7.11 (t, 1H, $^3J_{m,p}$ = 7.4 Hz, *p*-Ph), 6.16−6.15 (m, 1H, H-1^{CyH}), 2.20−2.18 (m, 2H, H-3^{CyH}), 2.17−2.16 (m, 2H, H-6^{CyH}), 1.71−1.67 (m, 2H, H-5^{CyH}), 1.65−1.61 (m, 2H, H-4^{CyH}) ppm; ^{13}C NMR, HSQC, HMBC (151 MHz, $CDCl_3$) δ = 155.6 (C-3), 148.9 (C-1), 146.1 (C-1^{Anil}), 135.2 (C-2^{CyH}), 134.9 (C-4a), 133.7 (C-1^{CyH}), 132.9 (C-6), 131.3 (C-5), 128.7 (C-7), 128.6 (C-3^{Anil}), 127.4 (C-8), 123.8(C-4^{Anil}), 123.7 (C-8a), 122.9 (C-2^{Anil}), 73.9 (C-I), 26.4 (C-3^{CyH}), 25.0 (C-6^{CyH}), 22.3 (C-5^{CyH}), 21.6 (C-4^{CyH}) ppm; ^{15}N HMBC (600/61 MHz) δ = 229.1 ppm; IR (ATR) ν (cm^{-1}) = 1652, 1591, 1025, 755; ESI-HRMS *m*/*z* calcd for $C_{21}H_{19}INO$ 428.0511, found 428.0497.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

General methods, spectra for all compounds, final energies and coordinates from DFT calculations, and crystallographic information files (CIFs) of **8**, **11a**, **11b**, **13a**, and **13b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank Dr. J. C. Liermann (University of Mainz) for NMR spectroscopy and Prof. Paul Margaretha (University of Hamburg) for helpful discussions. This work was supported by the German Federal Ministry for Education and Research (T.O., Grant 0315139).

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■ NOTE ADDED IN PROOF

After the submission of our manuscript, a related paper was submitted by Larock and coworkers. Mehta, S.; Yao, T.; Larock, R. C. *J. Org. Chem.* doi:10.1021/jo301958q.