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Nickel-Catalyzed Electrochemical Cyclization of Alkynyl Aryl Iodide and the Domino Reaction with Aldehydes

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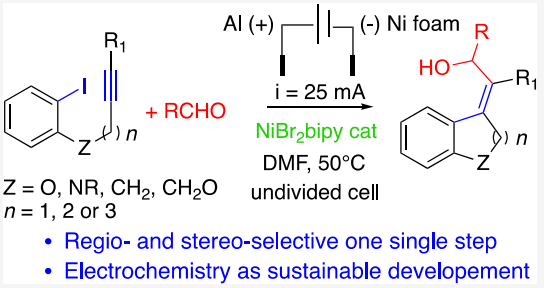
ABSTRACT: An intramolecular carbometallation of a triple bond promoted by electrochemistry and mediated by nickel catalysis is described. This domino process transforms various aryl halides bearing a propargyl chain into substituted heterocycles in one single operation, with high stereoselectivities and in good to high yields. This reaction, characterized by a cyclic voltammetry set of experiments, proceeds following a *syn-exo-dig* cyclization process. When run at 80 °C, vinylbenzofuranes that are suitable substrates for cycloaddition reactions are obtained.



INTRODUCTION

Indisputably, metal-catalyzed coupling reactions are, and now for years, one of the best ways to complete efficient syntheses of multifunctionalized scaffolds.[1] A typical catalytic cycle involves an unstable low-valent metal that is generally prepared in situ from salts of higher oxidation states to be reacted with a large excess of a reducing agent. But low-valent metals can also be generated by electrochemical reduction. Thus, the pioneering works by Périchon et al. in 1980 reported interesting results of electrosynthesis using a sacrificial anode process.[2] Combining this technique with nickel catalysis, some of us have described electrochemical processes allowing cross-coupling reactions based on the in situ generation of Ni(0). In particular, we have developed several processes, relying on the Ni(0)bipy system (resulting from the reduction of $NiBr_2$bipy), and this catalyst has been shown to be reactive toward an aryl or vinyl halide.[3] The recent revival of electrosynthesis,[4] likely to be related to the development of easy-to-handle commercial apparatus, has prompted us to re-explore the possibilities opened by this methodology.[5] Our first results are presented below.

Polycyclic oxygen or nitrogen heterocycles are found in numerous natural products or valuable building blocks, as illustrated in Figure 1. Because they give an effective access to carbon−carbon bonds,[6] carbometallation reactions can be regarded as a perfect showcase. The transition-metal-catalyzed functionalization of alkynes, which seems to be an easy-to-adapt transformation, is an attractive, possibly stereoselective transformation that provides substituted alkenes. In addition to carbolithiation[7] and carbomagnesation,[8] palladium has been widely used in recent decades to carry out this type of reaction.[9] The results presented underneath suggest that a nickel-based electrochemical system can afford a sustainable while competitive catalytic method, helping to clear large-scale

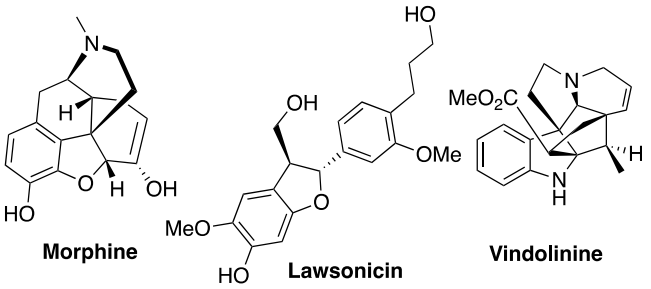


Figure 1. Representative polycyclic oxygen or nitrogen heterocycles found in natural products.

industrial processes from a rare and expensive metal, nowadays a societal requisite.[10]

We previously described the carbonickelation of alkynes followed by direct functionalization of the resulting vinylnickel, catalyzed by $NiBr_2$bipy. This handy process affords substituted dihydrobenzofurans, (iso)chromans, indoles, or indanes, in good to high yields from aryl iodides and a variety of electrophiles.[11] While our original protocol relied on the chemical reduction of stable Ni(II) complexes by Mn(0),[12] it appeared even simpler and certainly "cleaner" to us to use just electrons to generate Ni(0). This "minimal" and inexpensive reductant can indeed be regarded as a perfect alternative to manganese, avoiding metal powders and extra salt contami-

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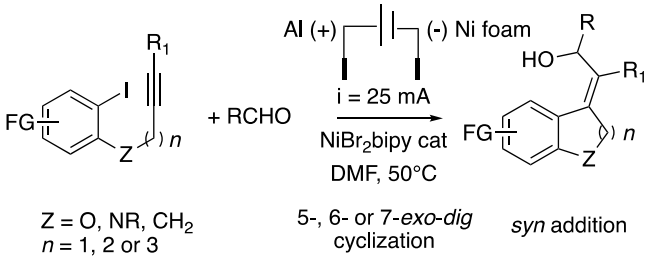
nation. If this attractive scenario casts relatively little doubt on the electrogeneration of the arylnickel intermediate, two key questions remain (i) will this elusive reagent be able to perform the cyclization step in the electrochemical conditions and (ii) will the second step of the domino process take place, that is will the transient vinylnickel react with the electrophile while avoiding its dimerization?

We present underneath our investigation on this nickel-catalyzed electroreductive intramolecular carbonickelation reaction, as well as its domino version, leading to various substituted heterocycles (Scheme 1). We also detail the

Scheme 1. Nickel-Catalyzed Electroreductive Intramolecular Carbonickelation Reaction Followed by a Barbier-Type Addition on Aldehydes



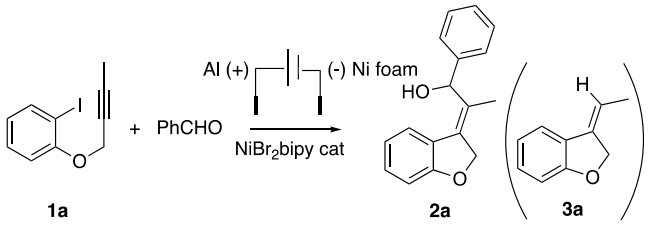
efficiency and scope of this procedure. In addition, the use of a simple nickel complex in an undivided cell, with a sacrificial anode, led us to expect an easy, cheap, little toxic, and innovative process.

RESULTS AND DISCUSSION

At first, different parameters such as the anode, the temperature, the intensity, and the solvent were studied; the results are reported in Table 1.

The optimization was run with aryl iodide **1a**,[11] which bears a simple propargyl chain, and benzaldehyde. Dimethylformamide (DMF), which is generally used when $NiBr_2$bipy is the catalyst,[11,12] immediately gave a very good result: the expected alcohol **2a**, resulting from the domino process cyclization + nucleophilic addition of the vinylnickel intermediate to benzaldehyde, was recovered in 90% isolated yields, provided the reaction was performed at 50 °C and a constant current of 25 mA (Table 1, entry 3). However, running the reaction at 50 or 100 mA revealed that some starting material was left unconsumed, and the time was too short for the cyclized vinylnickel intermediate to be added to benzaldehyde, as evidenced by significant amounts of vinylH **3a** recovered (Table 1, entries 1 and 2). At room temperature, the second step again seemed to slow down, and the current had to be decreased to 15 mA to obtain a complete conversion and, finally, to wait 15 min after electrolysis to obtain good yield of alcohol **2a** (Table 1, entries 4 and 5). Replacement of DMF by other solvents gave poor results, even in a mixture with DMF (Table 1, entries 6−9). Finally, we found that an aluminum rod provides the best anode (Table 1, entries 3−5), and resorting to Zn instead of Al slows down the process and **1a** is not fully consumed at 2 F/mol, probably because a competitive Zn^{2+} reduction occurs during the Ni(II) catalytic cycle (Table 1, entry 10). The same observation was made with a Ni anode (Table 1, entry 11). Finally, it is interesting to note that the reaction can take place under air instead of argon, although a lower yield is obtained, probably due to the loss of the catalyst

Table 1. Optimization of the Intramolecular Electrochemical Carbonickelation and Functionalization of 1a[a]



entry	solvent	i (mA)	T (°C)	anode	**2a** (%)[b]
1	DMF	100	50	Al	30[c]
2	DMF	50	50	Al	45[d]
3	DMF	25	50	Al	95 (90)
4	DMF	25	r.t.	Al	69[e]
5	DMF	15	r.t.	Al	93[f]
6	EtOH/DMF 9:1	25	50	Al	[g]
7	MeCN/DMF 4:1	25	50	Al	
8	THF	25	50	Al	
9	NMP	25	50	Al	33
10	DMF	25	50	Zn	53[h]
11	DMF	25	50	Ni	56[h]
12	DMF[i]	25	50	Al	62 (48)

[a]Reaction conditions unless otherwise specified: **1a** (1 mmol), PhCHO (1.3 mmol), $NiBr_2$bipy (0.10 mmol), NBu_4BF_4 (0.15 mmol), and DMF (5 mL). Electrolysis was run under argon, at constant current intensity until the aromatic halide was totally consumed (2 F/mol). [b]NMR yields, based on the initial aryl iodide **1a**. Isolated yields in brackets. [c]26% of the starting material and 44% of vinylH **3a** is recovered at the end of electrolysis. [d]15% of the starting material and 40% of **3a** is recovered at the end of electrolysis. [e]15% of the starting material and 15% of **3a** is recovered at the end of electrolysis. [f]Reaction is stirred 15 min after the end of electrolysis. [g]Acetal of benzaldehyde is recovered with the starting material. [h]15% of the starting material and 30% of **3a** are recovered at the end of electrolysis. [i]Reaction is run under air.

during electrolysis. This experimental study led us to apply the following typical procedure: electrolysis was run in a one-compartment cell fitted with nickel sponge (area ca. 2 cm^2) as a cathode and an aluminum plate as the anode. NBu_4BF_4 (0.15 equiv, 0.15 mmol, supporting electrolyte) was dissolved in 5 mL of dry DMF under argon atmosphere, and then $NiBr_2$bipy (0.10 equiv, 0.10 mmol), aryl iodide **1** (1.0 equiv, 1.0 mmol), and aldehyde (1.3 equiv, 1.3 mmol) were added. Electrolysis was run at 50 °C with an oil bath, under argon, at a constant current intensity of 25 mA until the aromatic halide **1** was totally consumed (2 F/mol, ∼2 h 15 min).

This process was applied to various aryl iodides **1a−h**, easily prepared from commercially available iodophenol, iodobenzoic acid, or iodobenzyl bromide.[11] Results for the tandem process with benzaldehyde are given in Table 2. In all cases, the conversion is complete in 2 F/mol (ca. 2 h 15 min), and the selectivity of the carbonickelation is totally in favor of *exo-dig syn*-addition, whatever the size of the ring (5-, 6-, or 7-membered). Moreover, the postfunctionalization is efficient, and the alcohols are obtained in good to excellent yields. Unfortunately, our isolated yields sometimes look inferior, due to the dehydration reaction and rearomatization during the purification on silica gel or alumina column chromatography. We have then studied the influence of the nature of the link between the aryl and the triple bond. Here again, moderate to

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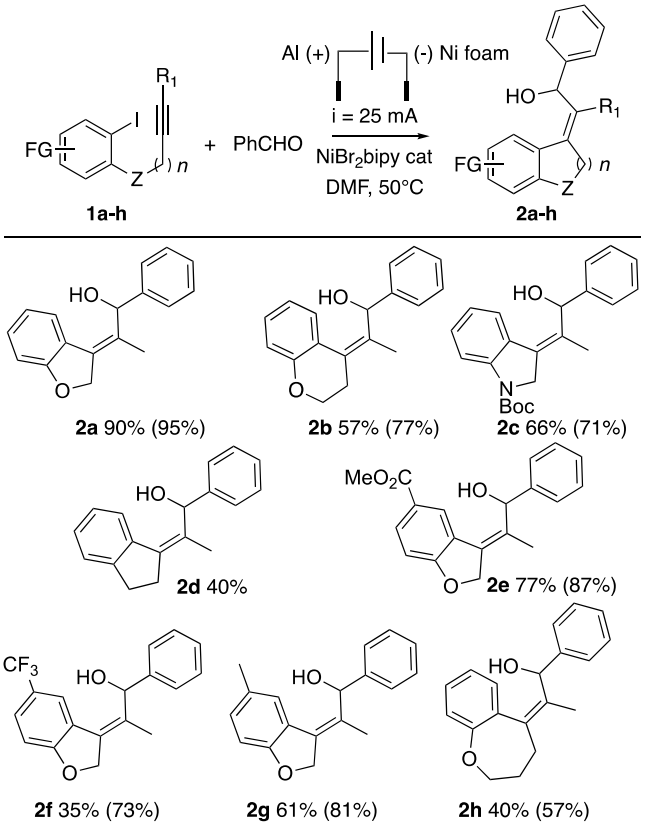
Table 2. Scope of the Electrochemical Carbonickelation of Aryl Iodides 1a–h in the Presence of Benzaldehyde[a]



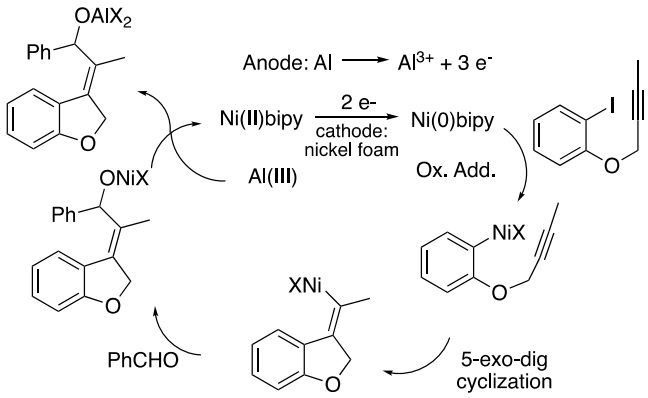
[a]Reaction conditions: **1a–h** (1 mmol), benzaldehyde (1.3 mmol), $NiBr_2$bipy (10 mol %), DMF (5mL), 50 °C, *i* = 25 mA, and 2 h 15 min. Yields of isolated products are given. NMR yields with respect to an internal standard based on the initial aryl iodide **1** are given within brackets.

good yields were obtained in the same experimental conditions, from the corresponding all-carbon (**2d**, Table 2) or nitrogenated (**2c**) alkynes. Note that the reaction tolerates electron-donating (**2g**) or -withdrawing (**2e,f**) substituents on the aromatic ring and remains highly chemoselective even in the presence of an ester group. We next checked whether this process could be scaled up. The reaction was performed on 4 mmol of the easily accessible substrate **1a**, using 5 mmol of benzaldehyde in 10 mL of DMF. To diminish the reaction time, the electrolysis was run at 50 mA, always with 2F/mol. Finally, alcohol **2a** was isolated in 69% isolated yield (75% NMR yield) after ≈4 h 30 min.

To explain the catalytic amount of the nickel salt in the case of this domino sequence cyclization/nucleophilic addition onto carbonyl, we propose the mechanism depicted in Scheme 2. The first likely step is the in situ generation of Ni(0) by reduction of nickel(II) at the cathode at −1.15 V/SCE.[13] After oxidative addition, the arylnickel intermediate reacts with the triple bond and triggers a stereoselective cyclization.[11] The nucleophilic addition of the resulting vinylnickel to benzaldehyde occurs, leading to the nickel alkoxide. Then, the nickel alkoxide transmetallates with Al(III) coming from the oxidation of the anode[14] releasing the nickel(II) salt, which can be reduced another time.

A cyclic voltammetry study was launched to support our mechanistic hypotheses. CV experiments were carried out in a

Scheme 2. Proposed Catalytic Cycle



0.1 M solution of *n*-NBu_4Br used as the supporting electrolyte in DMF at room temperature. The cyclic voltammograms of $NiBr_2$bipy in the absence and presence of 1 equiv of ArI **1a**, as obtained on a gold microelectrode at 200 mV/s, are given in Figure 2. By itself, the nickel(II) complex shows a quasi-

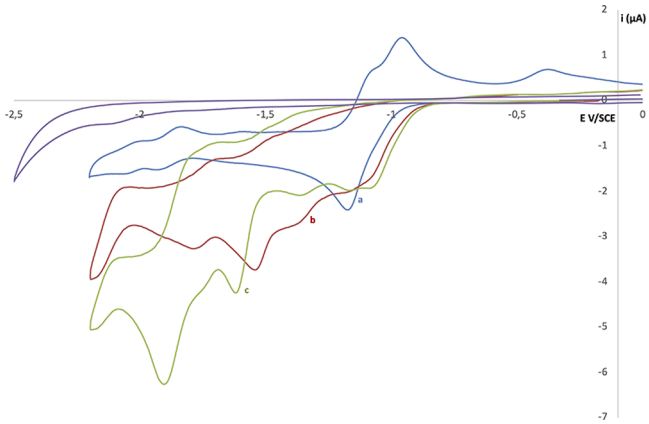


Figure 2. Cyclic voltammograms in DMF + 0.1 M NBu_4Br, at a gold disc microelectrode (0.25 mm diameter) at *v* = 0.2 V/s and at r.t (purple curve) of (a) 10^{-2} M $NiBr_2$bipy (blue curve), (b) 10^{-2} M $NiBr_2$bipy + 1 molar equiv of ArI **1a** (red curve), and (c) 10^{-2} M $NiBr_2$bipy + 1 molar equiv of ArI **1a** + 1.5 equiv of benzaldehyde (green curve).

reversible reduction system in DMF at −1.15 V/SCE, with the consumption of two electrons, giving Ni(0)bipy, which is then further reduced at −1.9 V/SCE to Ni(0)bipy^{-} (blue curve).[13b] In the presence of **1a**, an oxidative addition of electrogenerated Ni(0) to the aryl halide occurs, leading to a *σ*-arylnickel(II) entity, which can be reduced to ArNi(I) either at −1.35 or −1.5 V/SCE, depending on the complexation state[13a] (red curve). Simultaneously, the Ni(II) reduction occurs earlier, in agreement with a chemical reaction succeeding the electrochemical one, and the reoxidation of Ni(0) no longer takes place (EC mechanism). The addition of benzaldehyde modifies the curve again: the two peaks corresponding to the arylnickel(II) reduction disappear and a new system appears at −1.6 V/SCE, in addition to the reduction of benzaldehyde at −1.9 V/SCE (green curve).

The scope of this sequence is also defined by the variety of electrophiles that it can encompass. The results in Table 3 show the reactivity of aryl iodide **1a** toward various aldehydes. It turns out that the process is efficient, whatever the

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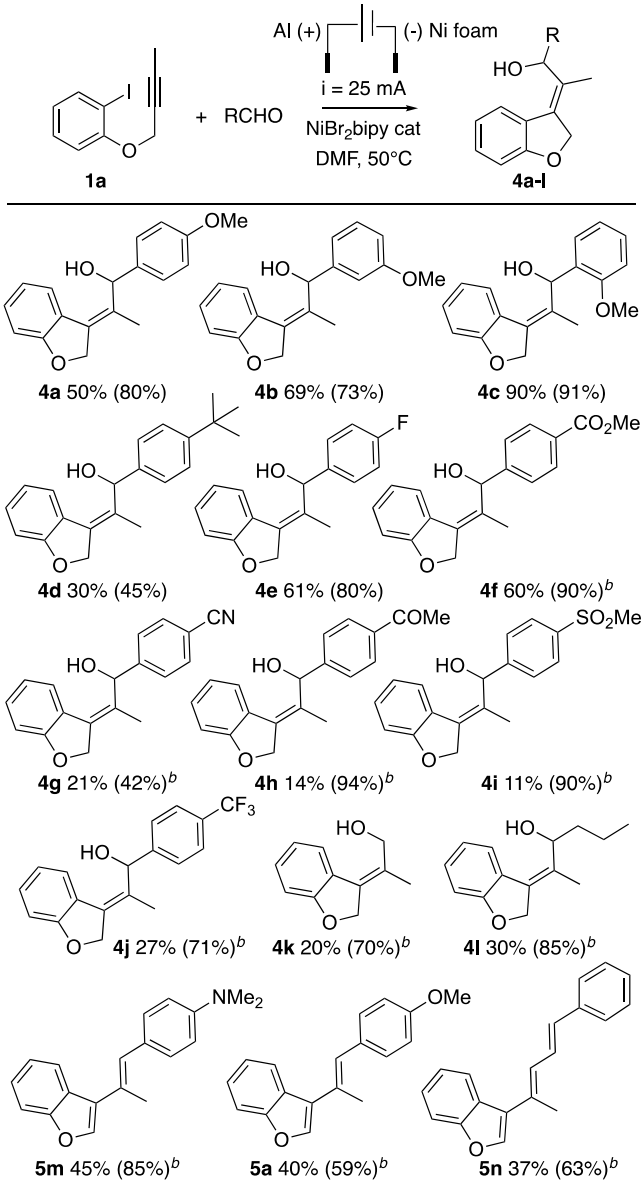
Table 3. Electrochemical Nickel-Catalyzed Cyclization of Iodoaryl 1a in the Presence of Various Aldehydes[a]



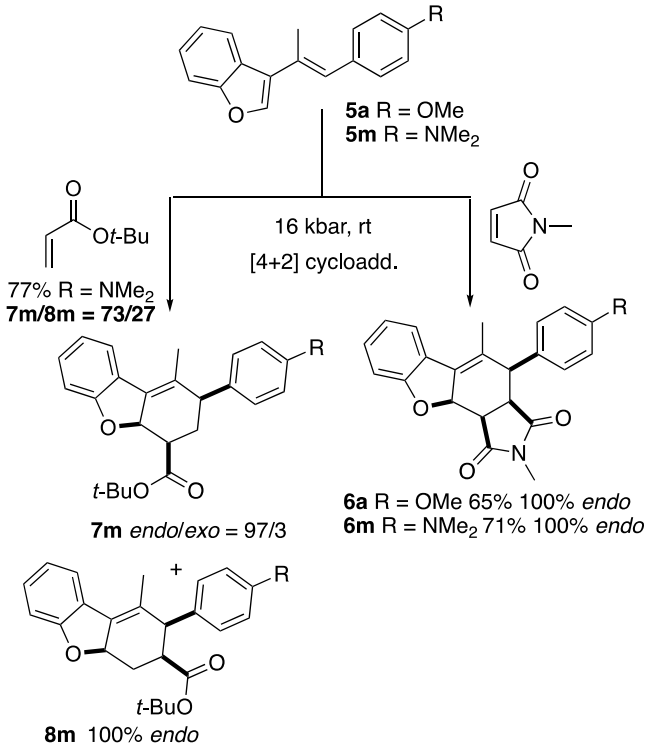
[a]Reaction conditions: **1a** (1 mmol), aldehyde (1.3 mmol), $NiBr_2$bipy (10 mol %), DMF (5 mL), 50 °C, *i* = 25 mA, and 2 h 15 min. Yields of isolated products are given. NMR yields with respect to an internal standard based on the initial aryl iodide **1a** are given within brackets. [b]Reaction run at 80 °C.

substituent formed by the aromatic aldehyde in *ortho*, *meta*, or *para* positions. For example, good to excellent NMR yields are obtained for anisaldehyde, and if the *para* isomer **4a** revealed to be unstable, the alcohols **4b** and **4c** could even be efficiently purified. If aromatic aldehydes bearing electron-donating or -withdrawing groups are suitable, the best results are obtained when the reaction is conducted at 80 °C on electron-depleted substrates. At 50 °C, a mixture of **4** and (*Z*)-3-ethylidene-2,3-dihydrobenzofuran **3a** was obtained. The formation of this latter is probably due to the sluggish nucleophilic addition of the vinylnickel intermediate on the electron-poor aldehydes, giving its chance, again, to a competitive protonation. Increasing the temperature to 80 °C allows a total conversion of the vinylnickel intermediate into the addition products **4**.

The reaction is highly chemoselective, and no competitive addition is observed on the ester, nitrile, or ketone groups (**4f–h**). Even if the reduction of aromatic aldehydes bearing electron-withdrawing groups is easy, compared to other aldehydes (−1.55 V/SCE for *p*-CF_3-PhCHO and −1.45 V/SCE for *p*-MeO_2C-pHCHO compared to −1.9 V/SCE for PhCHO),[15] and close to the Ni(II) reduction potential (−1.15 V/SCE),[13] no pinacolization is observed in these cases. Addition to aliphatic aldehydes at 80 °C also gave good NMR yield, but the purification by chromatography on silica or alumina gel led to severe losses of products (**4k–l**). Varying the temperature can afford, with electron-rich aldehydes, another product, the alcohol **4** can transform directly into the corresponding diene **5**, following a dehydration−aromatization process, as observed in the case of **5a** and **5m** and **5n**, derived, respectively, from anisaldehyde, *N,N*-dimethyl benzaldehyde, and cinnamaldehyde.

Since the 3-vinylbenzofuranes **5** we have prepared exhibit a peculiar dienic motive, we decided to end up this work by illustrating their synthetic potential in cycloaddition reactions. Previous works have shown that such substrates can react in dearomatizing (4 + 2) cycloadditions under hyperbaric conditions (Scheme 3).[11,16]

Scheme 3. Cycloaddition of Benzofurane 5 under Hyperbaric Conditions



Thus, **5a** was reacted with *N*-methylmaleimide at room temperature, under 16 kbar. The cycloaddition is efficient, allowing a single *endo* isomer **6a** in 65% yield. When **5m** is used under the same hyperbaric conditions, **6m** is isolated in a very good yield of 71% as a single *endo* isomer. The same reaction conducted in the presence of *t*-butyl acrylate as dienophile leads to the tricyclic adduct in a good yield of 77% but as a mixture of three isomers. Overall a good *endo*/*exo* selectivity of about 97/3 is observed for **7m** but associated

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with a moderate regioselectivity of 3/1 for **7m**/**8m**, probably due to the modest polarization of the diene.

CONCLUSIONS

In conclusion, this article describes an easy access to substituted dihydrobenzofuran, (iso)chroman, indole, or indane structures by an expedient electrochemical route that encompasses both a cyclization and a C−C bond formation step. We report on the first electroreductive catalytic intramolecular carbonickelation of alkynes that affords, in fine yields, a set of heterocycles, following a 5-, 6-, or 7-*exo-dig* cyclization. This transformation allows in one single *syn*-selective step the desired vinylnickel intermediate, which adds to aldehydes in Barbier conditions. The proposed mechanism was supported by a cyclic voltammetry set of experiments. Pushing the investigation further led us to show that the resulting 3-vinylbenzofuranes, obtained after dehydration of the alcohols, react with activated olefins to provide the (4 + 2) cycloaddition products, in high *endo*/*exo* selectivity. We believe that such a procedure presents significant advantages in terms of sustainable development over the more classical chemical method developed previously.

EXPERIMENTAL SECTION

GC analysis was carried out using a 24 m HP-methyl silicon capillary column. Mass spectra were recorded with a quadrupolar MS instrument coupled to a gas chromatograph. Elemental analyses were performed on a Thermo Fisher FLASH 2000. High-resolution mass spectra were obtained using a Thermo Finnigan MAT95XP mode. Column chromatography was performed on standard silica gel (230−400 mesh) or basic alumina. ^{1}H NMR spectra were recorded in $CDCl_3$ at 300 MHz and ^{13}C NMR spectra were recorded at 75 MHz; chemical shifts (δ) are given in parts per million (ppm) and the coupling constants (J) in hertz. IR spectra were recorded by transmission on an IRFT spectrometer. DMF was stored under argon. THF was distilled from sodium/benzophenone. The catalyst precursor $NiBr_2$bipy was prepared separately, according to the literature.[17]

Compounds **1a**, **1b**, **1c**, **1d**, and **1h** have been described previously, and prepared according to our previous reports.[11] **1e**, **1f**, and **1g** are prepared following a Williamson alkylation procedure.

The Williamson alkylation procedure, exemplified with **1e**. To a solution of substituted iodophenol (1,39 g, 5 mmol) and K_2CO_3 (1,05 g, 7.5 mmol, 1.5 equiv) in 10 mL of anhydrous DMF at room temperature under argon was added 1-bromo-but-2-yne (0.656 mL, 7.5 mmol, 1.5 equiv). The solution was stirred for 30 min and washed by adding HCl 0.5M (30 mL). The mixture was diluted with Et_2O (3 × 15 mL) and washed with 0.5 M NaOH (10 mL) and then NaCl (10 mL). The combined organic layers were dried over $MgSO_4$ and concentrated. We thus obtained 1,65 g (5.0 mmol, 100%) of the desired compound **1e**.

Methyl 4-(But-2-yn-1-yloxy)-3-iodobenzoate (1e). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.46 (d, 1H, J = 2.1 Hz), 8.01 (dd, 1H, J = 8.7, 2.1 Hz), 6.99 (d, 1H, J = 8.7 Hz), 4.79 (q, 2H, J = 2.3 Hz), 3.89 (s, 3H), 1.85 (t, 3H, J = 2.3 Hz). ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz): δ 165.5, 160.1, 141.1, 131.4, 124.7, 111.7, 85.8, 85.1, 72.9, 57.7, 52.2, 3.8. IR (neat): υ_{max} = 2947; 2241; 1703; 1592; 1436; 1296; 1259; 999 cm^{-1}. HRMS (ESI$^+$): theor for $C_{12}H_{12}IO_3$ (M + H$^+$): 330.9826, meas. 330.9831. Mp: 75−76 °C.

1-(But-2-yn-1-yloxy)-2-iodo-4-(trifluoromethyl)benzene (1f). Ether **1f** is obtained using 2-iodo-4-(trifluoromethyl)phenol (2.88 g, 10 mmol), potassium carbonate (2.10 g, 15 mmol, 1.5 equiv), and 1-bromo-but-2-yne (1.31 mL, 15 mmol, 1.5 equiv) in anhydrous DMF (10 mL) following the Williamson alkylation procedure. We thus obtained 3.257 g (9.58 mmol, 96%) of the desired compound **1f**. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.02 (d, 1H, J = 1.7 Hz), 7.58 (d, 1H, J = 8.6 Hz), 7.03 (d, 1H, J = 8.6 Hz), 4.78 (q, 2H, J = 2.3 Hz), 1.86 (t, 3H, J = 2.3 Hz). ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz): δ 159.1, 136.6 (q, J = 3.7 Hz), 126.8 (q, J = 3.7 Hz), 124.9 (q, J = 33.2 Hz), 123.3 (q, J = 271.3 Hz), 112.1, 86.1, 85.2, 72.8, 57.7, 3.7. ^{19}F NMR ($CDCl_3$, 282 MHz): −61.6; IR (neat): υ_{max} = 1602; 1496; 1324; 1268; 1117; 811; 670 cm^{-1}. MS (CI, methane) 341 (MH$^+$); 214 (base, MH$^+$ − I). HRMS (CI, methane): theor for $C_{11}H_9F_3IO$ (M + H$^+$): 340.9650, meas. 340.9634.

1-(But-2-yn-1-yloxy)-2-iodo-4-methylbenzene (1g). Ether **1g** is obtained using 2-iodo-4methylphenol (2.36 g, 10.1 mmol), potassium carbonate (2.12 g, 15.2 mmol, 1.5 equiv), and 1-bromo-but-2-yne (1.33 mL, 15.2 mmol, 1.5 equiv) in anhydrous DMF (10 mL) following the Williamson alkylation procedure. We thus obtained 2.885 g (10.08 mmol, 100%) of the desired compound **1g**. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.60 (d, 1H, J = 2.1 Hz), 7.09 (dd, 1H, J = 8.4, 2.1 Hz), 6.87 (d, 1H, J = 8.4 Hz), 4.68 (q, 2H, J = 2.3 Hz), 2.26 (s, 3H), 1.84 (t, 3H, J = 2.3 Hz). ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz): δ 154.3, 139.6, 132.4, 129.6, 112.7, 86.3, 83.9, 73.8, 57.5, 19.9, 3.6. IR (neat): υ_{max} = 2966; 2919; 2229; 1599; 1485; 1432; 1226; 1041; 698 cm^{-1}. MS (CI, methane) 286 (M$^+$); 159 (base, M$^+$ − I). HRMS (CI, methane): theor for $C_{11}H_{11}IO$ (M$^+$): 285.9855, meas. 285.9844.

General Procedure for Electroreductive Carbonickelation−Nucleoplile Addition, Exemplified with Compound 2a. Electrolysis was run in a one-compartment cell fitted with nickel sponge (area ca. 2 cm^2) as the cathode and an aluminum plate as the anode. NBu_4BF_4 (0.15 equiv, 0.15 mmol, 50 mg) was dissolved in 5 mL of dry DMF under argon atmosphere, then $NiBr_2$bipy (37 mg, 0.1 mmol, 0.1 equiv), 1-(but-2-yn-1-yloxy)-2-iodobenzene (1 mmol, 272 mg, 1 equiv), and benzaldehyde (130 μL, 1.3 equiv) were added. The electrolysis was run at 50 °C with an oil bath, under argon, at a constant current intensity of 25 mA until the aromatic halide was totally consumed (2 F/mol, ∼2 h 15 min). The reaction was monitored by TLC. Finally, the reaction was diluted with 5 mL of water and extracted with 3 × 10 mL of ethyl acetate and organic layers were washed with water.

(*E*)-2-(Benzofuran-3(2*H*)-ylidene)-1-phenylpropan-1-ol (2a). The pure compound **2a** was obtained by recrystallization in pentane (227 mg, 0.90 mmol, 90%) as a white solid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.58 (d, 1H, J = 7.9 Hz), 7.45 (d, 2H, J = 7.9 Hz), 7.35 (t, 2H, J = 7.9 Hz), 7.29 (d, 1H, J = 7.1 Hz), 7.19 (t, 1H, J = 7.9 Hz), 6.89 (d, 1H, J = 8.0 Hz), 6.88 (t, 1H, J = 7.9 Hz), 6.37 (s, 1H), 5.10 (bs, 2H), 2.00 (s, 1H), 1.61 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz): δ 128.8 (2C), 128.5, 127.8, 126.0 (2C), 125.0, 124.5, 121.2, 111.1, 75.0, 71.6, 15.0. NMR 2D NOESY correlation between 1.61 (s, 3H) and 5.12 (bs, 2H). MS 234 (M − H_2O), 219 (base), 218, 191, 189. Anal. calcd for $C_{17}H_{16}O_2$: C, 80.93; H, 6.39. Found: C, 80.89; H, 6.35.

(*Z*)-3-Ethylidene-2,3-dihydrobenzofuran (3a). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.34 (dd, 1H, J = 7.5 Hz J = 1.2 Hz), 7.13 (td, 1H, J = 7.5 Hz J = 1.2 Hz), 6.86 (td, 1H, J = 7.6 Hz J = 1.0 Hz), 6.84 (dd, 1H, J = 7.3 Hz J = 1.0 Hz), 5.86 (qt, 1H, J = 7.1 Hz J = 3.6 Hz), 5.10 (bs, 2H), 1.74 (dt, 3H, J = 7.1 Hz J = 1.9 Hz). ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz): δ 163.4, 136.7, 129.5, 126.6, 120.9, 120.4, 111.8, 110.6, 73.9, 15.3. NMR 2D NOESY correlation between 1.74 (dt, 3H, J = 7.1 Hz J = 1.9 Hz) and 5.10 (s, 2H). MS 146 (M$^+$), 131 (base), 115, 103, 77. Anal. calcd for $C_{10}H_{10}O$: C, 82.16; H, 6.89. Found: C, 81.77; H, 6.64.

(*Z*)-2-(Chroman-4-ylidene)-1-phenylpropan-1-ol (2b). The pure compound **2b** was isolated by flash column chromatography (SiO_2, cyclohexane/AcOEt: 95:5) (151 mg, 0.57 mmol, 57%) as a white solid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.43-7.32 (m, 4H), 7.30−7.26 (m, 2H), 7,17 (td, 1H, J = 8.0 Hz J = 1.5 Hz), 6.86 (dd, 1H, J = 8.0 Hz J = 1.2 Hz), 6.80 (td, 1H, J = 7.8 Hz J = 1.2 Hz), 6.16 (d, 1H, J = 3.9 Hz), 4.43−4.27 (m, 2H), 2.76−2.62 (m, 2H), 1.99 (d, 1H, J = 3.9 Hz), 1.69 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz): δ 154.9, 142.6, 130.3, 130.1, 129.2, 128.7, 128.5 (2C), 127.3, 126.2 (2C), 123.0, 119.9, 116.9, 72.9, 67.7, 28.0, 13.8. NMR 2D NOESY correlation between 1.68 (s, 3H) and 2.69 (m, 2H). MS 248 (M − H_2O), 233 (base), 215, 205, 171, 131, 91, 77. IR (neat): υ_{max} = 3418, 2976, 2869, 2359, 1486,1449, 1119 cm^{-1}. Mp: 117−118 °C.

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(*E*)-*tert*-Butyl 3-(1-hydroxy-1-phenylpropan-2-ylidene)-indoline-1-carboxylate (2c). The pure compound **2c** was isolated by flash column chromatography (SiO_2, cyclohexane/AcOEt: 9:1) (232 mg, 0.66 mmol, 66%) as a white solid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.92 (sl, 1H), 7.57 (d, 1H, J = 7.8 Hz), 7.43 (d, 2H, J = 7.4 Hz), 7.30−7.35 (m, 3H), 7.21 (d, 1H, J = 8.1 Hz), 6.93 (td, 1H, J = 7.8 Hz J = 0.9 Hz), 6.38 (s, 1H), 4.53 (s, 2H), 1.99 (bs, 1H), 1.68 (t, 3H, J = 1.7 Hz), 1.60 (bs, 9H).^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz): δ 151.9, 145.8, 141.5, 130.5, 129.7, 128.8, 128.4 (2C), 127.3, 127.0, 125.8 (2C), 123.9, 122.4, 115.3, 81.2, 70.6, 53.0, 28.5 (3C), 15.2. NMR 2D NOESY correlation between 1.65 (s, 3H) and 4.34−4.50 (m, 2H). MS 350 (M^+ − H), 349, 233 (base), 218. IR (neat): υ_{max} = 3412, 3052, 2980, 1703, 1472, 1383, 1163, 725 cm^{-1}. Anal. Calcd for $C_{22}H_{25}NO_3$: C, 75.19; H, 7.17; N, 3.99. Found: C, 74.91; H, 7.69; N, 3.90.

(*Z*)-2-(1,2-Dihydroinden-3-ylidene)-1-phenylpropan-1-ol (2d). The pure compound **2d** was isolated by flash column chromatography (SiO_2, cyclohexane/AcOEt: 97:3) (100 mg, 0.40 mmol, 40%) as a yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.53 (d, 1H, J = 7.5 Hz), 7.45−7.56 (m, 2H), 7.14−7.39 (m, 6H), 6.37 (d, 1H, J = 3.9 Hz), 2.98−3.03 (m, 2H), 2.74−2.89 (m, 2H), 2.35 (d, 1H, J = 3.9 Hz), 1. 72 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 148.1, 142.1, 140.3, 140.2, 130.0, 128.4 (2C), 127.5, 127.1, 126.5, 126.0 (2C), 125.5, 124.5, 71.8, 31.8, 30.2, 15.4. NMR 2D NOESY correlation between 1.72 (s, 3H) and 2.74−2.89 (m, 2H) and between 6.37 (d, 1H, J = 3.9 Hz) and 7.53 (d, 1H, J = 7.5 Hz). MS 250 (M^+), 232 (M^+ − H_2O), 217 (base), 202, 115. IR (neat): υ_{max} = 3405, 2919, 1447, 1016, 754 cm^{-1}. HRMS (EI): calcd for $C_{18}H_{16}$ (M − H_2O) 232.1252, found 232.1260.

Methyl (*E*)-3-(1-Hydroxy-1-phenylpropan-2-ylidene)-2,3-dihydrobenzofuran-5-carboxylate (2e). The pure compound **2e** was obtained by recrystallization in pentane (240 mg, 0.77 mmol, 77%) as a cream solid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.32 (d, 1H, J = 1.7 Hz), 7.93 (dd, 1H, J = 8.5Hz J = 1.7 Hz), 7.42−7.47 (m, 2H), 7.32−7.38 (m, 2H), 7.27−7.31 (m, 1H), 6.90 (d, 1H, J = 8.5 Hz), 6.42 (s, 1H), 5.16 (m, 2H), 3.86 (s, 3H), 2.20 (s, 1H), 1.62 (t, 3H, J = 1.9 Hz). ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz): δ 168.5, 167.0, 141.6, 132.2, 131.2, 130.3, 128.7 (2C), 127.7, 125.9, 125.8 (2C), 125.1, 123.0, 110.5, 75.8, 71.3, 52.2, 15.0. NMR 2D NOESY correlation between 1.62 (t, 3H, J = 1.9 Hz) and 5.16 (m, 2H). IR (neat): υ_{max} = 3472; 2949; 1695; 1588; 1482; 1433; 1363; 1328; 1295; 1243; 1114; 1100; 987; 841; 706 cm^{-1}. HRMS (API$^+$): calcd for $C_{19}H_{17}O_3$ (M − H_2O+H^+) 293.1172, found 293.1175. Mp: 151−152 °C.

(*E*)-1-Phenyl-2-(5-(trifluoromethyl)benzofuran-3(2*H*)-ylidene)propan-1-ol (2f). The pure compound **2f** was isolated by flash column chromatography (neutralized alumina, cyclohexane/AcOEt: 95:5) (112 mg, 0.35 mmol, 35%) as a yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.82 (s, 1H), 7.42−7.47 (m, 3H), 7.27−7.40 (m, 3H), 6.94 (d, J = 8.5Hz, 1H), 6.29 (s, 1H), 5.17 (m, 2H), 2.09 (s, 1H), 1.64 (t, 3H, J = 1.9 Hz). ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz): δ 167.0, 141.3, 131.2, 130.8, 128.8 (2C), 127.9, 127.2 (q, J = 3.9 Hz), 125.8 (2C), 125.3, 124.3 (q, J = 271.2 Hz), 123.3 (q, J = 32.5 Hz), 121.5 (q, J = 3.9 Hz), 110.8, 75.6, 71.5, 15.2. ^{19}F NMR ($CDCl_3$, 282 MHz): −61.16. NMR 2D NOESY correlation between 1.64 (t, 3H, J = 1.9 Hz) and 5.16 (m, 2H). IR (neat): υ_{max} = 3290; 3076; 3034; 2933; 1658; 1613; 1494; 1452; 1319; 1280; 1246; 1102; 1064; 994 cm^{-1}. HRMS (EI): calcd for $C_{18}H_{13}F_3O$ (M − H_2O) 302.0918, found 302.0924. Mp: 84−85 °C.

(*E*)-2-(5-Methylbenzofuran-3(2*H*)-ylidene)-1-phenylpropan-1-ol (2g). The pure compound **2g** was obtained by recrystallization in pentane (162 mg, 0.61 mmol, 61%) as a cream solid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.40−7.50 (m, 3H), 7.33−7.39 (m, 2H), 7.27−7.32 (m, 1H), 7.00 (d, 1H, J = 8.2 Hz), 6.80 (d, 1H, J = 8.2 Hz), 6.39 (s, 1H), 5.06 (m, 2H), 2.28 (s, 3H), 2.13 (s, 1H), 1.57 (t, 3H, J = 1.9 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz): δ 162.9, 141.7, 133.3, 130.4, 130.1, 128.6 (2C), 127.9, 127.4, 125.7 (2C), 124.6, 124.5, 110.4, 74.9, 71.3, 21.2, 14.7. NMR 2D NOESY correlation between 1.57 (t, 3H, J = 1.9 Hz) and 5.06 (m, 2H). IR (neat): υ_{max} = 3457; 3058; 3029; 2927; 1489; 1449; 1395; 1306; 1208; 1025; 1117; 987; 807; 749; 698 cm^{-1}. HRMS (EI$^+$): calcd for $C_{18}H_{16}O$ (M − H_2O) 248.1201, found 248.1203. Mp: 128−129 °C.

(*Z*)-2-(3,4-Dihydrobenzo[*b*]oxepin-5(2*H*)-ylidene)-1-phenylpropan-1-ol (2h). The pure compound **2h** was isolated by flash column chromatography (SiO_2, cyclohexane/Et_2O 8:2) (123 mg, 0.44 mmol, 44%) as a white solid. ^{1}H NMR (DMSO, 300 MHz, 60 °C): δ 7.16−7.41 (m, 7H), 6.97−7.03 (m, 2H), 5.42 (d, 1H, J = 4.1 Hz), 5.18 (d, J = 4.1 Hz, 1H), 4.23 (bs, 1H), 3.95 (bs, 1H), 2.68 (bs, 1H), 2.19 (bs, 1H), 1.78−2.01 (m, 2H), 1.56 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz): δ 157.7, 142.9, 136.9, 134.6, 133.2, 129.7, 128.5, 128.2 (2C), 126.7, 125.3, 123.3, 121.5 (2C), 73.3, 72.4, 30.6, 29.5, 11.8. NMR 2D NOESY correlation between 1.56 (s, 3H) and 1.78−2.01 (m, 2H). MS: 280 (M^+), 262 (M − H_2O), 247 (M − H_2O − CH_3), 147 (base). IR (neat): υ_{max} = 3424, 3025, 2930, 1599, 1480, 1228, 1054, 1008 cm^{-1}. HRMS (EI): calcd for $C_{19}H_{20}O_2$ 280.1463, found 280.1477. Mp: 92−94 °C.

(*E*)-2-(Benzofuran-3(2*H*)-ylidene)-1-(4-methoxyphenyl)-propan-1-ol (4a). The pure compound **4a** was isolated by reversed-phase columns (water/acetonitrile: 54/46) (141 mg, 0.50 mmol, 50%) as a yellow solid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.54 (d, 1H, J = 7.9 Hz), 7.36 (d, 2H, J = 8.8 Hz), 7.18 (t, 1H, J = 7.7 Hz), 6.85−6.91 (m, 4H), 6.29 (d, 1H, J = 3.5 Hz), 5.09 (m, 2H), 3.80 (s, 3H), 1.97 (d, 1H, J = 3.5 Hz), 1.62 (t, 3H, J = 1.7 Hz). ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz): δ 164.7, 159.1, 133.7, 132.5, 129.6, 128.5, 127.1 (2C), 124.7, 124.3, 120.9, 114.0 (2C), 110.8, 74.7, 71.2, 55.4, 14.8. NMR 2D NOESY correlation between 1.62 (t, 3H, J = 3.0 Hz) and 5.09 (m, 2H) and between 6.26 (s, 1H) and 7.54 (d, 1H, J = 7.9 Hz). MS: 280 (M^+), 262 (M − H_2O), 247 (M − H_2O − CH_3), 147 (base). IR (neat): υ_{max} = 3492, 2911, 1240, 1023 cm^{-1}. HRMS (API$^+$): calcd for $C_{18}H_{17}O_2$ (M − H_2O + H^+) 265.1229, found 265,1233. Mp: 132−133 °C.

(*E*)-2-(Benzofuran-3(2*H*)-ylidene)-1-(3-methoxyphenyl)-propan-1-ol (4b). The pure compound **4b** was obtained by recrystallization in pentane (195 mg, 0.69 mmol, 69%) as a cream solid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.58 (d, 1H, J = 7.7 Hz), 7.24−7.30 (m, 1H), 7.19 (t, 1H, J = 7.5 Hz), 6.97−7.05 (m, 2H), 6.86−6.95 (m, 2H), 6.78−6.84 (m, 1H), 6.33 (s, 1H), 5.08 (bs, 2H), 3.80 (s, 3H), 2.07 (s, 1H), 1.60 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz): δ 164.8, 160.0, 143.4, 133.1, 129.8, 129.6, 128.1, 124.7, 124.2, 120.9, 118.1, 112.8, 111.6, 110.9, 74.7, 71.3, 55.4, 14.7. NMR 2D NOESY correlation between 1.60 (s, 3H) and 5.08 (m, 2H). IR (neat): υ_{max} = 3489, 1585, 1462, 1435, 1136, 1050, 1022 cm^{-1}. HRMS (API$^+$): calcd for $C_{18}H_{17}O_2$ (M + H^+ − H_2O) 265.1229, found 265.1225. Mp: 129−130 °C.

(*E*)-2-(Benzofuran-3(2*H*)-ylidene)-1-(2-methoxyphenyl)-propan-1-ol (4c). The pure compound **4c** was obtained by recrystallization in pentane (254 mg, 0.90 mmol, 90%) as a cream solid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.44 (d, 1H, J = 7.6 Hz), 7.34 (dd, 1H, J = 7.5, 1.4 Hz), 7.25−7.31 (m, 1H), 7.13 (t, 1H, J = 7.7 Hz), 6.91−6.97 (m, 2H), 6.79−6.87 (m, 2H), 6.42 (s, 1H), 5.12 (m, 2H), 3.83 (s, 3H), 2.93 (s, 1H), 1.74 (t, 3H, J = 1.9 Hz). ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz): δ 164.7, 157.4, 132.7, 129.6, 129.2, 128.9, 127.2, 126.8, 125.2, 124.9, 120.9, 120.7, 110.6, 110.3, 74.8, 68.7, 55.4, 15.5. NMR 2D NOESY correlation between 1.74 (t, 3H, J = 1.9 Hz) and 5.12 (m, 2H). IR (neat): υ_{max} = 3482, 2935, 2840, 1598, 1586, 1463, 1239, 1118, 744 cm$^{-1.}$ HRMS (API$^+$): calcd for $C_{18}H_{17}O_2$ (M + H^+ − H_2O) 265.1229, found 265.1227. Mp: 126−127 °C.

(*E*)-2-(Benzofuran-3(2*H*)-ylidene)-1-(4-(tert-butyl)phenyl)-propan-1-ol (4d). The pure compound **4d** was isolated by flash column chromatography (neutralized alumina, cyclohexane/AcOEt: 95:5) (92 mg, 0.30 mmol, 30%) as a yellow solid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.57 (d, 1H, J = 7.8 Hz), 7.37 (s, 4H), 7.18 (td, 1H, J = 7.8 1.2 Hz), 6.84−6.91 (m, 2H), 6.33 (bs, 1H), 5.09 (m, 2H), 2.08 (bs, 1H), 1.63 (t, 3H, J = 1.7 Hz), 1.32 (s, 9H). ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz): δ 164.8, 150.5, 138.6, 132.6, 129.6, 128.5, 125.5 (4C), 124.8, 124.3, 120.9, 110.8, 74.8, 71.4, 34.6, 31.5 (3C), 14.8. NMR 2D NOESY correlation between 1.64 (t, 3H, J = 1.7 Hz) and 5.10 (m, 2H). IR (neat): υ_{max} = 3494, 2961, 2869, 1584, 1463, 1364, 1215, 1107, 1027, 987, 749 cm^{-1}. HRMS (ESI): calcd for $C_{21}H_{23}O_2$ (M − H^+) 307.1698, found 307.1691. Mp: 133−134 °C.

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(*E*)-2-(Benzofuran-3(2*H*)-ylidene)-1-(4-fluorophenyl)-propan-1-ol (4e). The pure compound **4e** was obtained by recrystallization in pentane (165 mg, 0.61 mmol, 61%) as a cream solid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.55 (d, 1H, J = 7.7 Hz), 7.39−7.43 (m, 2H), 7.17−7.22 (m, 1H), 7.00−7.06 (m, 2H), 6.84−6.92 (m, 2H), 6.34 (s, 1H), 5.09 (m, 2H), 1.98 (bs, 1H), 1.59 (t, 3H, J = 1.8 Hz). ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz): δ 164.9, 161.9 (d, J = 246.1 Hz), 133.3, 129.9, 128.9 (d, J = 8.7 Hz), 127.5 (d, 2C, J = 9.7 Hz), 124.6, 124.2, 121.0, 116.7, 115.4 (d, 2C, J = 19.4 Hz), 111.0, 74.7, 71.0, 14.6. ^{19}F NMR ($CDCl_3$, 282 MHz): −115.40. NMR 2D NOESY correlation between 1.59 (t, 3H, J = 1.8 Hz) and 5.09 (m, 2H). IR (neat): υ_{max} = 3469, 2910, 1653, 1602, 1508, 1464, 1377, 1222, 1156, 1016, 748 cm^{-1}. HRMS (API$^+$): calcd for $C_{17}H_{14}OF$ (M + H$^+$ − H_2O) 253.1029, found 253.1027. Mp: 138−139 °C.

(*E*)-Methyl 4-(2-(Benzofuran-3(2*H*)-ylidene)-1-hydroxypropyl)benzoate (4f). The pure compound **4f** was isolated by flash column chromatography (neutralized alumina, cyclohexane/AcOEt: 9:1) (186 mg, 0.60 mmol, 60%) as a yellow solid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.02 (d, 2H, J = 8.3 Hz), 7.60 (d, 1H, J = 7.7 Hz), 7.52 (d, 2H, J = 8.3 Hz), 7.21 (td, 1H, J = 7.8 1.5 Hz), 6.87−6.94 (m, 2H), 6.42 (d, 1H, J = 3.3 Hz), 5.09 (m, 2H), 3.91 (s, 3H), 2.07 (d, 1H, J = 3.3 Hz), 1.56 (t, 3H, J = 2.1 Hz). ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz): δ 167.1, 164.9, 146.9, 133.6, 130.0, 129.8 (2C), 129.3, 127.6, 125.8 (2C), 124.5, 124.0, 121.0, 111.0, 74.7, 71.1, 52.2, 14.6. NMR 2D NOESY correlation between 1.56 (t, 3H, J = 1.8 Hz) and 5.09 (m, 2H). IR (neat): υ_{max} = 3469, 2908, 1896, 1603, 1508, 1464, 1377, 1222, 1156, 1017, 748 cm^{-1}. HRMS (API$^+$): calcd for $C_{19}H_{17}O_3$ (M + H$^+$ − H_2O) 293.1178, found 293.1174. Mp: 100−101 °C.

(*E*)-4-(2-(Benzofuran-3(2*H*)-ylidene)-1-hydroxypropyl)-benzonitrile (4g). The pure compound **4g** was isolated by flash column chromatography (neutralized alumina, cyclohexane/AcOEt: 9:1) (59 mg, 0.21 mmol, 21%) as a yellow solid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.55−7.66 (m, 5H), 7.21−7.23 (m, 1H), 6.88−6.94 (m, 2H), 6.42 (s, 1H), 5.09 (m, 2H), 2.07 (s, 1H), 1.54 (t, 3H, J = 1.9 Hz). ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz): δ 165.0, 147.0, 134.1, 132.4 (2C), 130.2, 130.0, 127.0, 126.5 (2C), 124.3, 123.9, 121.1, 119.0, 111.2, 74.7, 70.8, 14.5. NMR 2D NOESY correlation between 1.54 (t, 3H, J = 1.9 Hz) and 5.09 (m, 2H). IR (neat): υ_{max} = 3468, 2910, 1653, 1603, 1508, 1464, 1377, 1222, 1156, 1115, 748 cm^{-1}. HRMS (API$^+$): calcd for $C_{18}H_{14}NO$ (M + H$^+$ − H_2O) 260.1075, found 260.1082. Mp: 139−140 °C.

(*E*)-1-(4-(2-(Benzofuran-3(2*H*)-ylidene)-1-hydroxypropyl)-phenyl)ethan-1-one (4h). The pure compound **4h** was isolated by flash column chromatography (neutralized alumina, cyclohexane/AcOEt: 9:1) (41 mg, 0.14 mmol, 14%) as a yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz,): δ 7.93 (d, 2H, J = 8.3 Hz), 7.59 (d, 1H, J = 7.6 Hz), 7.54 (d, 2H, J = 8.3 Hz), 7.21 (td, 1H, J = 7.8 1.1 Hz), 6.86−6.93 (m, 2H), 6.41 (bs, 1H), 5.07 (m, 2H), 2.59 (s, 3H), 2.32 (bs, 1H), 1.55 (t, 3H, J = 2.1 Hz). ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz,): δ 198.0, 164.9, 147.0, 136.4, 133.7, 130.0, 128.7 (2C), 127.5, 126.0 (2C), 124.5, 124.0, 121.0, 111.1, 74.7, 71.1, 26.8, 14.6. NMR 2D NOESY correlation between 1.56 (t, 3H, J = 2.1 Hz,) and 5.10 (m, 2H). IR (neat): υ_{max} = 3488, 2923, 2857, 1686, 1606, 1461, 1359, 1266, 1077, 747 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{19}H_{17}O_2$ (M + H$^+$ − H_2O) 277.1229, found 277.1219. Mp: 125−126 °C.

(*E*)-2-(Benzofuran-3(2*H*)-ylidene)-1-(4-(methylsulfonyl)-phenyl)propan-1-ol (4i). The pure compound **4i** was isolated by flash column chromatography (neutralized alumina, Toluene/AcOEt 9:1) (36 mg, 0.11 mmol, 11%) as a white solid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.87 (d, 2H, J = 8.3 Hz), 7.63 (d, 2H, J = 8.3 Hz), 7.57 (d, 1H, J = 7.9 Hz), 7.21 (td, 1H, J = 7.8 1.1 Hz), 6.86−6.95 (m, 2H), 6.42 (bs, 1H), 5.06 (m, 2H), 3.03 (s, 3H), 2.63 (bs, 1H), 1.56 (t, 3H, J = 1.2 Hz). ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz): δ 164.9, 148.2, 139.4, 134.0, 130.2, 127.6 (2C), 127.1, 126.8 (2C), 124.3, 123.9, 121.1, 111.1, 74.7, 70.7, 44.6, 14.5. NMR 2D NOESY correlation between 1.56 (t, 3H, J = 1.2 Hz) and 5.10 (m, 2H). IR (neat): υ_{max} = 3431; 2921; 1603; 1464; 1321; 1299; 1141; 959; 742 cm^{-1}. HRMS (ESI$^-$): calcd for $C_{18}H_{17}O_4S$ (M − H$^+$) 329.0848, found 329.0847. Mp: 155−156 °C.

(*E*)-2-(Benzofuran-3(2*H*)-ylidene)-1-(4-(trifluoromethyl)-phenyl)-1-ol (4j). The pure compound **4j** was obtained by recrystallization in pentane (86 mg, 0.27 mmol, 27%) as a cream solid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.55−7.62 (m, 5H), 7.22 (td, 1H, J = 7.8 1.0 Hz), 6.87−6.94 (m, 2H), 6.42 (s, 1H), 5.09 (m, 2H), 2.17 (bs, 1H), 1.56 (t, 3H, J = 1.9 Hz). ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz): δ 165.0, 145.6, 133.9, 130.1, 129.8 (q, J = 31.5 Hz), 127.4, 126.1 (2C), 125.6 (q, J = 3.8Hz, 2C), 124.4, 124.2 (q, J = 247.7 Hz), 124.0, 121.1, 111.1, 74.7, 71.0, 14.6. ^{19}F NMR ($CDCl_3$, 282 MHz): −62.40. NMR 2D NOESY correlation between 1.56 (t, 3H, J = 1.9 Hz) and 5.09 (m, 2H). IR (neat): υ_{max} = 3479; 1621; 1465; 1323; 1115; 1067; 742 cm^{-1}. HRMS (ESI): calcd for $C_{18}H_{14}O_2F_3$ (M − H$^+$) 319.0946, found 319.0959. Mp: 148−149 °C.

(*E*)-2-(Benzofuran-3(2*H*)-ylidene)propan-1-ol (4k). The pure compound **4k** was isolated by flash column chromatography (neutralized alumina, cyclohexane/AcOEt: 95:5) (35 mg, 0.20 mmol, 20%) as a white solid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.57 (d, 1H, J = 7.7 Hz), 7.16 (t, 1H, J = 7.8 Hz), 6.84−6.93 (m, 2H), 5.04 (m, 2H), 4.49 (bs, 2H), 1.83 (t, 3H, J = 1.8 Hz), 1.69 (bs, 1H). ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz,): δ 164.5, 133.2, 129.5, 125.7, 124.8, 124.3, 120.9, 110.6, 74.6, 63.5, 19.0. NMR 2D NOESY correlation between 1.85 (t, 3H, J = 1.8 Hz) and 5.06 (m, 2H). IR (neat): υ_{max} = 3204, 2924, 1668, 1601, 1585, 1463, 1242, 1212, 1112, 1000, 986, 742 cm^{-1}. HRMS (EI): calcd for $C_{11}H_{10}O_1$ (M − H_2O + H$^+$) 158.0732, found 158.0736. Mp: 90−91 °C.

(*E*)-2-(Benzofuran-3(2*H*)-ylidene)hexan-3-ol (4l). The pure compound **4l** was isolated by flash column chromatography (neutralized alumina, cyclohexane/AcOEt: 95:5) (65 mg, 0.30 mmol, 30%) as a yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.45 (d, 1H, J = 7.3 Hz), 7.14 (td, 1H, J = 7.8 1.1 Hz), 6.87 (td, 1H, J = 7.6 1.1 Hz), 6.85 (d, 1H, J = 8.0 Hz), 5.11−5.15 (m, 1H), 5.00 (bs, 2H), 1.94 (bs, 1H), 1.69 (t, 3H, J = 1.8 Hz), 1.27−1.62 (m, 4H), 0.97 (t, 3H, J = 7.1 Hz). ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz): δ 164.5, 131.0, 129.8, 129.1, 124.8, 124.5, 120.7, 110.6, 74.6, 70.1, 37.0, 19.1, 14.2, 14.1. NMR 2D NOESY correlation between 1.69 (t, 3H, J = 1.8 Hz) and 5.00 (m, 2H) and between 5.11−5.15 (m, 1H) and 7.45 (d, 1H, J = 7.3 Hz). IR (neat): υ_{max} = 3492, 2957, 2929, 2870, 1710, 1600, 1585, 1465, 1454, 1226, 985, 748 cm^{-1}. HRMS (EI): calcd for $C_{14}H_{16}O_1$ (M − H_2O) 200.1201, found 200.1207.

(*E*)-3-(1-(4-Methoxyphenyl)prop-1-en-2-yl)benzofuran (5a). The pure compound **5a** was isolated by flash column chromatography (SiO_2, cyclohexane/AcOEt: 95:5) (106 mg, 0.40 mmol, 40%) as a yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.93 (dd, 1H, J = 7.5 1.9 Hz), 7.71 (s, 1H), 7.52 (dd, 1H, J = 7.5 1.9 Hz), 7.28−7.37 (m, 4H), 7.09 (bs, 1H), 6.94 (d, 2H, J = 8.8 Hz), 3.85 (s, 3H), 2.30 (d, 3H, J = 1.3 Hz). ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz): δ 158.4, 156.0, 142.1, 130.49 (2C), 130.46, 127.5, 127.2, 126.0, 124.7, 124.5, 122.9, 121.5, 113.8 (2C), 111.8, 55.3, 17.8. NMR 2D NOESY correlation between 2.30 (d, 3H, J = 3.0 Hz) and 7.32−7.36 (m, 4H) and between 2.30 (d, 3H, J = 3.0 Hz) and 7.71 (s, 1H). IR (neat): υ_{max} = 2917, 1507, 1244, 1026 cm^{-1}. HRMS (API$^+$): calcd for $C_{18}H_{16}O_2$ 264.1150, found 264.1159.

(*E*)-2-((Benzofuran-3-yl)prop-1-en-1-yl)-*N*, *N*-dimethylaniline (5m). The pure compound **5m** was isolated by flash column chromatography (neutralized alumina, cyclohexane) (125 mg, 0.45 mmol, 45%) as a white solid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.93 (dd, 1H, J = 6.4 1.8 Hz), 7.69 (s, 1H), 7.51 (d, 1H, J = 7.2 Hz), 7.25−7.34 (m, 4H), 7.06 (s, 1H), 6.77 (d, 2H, J = 8.6 Hz), 3.00 (s, 6H), 2.32 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz): δ 156.1, 149.3, 141.9, 130.4 (2C), 127.9, 126.29, 126.25, 125.8, 125.2, 124.4, 122.9, 121.7, 112.3 (2C), 111.8, 40.7 (2C), 18.1. NMR 2D NOESY correlation between 2.32 (s, 3H) and 6.77 (d, 2H, J = 8.4 Hz). IR (neat): υ_{max} = 3137, 3030, 2983, 2911, 2853, 2792, 1603, 1449, 1336, 1224, 744 cm^{-1}. HRMS (ESI$^+$): calcd for $C_{19}H_{20}NO$ (M + H$^+$) 278.1545, found 278.1541. Mp: 88−89 °C.

3-((2*Z*,4*E*)-5-Phenylpenta-2,4-dien-2-yl)benzofuran (5n). The pure compound **5n** was isolated by flash column chromatography (neutralized alumina, cyclohexane) (96 mg, 0.37 mmol, 37%) as a yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.93−8.00 (m, 1H), 7.71 (s, 1H), 7.51−7.55 (m, 1H), 7.47−7.51 (m, 2H), 7.32−7.39 (m, 4H),

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7.26 (d, 1H, J = 1.1 Hz), 7.25 (d, 1H, J = 15.4 Hz), 6.94 (d, 1H, J = 11.0 Hz), 6.72 (d, 1H, J = 15.4 Hz), 2.31 (d, 3H, J = 1.1 Hz). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz): δ 156.1, 142.5, 137.8, 132.7, 128.9, 128.8 (2C), 127.6, 127.3, 126.5 (2C), 125.8, 125.3, 124.6, 124.2, 123.1, 121.7, 111.9, 16.7. NMR 2D NOESY correlation between 2.30 (s, 3H) and 7.71 (s, 1H) and between 2.30 (s, 3H) and 7.25 (d, 1H, J = 15.4 Hz). IR (neat): υ_{max} = 3070, 3023, 2919, 1765, 1615, 1477, 1461, 1378, 1330, 1288, 1231, 1135, 1079, 747 cm^{-1}. HRMS (EI): calcd for $C_{19}H_{16}O$ 260.1201, found 260.1195.

General Procedure for Cycloaddition Exemplified with Compound 6a *endo*. The reaction was realized from diene **5a** (0.129 g, 0.49 mmol, 1 equiv) and *N*-methylmaleimide (0.108 g, 0.98 mmol, 2 equiv) in solution in THF (5 mL). After 24 h under hyperbaric conditions (16 Kbar) at room temperature, the solvent was concentrated, and the crude solid was purified by column chromatography.

*Cycloadduct (**6a** endo).* The pure compound **6a** was isolated by flash column chromatography (SiO_2, cyclohexane/AcOEt: 80/20) (120 mg, 0.32 mmol, 65%) as a yellow solid. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.52 (d, 2H, J = 8.6 Hz), 7.48 (d, 1H, J = 7.9 Hz), 7.20 (t, 1H, J = 7.9 Hz), 7.02 (d, 1H, J = 8.0 Hz), 6.94 (d, 2H, J = 8.6 Hz), 6.92 (t, 1H, J = 8.4 Hz), 5.36−5.29 (m, 1H), 3.84 (s, 3H), 3.81 (t, 1H, J = 8.4 Hz), 3.54−3.49 (m, 2H), 2.78 (s, 3H), 1.92 (d, 3H, J = 2.4 Hz). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz): δ 176.7, 173.6, 163.4, 158.8, 132.0 (2C), 130.9, 129.6, 129.2, 129.1, 124.0, 123.4, 121.3, 113.6 (2C), 110.9, 80.2, 55.4, 47.7, 44.2, 43.6, 25.1, 17.0. NMR 2D NOESY correlation between 3.54−3.51 (m, 2H) and 5.36−5.32 (m, 1H) and between 3.83 (t, 1H, J = 8.4 Hz) and 5.36−5.32 (m, 1H). IR (neat): υ_{max} = 2929, 2835, 1777, 1699, 1513, 1462, 1434, 1384, 1306, 1248, 1182, 1110, 1032, 1003, 752. HRMS (ESI^+): calcd for $C_{23}H_{22}NO_4$ ($M + H^+$) 376.1543, found 376.1549. Mp: 208−209 °C.

*Cycloadduct (**6m** endo).* The pure compound **6m** was isolated by flash column chromatography (SiO_2, cyclohexane/AcOEt: 80/20) (135 mg, 0.35 mmol, 71%) as a white solid. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.47 (d, 1H, J = 8.7 Hz), 7.44 (d, 2H, J = 8.7 Hz), 7.18 (t, 1H, J = 7.6 Hz), 7.01 (d, 1H, J = 8.4 Hz), 6.91 (t, 1H, J = 7.7 Hz), 6.76 (d, 2H, J = 8.7 Hz), 5.32−5.28 (m, 1H), 3.77 (t, 1H, J = 7.7 Hz), 3.45 (t, 1H, J = 3.4 Hz), 3.43 (bs, 1H), 2.98 (s, 6H), 2.77 (s, 3H), 1.94 (d, 3H, J = 1.6 Hz). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz): δ 176.7, 173.7, 163.3, 149.6, 131.6 (2C), 130.5, 129.7, 129.3, 124.7, 124.1, 123.3, 121.1, 112.0 (2C), 110.7, 80.2, 47.6, 44.2, 43.6, 40.6 (2C), 25.0, 17.0. NMR 2D NOESY correlation between 5.38−5.29 (m, 1H) and 3.81 (t, 1H, J = 7.7 Hz) and between 5.38−5.29 (m, 1H) and 3.49−3.47 (m, 2H). IR (neat): υ_{max} = 2888, 2800, 1690, 1607, 1520, 1462, 1436, 1389, 1339, 1217, 1150, 1029, 824, 744. HRMS (ESI^+): calcd for $C_{24}H_{25}N_2O_3$ ($M + H^+$) 389.1860, found 389.1847. Mp: 221−222 °C.

Cycloaddition in the Presence of *t*-Butyl Acrylate. The cycloaddition reaction is conducted in similar conditions (16 kbar, room temperature) in the presence of *t*-butyl acrylate as dienophile and leads to the tricyclic adducts **7m** *endo*/**7m** *exo*/**8m** *endo* in a good isolated yield of 77% but as a mixture of three inseparable isomers in a ratio of 70/3/27. A fraction of the pure compound **8m** *endo* is isolated by flash column chromatography (SiO_2, cyclohexane/AcOEt: 98/2) (21 mg, 0.052 mmol, 13%) as a colorless oil.

*Cycloadduct (**7m** endo).* ^1H NMR ($CDCl_3$, 300 MHz): δ 7.45 (d, 1H, J = 7.9 Hz), 7.19 (t, 1H, J = 7.7 Hz), 7.07 (d, 2H, J = 8.6 Hz), 6.90−6.97 (m, 2H), 6.61 (d, 2H, J = 8.6 Hz), 4.97−5.09 (m, 1H), 3.81 (dd, 1H, J = 6.6 2.4 Hz), 2.94−3.02 (m, 1H), 2.89 (s, 6H), 2.37−2.44 (m, 1H), 2.19 (q, 1H, J = 12.1 Hz), 1.75 (d, 3H, J = 2.5 Hz), 1.28 (s, 9H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz): δ 171.6, 162.5, 150.0, 132.0, 130.8 (2C), 129.2, 128.9, 127.6, 126.8, 124.0, 120.9, 112.4 (2C), 110.4, 83.2, 80.6, 48.4, 44.8, 40.8 (2C), 28.1 (3C), 24.9, 17.9. NMR 2D NOESY correlation between 4.97−5.09 (m, 1H) and 2.94−3.02 (m, 1H), between 4.97−5.09 (m, 1H) and 2.37−2.44 (m, 1H) and between 3.81 (dd, 1H, J = 6.6 2.4 Hz) and 2.94−3.02 (m, 1H). IR (neat): υ_{max} = 2974, 2884, 1724, 1612, 1519, 1457, 1366, 1339, 1223, 1151, 1022, 820, 747. HRMS (ESI^+): calcd for $C_{26}H_{32}NO_3$ ($M + H^+$) 406.2377, found 406.2383.

*Cycloadduct (**8m** endo).* ^1H NMR ($CDCl_3$, 300 MHz): δ 7.48 (dd, 1H, J = 7.6 1.4 Hz), 7.18 (td, 1H, J = 7.7 1.4 Hz), 7.06 (d, 2H, J = 8.7 Hz), 6.94 (td, 1H, J = 7.5 1.1 Hz), 6.90 (d, 1H, J = 7.7 Hz), 6.66 (d, 2H, J = 8.7 Hz), 4.98−4.90 (m, 1H), 3.93 (s, 1H), 2.92 (s, 6H), 2.76 (t, 1H, J = 4.8 Hz), 2.57−2.50 (m, 1H), 2.05 (td, 1H, J = 11.8 4.8 Hz), 1.84 (d, 3H, J = 2.5 Hz), 1.47 (s, 9H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz): δ 173.6, 162.3, 149.6, 132.1, 131.5, 129.3 (2C), 128.7, 128.2, 127.0, 124.1, 120.9, 112.8 (2C), 110.3, 81.1, 80.6, 47.2, 46.8, 40.8 (2C), 28.2 (3C), 25.1, 18.3. NMR 2D NOESY correlation between 4.98−4.90 (m, 1H) and 2.57−2.50 (m, 1H) and between 3.93 (s, 1H) and 2.76 (t, 1H, J = 4.8 Hz). IR (neat): υ_{max} = 2974, 2800, 1723, 1611, 1518, 1458, 1367, 1340, 1217, 1146, 1020, 829, 816, 748. HRMS (ESI^+): calcd for $C_{26}H_{32}NO_3$ ($M + H^+$) 406.2377, found 406.2363.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c00811.

^1H and ^{13}C NMR spectra of the new compounds (PDF)

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All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

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