JOC The Journal of Organic Chemistry

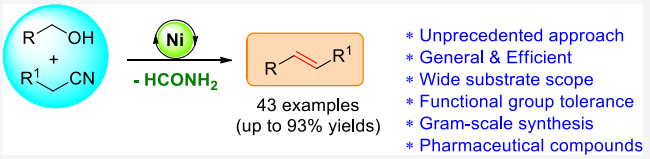
pubs.acs.org/joc Article

Tandem Acceptorless Dehydrogenative Coupling–Decyanation under Nickel Catalysis

Siba P. Midya, Murugan Subaramanian, Reshma Babu, Vinita Yadav, and Ekambaram Balaraman*

Cite This: J. Org. Chem. 2021, 86, 7552–7562 Read Online

ABSTRACT: The development of new catalytic processes based on abundantly available starting materials by cheap metals is always a fascinating task and marks an important transition in the chemical industry. Herein, a nickel-catalyzed acceptorless dehydrogenative coupling of alcohols with nitriles followed by decyanation of nitriles to access diversely substituted olefins is reported. This unprecedented C=C bond-forming methodology takes place in a tandem manner with the formation of formamide as a sole byproduct. The significant advantages of this strategy are the low-cost nickel catalyst, good functional group compatibility (ether, thioether, halo, cyano, ester, amino, N/O/S heterocycles; 43 examples), synthetic convenience, and high reaction selectivity and efficiency.

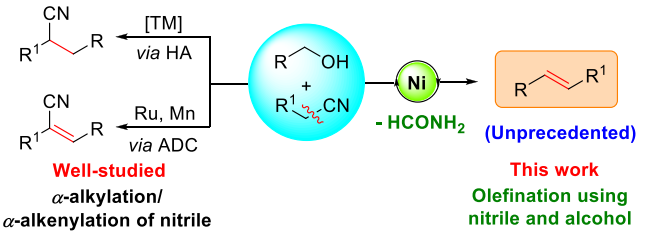


INTRODUCTION

Olefins are one of the most important organic scaffolds widely found in many natural products and have been effectively utilized as fundamental building blocks in the large-scale production of plastics and pharmaceuticals.[1] The Wittig reaction is the most commonly employed synthetic methodology for the selective synthesis of *E*-alkenes from carbonyl compounds.[2] Equally, Julia olefination,[3] the Peterson reaction,[4] and Tebbe olefination[5] are also broadly used approaches to access the substituted olefins. The classical approach to access linear or cyclic olefins is mainly based on a ruthenium-catalyzed metathesis reaction.[6] A significant number of transition-metal-catalyzed cross-coupling reactions have paid much attention to the (*E*)-olefin synthesis, including a Pd-catalyzed Heck-type coupling.[7]

In recent times, transition-metal-catalyzed acceptorless dehydrogenation (AD) and the hydrogen autotransfer (HA) strategy have been widely explored for the formation of C–C and C–N bonds using abundantly available alcohols as feedstocks.[8,9] Seminal works on ruthenium-catalyzed dehydrogenative Wittig and Julia-type olefination of alcohol were reported by the research group of Milstein[10a,b] and by others with different catalytic systems (Scheme 1).[10c] The same group reported an earth-abundant manganese-catalyzed direct condensation of alcohols into alkenes using hydrazine or hydrazone via acceptorless dehydrogenative coupling (ADC).[11] Of late, transition-metal-catalyzed dehydrogenative coupling of alcohols with nitrile to lead to α-alkylated or α-alkenylated arylacetonitriles with the liberation of hydrogen and/or water has been well studied via ADC and hydrogen autotransfer (HA) strategies.[12] It is noteworthy that Li and co-workers reported a rhodium-catalyzed direct coupling of arylacetonitriles and primary alcohols to α-alkylated arylacetamides.[13] Recent years have witnessed tremendous interest by various research groups in the use of well-defined nickel catalysts for the C–C and C–N bond formation via ADC and HA reactions.[14] Herein, an unprecedented reactivity in the dehydrogenative coupling of alcohols with nitriles to access diversely substituted (*E*)-olefins in contrast to the archetypical α-alkylated/alkenylated products is reported. This new C=C bond-forming methodology takes place via the ADC/decyanation tandem with the formation of formamide as the byproduct. Notably, the removal of the cyano group from organic molecules is very challenging.[15]

Scheme 1. Tandem Acceptorless Dehydrogenative Coupling–Decyanation in the Olefin Synthesis



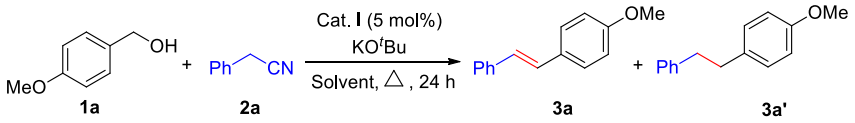
RESULT AND DISCUSSION

Initially, the reaction of 4-methoxybenzyl alcohol (**1a**) and 2-phenylacetonitrile (**2a**) was chosen as a model system for the Ni-catalyzed dehydrogenative coupling to form (*E*)-1-me-

Received: March 12, 2021
Published: May 25, 2021

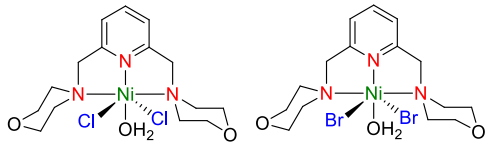
https://doi.org/10.1021/acs.joc.1c00592
J. Org. Chem. 2021, 86, 7552–7562

Table 1. Optimization Studies[a]



entry	Ni catalyst	base	solvent	temp (°C)	yield[b] (%) 3a/3a′
1	Cat. **I**	KO^{t}Bu	*n*-octane	135	64/22
2	Cat. **II**	KO^{t}Bu	*n*-octane	135	52/25
3	$NiCl_2{\cdot}6H_2O$	KO^{t}Bu	*n*-octane	135	27/15
4	Cat. **I**	KO^{t}Bu	toluene	135	42/20
5	Cat. **I**	KO^{t}Bu	THF	110	20/8
6	Cat. **I**	KO^{t}Bu	1,4-dioxane	135	33/18
7	Cat. **I**	KO^{t}Bu	*n*-octane	120	87/5[c]
8	Cat. **I**	KO^{t}Bu	*n*-octane	100	48/14[c]
9	–	KO^{t}Bu	*n*-octane	120	trace
10	Cat. **I**	–	*n*-octane	120	NR

[a]Reaction conditions: alcohol **1a** (1.2 mmol), nitrile **2a** (1.0 mmol), Cat. [**Ni**] (5 mol %), KO^{t}Bu (1.0 equiv), and solvent (1.5 mL) heated at 100−135 °C (oil-bath temperature) for 24 h. [b]Yield determined by GC using 1,4-dibromobutane as an internal standard. [c]Reaction using 1.2 mmol of KO^{t}Bu.



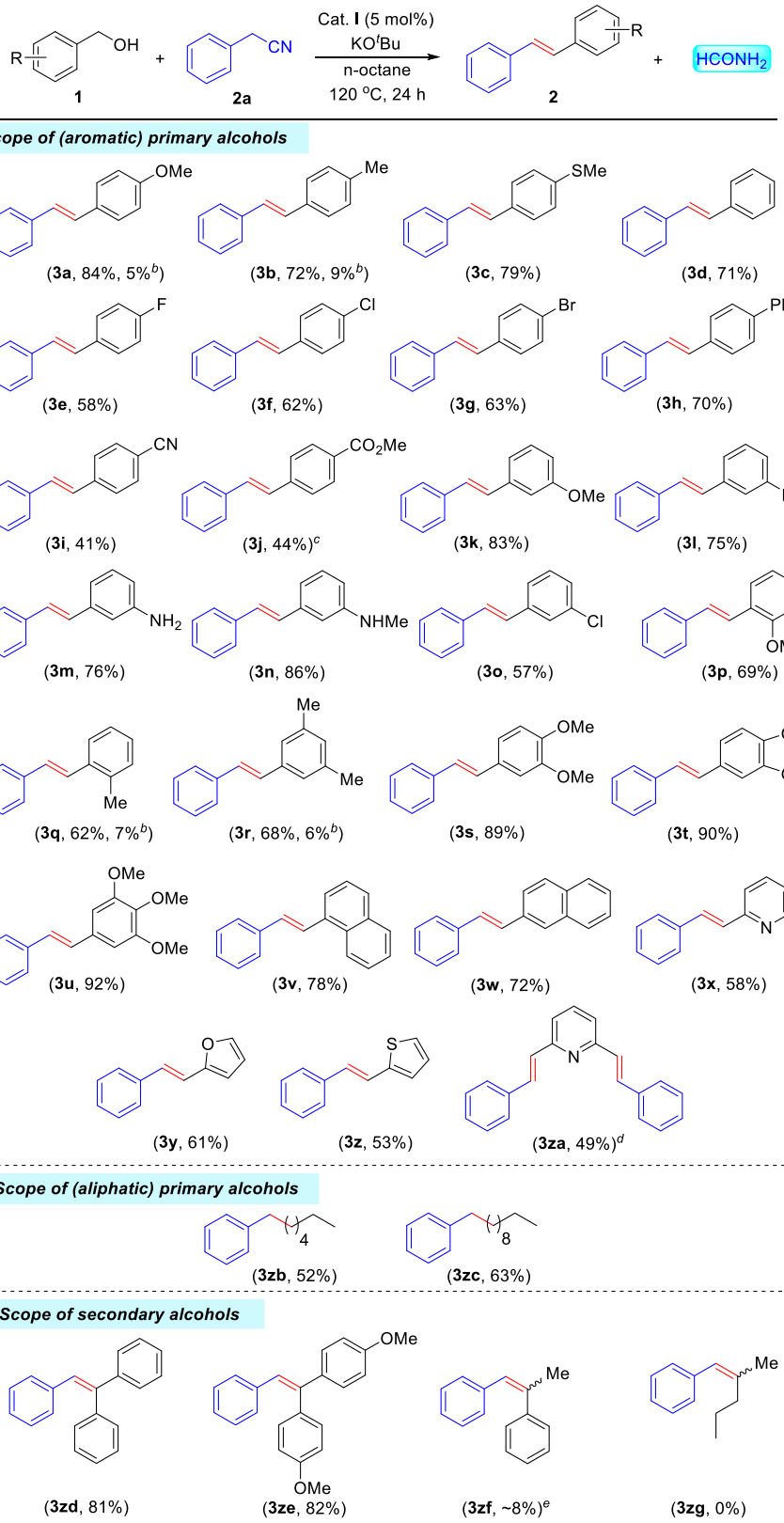
thoxy-4-styrylbenzene. After careful investigation of various parameters, such as the use of nickel catalysts, bases, solvents, and temperature (Table 1), the optimal reaction conditions were determined. Refluxing at 135 °C of **1a** (1.2 mmol), **2a** (1.0 mmol), and KO^{t}Bu (1.0 mmol) in *n*-octane in the presence of complex **I** (5 mol %) gave a 64% yield of (*E*)-1-methoxy-4-styrylbenzene **3a** along with 22% of 1-methoxy-4-phenethylbenzene **3a′** (Table 1, entry 1). Under similar reaction conditions, complex **II** gave **3a** and **3a′** in 52% and 25% yields, respectively (Table 1, entry 2). Other commercially available nickel salts such as $NiCl_2$, $Ni(acac)_2$, $Ni(OTf)_2$, and $NiCl_2(PMe_3)_2$ gave the product **3a** in poor yield (<32%; see the SI). Other solvents such as toluene, THF, and 1,4-dioxane were found to not be suitable for this transformation, and the results are unsatisfactory (Table 1, entries 4−6). Performing the reaction at 120 °C reduces the formation of **3a′** and selectively yields 87% of product **3a** (Table 1, entry 7). As the temperature is further lowered, a poor result was obtained (Table 1, entry 8). Decreasing the catalyst load and replacing KO^{t}Bu with either NaO^{t}Bu or LiO^{t}Bu provided considerably lower yields (see the SI). In control experiments performed by employing only base and without catalyst and base, no product formation was observed, indicating that the catalyst and base are essential for the success of the reaction.

Having optimal reaction conditions in hand, the scope of the various alcohols on dehydrogenative coupling with **2a** to access diverse (*E*)-alkenes was investigated. As shown in Table 2, a range of electron-rich primary alcohols (*p*-OMe, *p*-Me, and *p*-SMe) efficiently reacted with **2a** under the present Ni(II)-catalyzed conditions and afforded the corresponding alkene derivatives in excellent yields (products **3a**−**3c**; up to 84% yield). Electron-withdrawing halogen substituents (F-, Cl-, and Br-) at the *para* position of benzyl alcohol provided the products **3e**−**3g** in 58%, 62%, and 63% yields, respectively. A similar result was obtained in the case of *p*-CN- and *p*-CO_2Me-substituted benzyl alcohols (products **3i** in 41% and **3j** in 44% yields). However, *p*-CF_3-substituted benzyl alcohol did not yield the desired product under standard reaction conditions. This result indicates that the electronic nature of the substituent may play an important role in the present transformation. Thus, electron-rich *meta*-substituted alcohols were reacted smoothly with **2a** and yielded the corresponding stilbenes (**3k**−**3n**) in excellent yields. It is noteworthy that the unprotected amine group such as 3-aminobenzyl alcohol (**1m**) underwent the (*E*)-olefination reaction selectively and gave **3m** as a sole product in 76% yield. Remarkably, both sterically demanding *ortho*-substituted benzyl alcohols and multisubstituted benzyl alcohols were smoothly reacted with **2a** and afforded the desired products **3p**−**3u** in excellent yields (up to 92% yield). The bicyclic aromatic primary alcohols (1-naphthyl and 2-naphthyl) proceeded efficiently and yielded the corresponding (*E*)-alkenes in good yields (products **3v** in 78% and **3w** in 72% isolated yields). Notably, heteroaryl aromatic primary alcohols were well tolerated, and the corresponding olefinic products **3x**−**3z** were obtained in good yields. Interestingly, 2,6-pyridinedimethanol provided the corresponding diolefinated product **3za** in moderate yield. Under our optimal reaction conditions, aliphatic alcohols (1-hexanol and 1-decanol) selectively led to the saturated alkanes as the major product (**3zb** in 52% yield and **3zc** in 63% yield). Indeed, sterically hindered secondary alcohols such as 1,1-diarylmethanols (**1zd**−**1ze**) delivered the corresponding trisubstituted alkene derivatives **3zd** and **3ze** in good yields. However, α-methylbenzyl alcohol (**1zf**) and 2-pentanol (**1zg**) failed to yield the corresponding olefinated products **3zf** (~8% only) and **3zg**.

Next, the scope of this unprecedented catalytic dehydrogenative coupling of alcohols with nitriles was explored using various aryl nitriles (Table 3). Initially, 4-methoxybenzyl alcohol (**1a**) was chosen as a benchmark substrate to show the versatility of this transformation. Thus, the reaction of **1a** with electron-rich aryl nitriles proceeded smoothly and led to

https://doi.org/10.1021/acs.joc.1c00592
J. Org. Chem. 2021, 86, 7552−7562

Table 2. Nickel-Catalyzed Acceptorless Dehydrogenative Coupling–Decyanation: Scope of Alcohols[a]

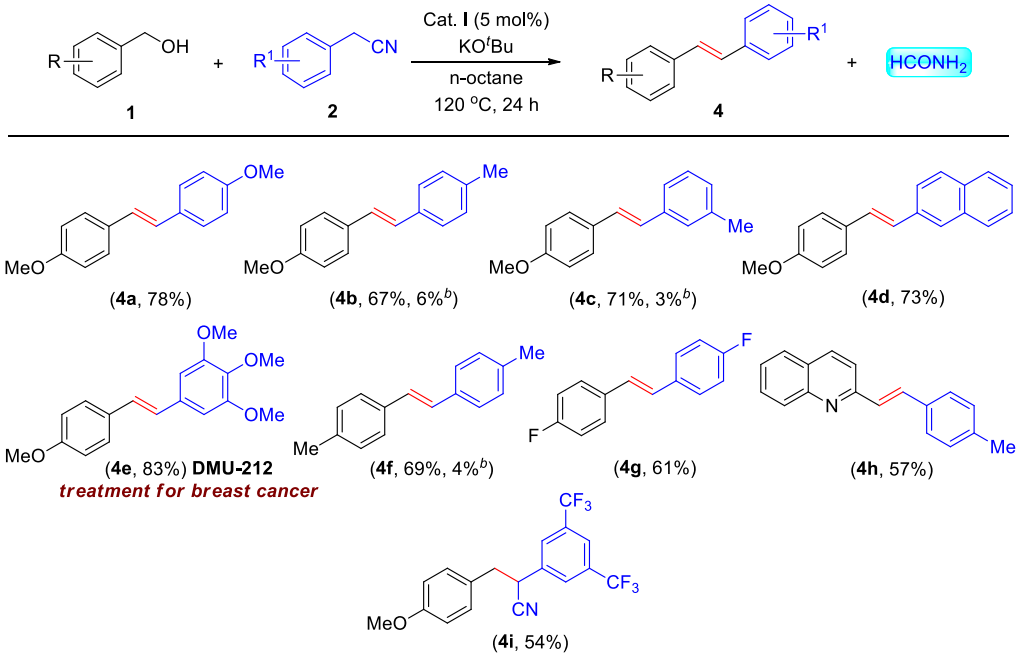


[a]Reaction conditions: alcohol **1** (1.2 mmol), nitrile **2a** (1.0 mmol), Cat. **I** (5 mol %), KO^{t}Bu (1.2 equiv), and *n*-octane (1.5 mL) heated at 120 °C (oil-bath temperature) for 24 h (isolated yields). [b]Yield of the corresponding hydrogenated product. [c]CH_3ONa was used as a base. [d]0.5 mmol of **2a**. [e]By GC and GC-MS.

the desired products **4a** in 78%, **4b** in 67%, **4c** in 71%, **4d** in 73%, and **4f** in 69% yields, respectively. To our delight, direct synthesis of DMU-212 (**4e**), a drug used for breast cancer treatment, has been achieved in excellent yield (83%). The

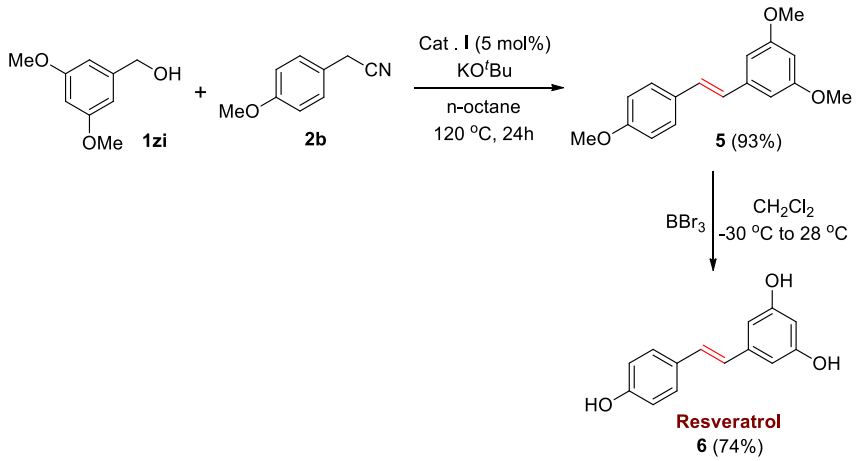
https://doi.org/10.1021/acs.joc.1c00592
J. Org. Chem. 2021, 86, 7552–7562

Table 3. Nickel-Catalyzed Acceptorless Dehydrogenative Coupling−Decyanation: Scope of Nitriles[a]



[a]Reaction conditions: alcohol **1** (1.2 mmol), nitrile **2** (1.0 mmol), Cat. **I** (5 mol %), KO^{t}Bu (1.2 equiv), and *n*-octane (1.5 mL) heated at 120 °C (oil-bath temperature) for 24 h (isolated yields). [b]Yield of the corresponding hydrogenated product.

Scheme 2. Direct Synthesis of Resveratrol (6)



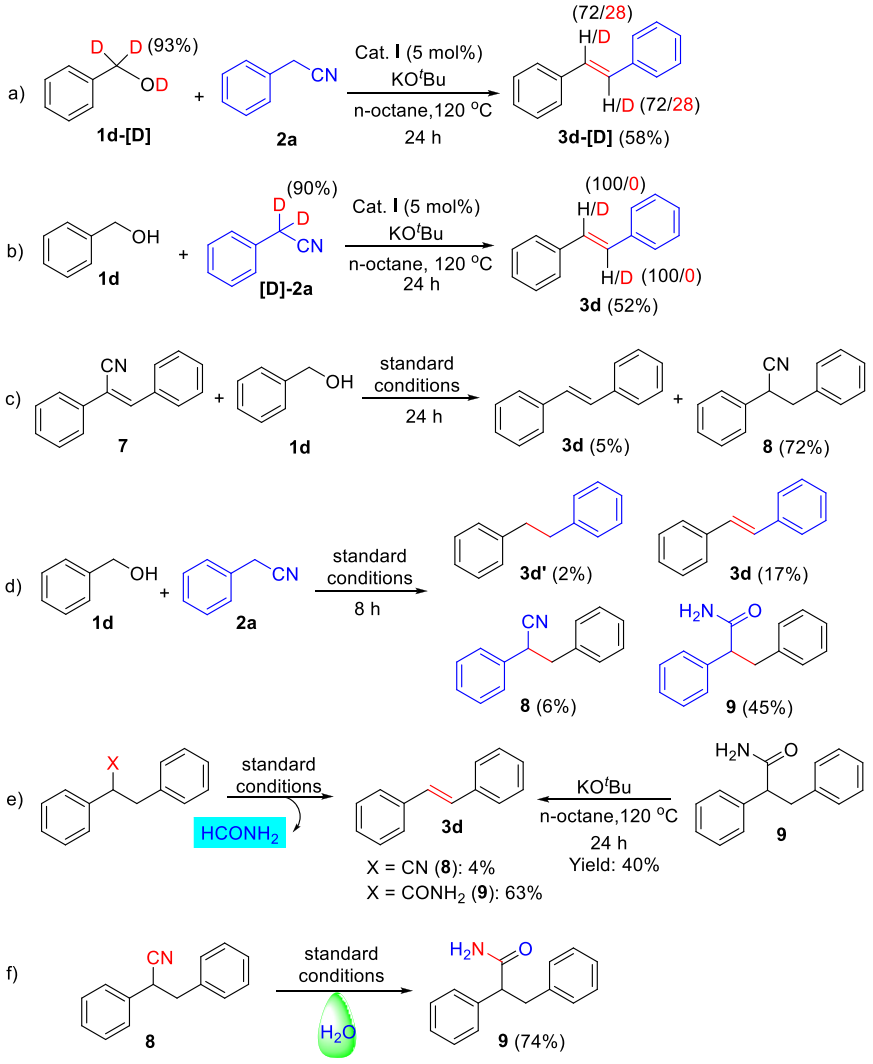
reaction of electron-deficient aryl nitrile such as 2-(4-fluorophenyl)acetonitrile **2g** with 4-fluorobenzyl alcohol **1g** under the optimal conditions provided **4g** in moderate yield. Moreover, heterocyclic alcohol **1h** with 4-methyl phenylacetonitrile resulted in the corresponding *trans*-alkene **4h** in 57% yield. Notably, the reaction of **1a** and highly electron-deficient 3,5-bis(trifluoromethyl) phenylacetonitrile **2i** led to the α-alkylated nitrile product **4i** in moderate yield (54%) as the sole product.

Gratifyingly, we have successfully demonstrated the scalability of this catalytic protocol under mild conditions. In this regard, the present nickel-catalyzed dehydrogenative coupling was tested for a large-scale synthesis of **3d**, **3v**, and **3zd** (5.0 mmol scale), and it worked excellently and afforded the corresponding products in good yields. Next, we have extended our synthetic strategy for synthesis of pharmaceutically important molecules. As a result, we have established a step-economic process to *resveratrol* (**6**), a pan-assay interference compound[16] (Scheme 2).

To gain insight into the reaction mechanism, several control experiments were performed (Scheme 3). GC analysis of the model reaction system (in the absence of **2a**) indicated the formation of the dehydrogenated product (4-methoxybenzaldehyde) and hydrogen gas. This result shows that the initial step is the acceptorless dehydrogenation pathway of alcohol. Deuterium-labeling experiments were conducted, and the results suggest the involvement of hydrogen autotransfer strategy in the overall process and that one of the two benzylic C−D/H bonds of alcohol needs to be cleaved in order to initiate the α-alkylation reaction (Scheme 3a). Reaction of benzyl alcohol (**1d**) with deuterated phenyl acetonitrile [**D**]-**2a** resulted in 52% yield of **3d** without deuterium incorporation. No deuteration in the olefinic product suggests that the benzylic hydrogen of the nitrile derivative is not taking part in

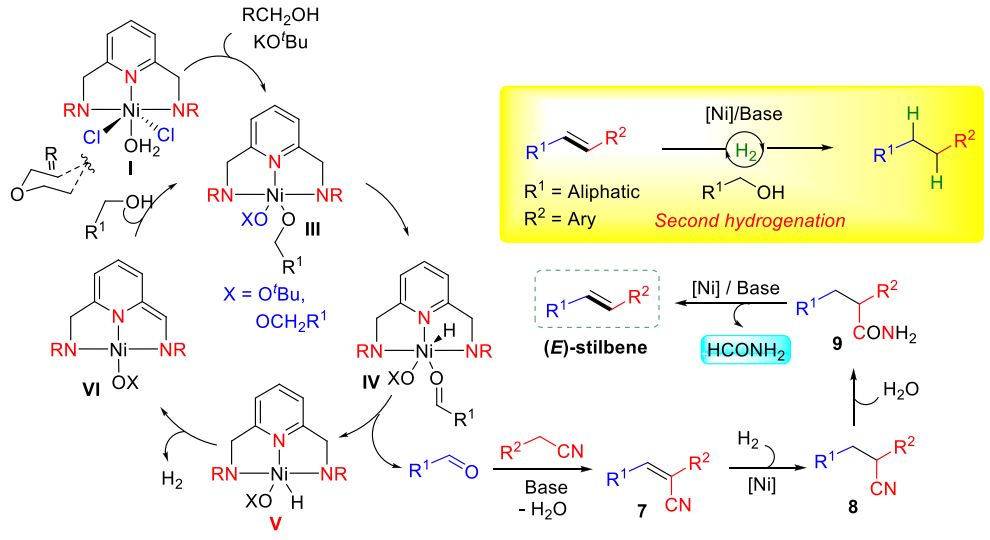
https://doi.org/10.1021/acs.joc.1c00592
J. Org. Chem. 2021, 86, 7552−7562

Scheme 3. Mechanistic Studies[a]



[a]Standard conditions: Cat. **I** (5 mol %), KO^{t}Bu (1.2 equiv), and *n*-octane (1.5 mL) heated at 120 °C (oil-bath temperature).

Scheme 4. Plausible Mechanism



the hydrogen autotransfer reaction (Scheme 3b). A control experiment showed that phenylacetonitrile undergoes the base-catalyzed Knoevenagel condensation with the *in situ* generated aldehyde intermediate. Treatment of α-alkenylated nitrile

https://doi.org/10.1021/acs.joc.1c00592
J. Org. Chem. 2021, 86, 7552−7562

(7)[12h] with benzyl alcohol (**1d**) resulted in 72% yield of the α-alkylated nitrile (**8**) and 5% yield of the desired product (**3d**), which suggests the involvement of the hydrogen autotransfer step in the present catalysis. Furthermore, experiments aimed at identifying the possible potential intermediates were performed (Scheme 3c,d). When alcohol **1d** was reacted with nitrile **2a** under standard reaction conditions for 8 h, it resulted in a mixture of products. GC and GC-MS analyses of this reaction mixture exhibited the formation of 1,2-diphenylethane (**3d′**, 2%), (*E*)-stilbene (**3d**, 17%), α-alkylated nitrile (**8**, 6%), and α-alkylated amide (**9**, 45%). This observation signifies that α-alkylated amide and/or α-alkylated nitrile are the potential intermediates. To gain insight into the final elimination step, both α-alkylated nitrile (**8**) and α-alkylated amide (**9**) were separately prepared[12e,13] and employed in the present nickel catalysis (Scheme 3e). This result clearly indicates that the final elimination step is more facile in the case of α-alkylated amide and leads to the formation of formamide as the sole byproduct. The control experiment also indicates that a base-mediated E2 elimination is operative, and nickel catalyst promotes the E2 elimination. Finally, the hydration of **8** was examined. We believe that the hydration of α-alkylated arylacetonitriles **8** with water, which results from the Knoevenagel condensation step, produces the α-alkylated arylacetamide **9** suggested by Li and coworkers.[13] When the N^3−Ni(II) complex/KO^{t}Bu system was employed, the reaction of **8** with an equimolar amount of water was performed and yielded **9** in 74% yield (Scheme 3f).

Based on the mechanistic studies and our previous works, a plausible mechanism for the *N*,*N*,*N*-nickel(II)-catalyzed tandem acceptorless dehydrogenative coupling−decyanation in the olefin synthesis is depicted in Scheme 4. Initially, in the presence of alcohol and base, the *N*,*N*,*N*-Ni(II)Cl_2 complex **I** undergoes a displacement reaction with chloride ligand to give complex **III**. The complex **III** undergoes β-hydride elimination (of alkoxide) to lead to the corresponding aldehyde and with the formation of Ni−H species **IV**. The complex **VI** was generated from complex **V** with the liberation of H_2. Finally, the complex **VI** reacts with alcohol to regenerate the catalyst **I**. Followed by the initial dehydrogenation of alcohol under Ni catalysis, the *in situ* generated aldehyde undergoes the Knoevenagel condensation with nitrile and led to vinyl nitrile (**7**) by the elimination of a water molecule. Next, the α-alkenylated intermediate **7** undergoes catalytic (transfer)-hydrogenation to lead to the α-alkylated product **8** by *in situ* generated hydrogen from the initial dehydrogenation of alcohol. Finally, intermediate **8** undergoes hydrolysis (by water resulting from the α-alkenylation step) to produce α-alkylated arylacetamide (**9**). Subsequent elimination of formamide from **9** eventually delivers the product (*E*)-stilbene. The formation of saturated alkanes was observed in the case of aliphatic alcohols due to the further hydrogenation (double HA) of the corresponding olefinated product.

CONCLUSION

In summary, we have disclosed an unprecedented tandem acceptorless dehydrogenative coupling−decyanation in the olefin synthesis. This new C=C bond forming methodology is catalyzed by nickel and affords diversely substituted (*E*)-olefins (43 examples; up to 92% yield) with the formation of formamide as the only byproduct. Several control and labeling experiments provide the basis for our assertion that the reaction proceeds via the borrowing hydrogenation.

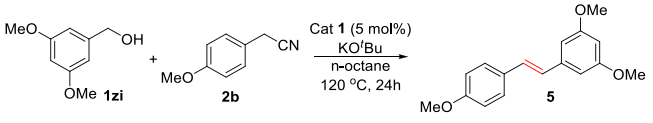
EXPERIMENTAL SECTION

1. General Information. All catalytic experiments were carried out using standard Schlenk techniques. All solvents were reagent grade or better. Deuterated solvents were used as received. Nickel salt precursors were used without additional purification. All the starting materials (alcohols (**1**) and nitriles (**2**)) are commercially available and were purified according to the standard procedure.[17] The ligand 2,6-bis(morpholinomethyl)pyridine and the corresponding Ni(II) complexes (**I**−**II**) were synthesized based on the reported procedure. Thin-layer chromatography (TLC) was performed using silica gel 60 F_{254} coated on an aluminum sheet purchased from Merck, which was visualized with UV light at 254 nm or under iodine. Column chromatography was performed with SiO_2 (SilicycleSilicaflash F60 (230−400 mesh)). ^{1}H NMR (200, 400, or 500 MHz) and ^{13}C NMR (50, 100, or 126 MHz) spectra were recorded on the NMR spectrometer. Deuterated chloroform was used as the solvent, and chemical shift values (δ) are reported in parts per million relative to the residual signals of this solvent [δ 7.27 for ^{1}H (chloroform-*d*), δ 77.0 for ^{13}C (chloroform-*d*)]. Abbreviations used in the NMR follow-up experiments: br, broad; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. GC analysis was carried out using an HP-5 column (30 m, 0.25 mm, 0.25 μ). Mass spectra were obtained on a GCMS-QP 5000 instrument with ionization voltages of 70 eV. High-resolution mass spectra (HRMS) were obtained by fast atom bombardment (FAB) using a double focusing magnetic sector mass spectrometer and electron impact (EI) ionization technique (magnetic sector−electric sector double focusing mass analyzer).

2A. General Procedure for the Ni-Catalyzed Synthesis of (*E*)-Stilbene. To an oven-dried 15 mL ace pressure tube were added alcohol **1** (1.2 mmol), nitrile **2** (1.0 mmol), Ni-complex **I** (5 mol %, 21 mg), and KO^{t}Bu (1.2 mmol, 134 mg) in *n*-octane (1.5 mL) under a gentle stream of argon. The mixture was heated at 120 °C (oil-bath temperature) for 24 h followed by cooling to room temperature. The reaction mixture was diluted with water (4 mL) and extracted with dichloromethane (3 × 5 mL). The resultant organic layer was dried over anhydrous Na_2SO_4, and the solvent was evaporated under reduced pressure. The crude mixture was purified by silica gel column chromatography (230−400 mesh size) using petroleum-ether/ethyl acetate as an eluting system.

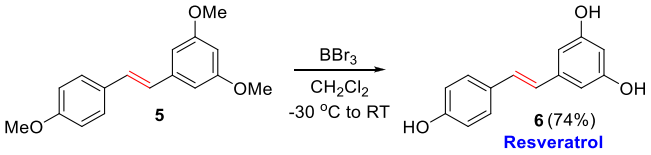
2B. Large-Scale Synthesis of 3d, 3v, and 3zd. To an oven-dried 35 mL ace pressure tube were added alcohol **1d** or **1v** or **1zd** (5.5 mmol), nitrile **2** (5.0 mmol), Ni-complex **I** (5 mol %, 105 mg), and KO^{t}Bu (5.5 mmol, 616 mg) in *n*-octane (8 mL) under a gentle stream of argon. The mixture was heated at 120 °C (oil-bath temperature) for 36 h followed by cooling to room temperature. The reaction mixture was diluted with water (15 mL) and extracted with dichloromethane (3 × 10 mL). The resultant organic layer was dried over anhydrous Na_2SO_4, and the solvent was evaporated under reduced pressure. The crude mixture was purified by silica gel column chromatography (230−400 mesh size) using petroleum-ether/ethyl acetate as an eluting system and yielded the desired products **3d**, **3v**, and **3zd** in 68% (612 mg), 80% (920 mg), and 87% (1.11 g) yields, respectively.

2C. Two-Step synthesis of *Resveratrol*. To an oven-dried 15 mL ace pressure tube were added alcohol **1zi** (1.2 mmol, 201 mg),



nitrile **2b** (1.0 mmol, 147 mg), Ni-complex **I** (5 mol %, 21 mg), and KO^{t}Bu (1.2 mmol, 134 mg) in *n*-octane (1.5 mL) under a gentle stream of argon. The mixture was of heated at 120 °C for 24 h followed by cooling to room temperature. The reaction mixture was diluted with water (4 mL) and extracted with dichloromethane (3 × 5 mL). The resultant organic layer was dried over anhydrous Na_2SO_4, and the solvent was evaporated under reduced pressure. The crude mixture was purified by silica gel column chromatography (230−400 mesh size) using petroleum-ether/ethyl acetate as an eluting system.

https://doi.org/10.1021/acs.joc.1c00592
J. Org. Chem. 2021, 86, 7552−7562



To a 15 mL clean, oven-dried screw cap reaction tube were added **5** (0.5 mmol, 135 mg) and samarium(II) iodide (THF solution, 8 equiv, 1.6 g) followed by Et_3N (72 equiv, 0.5 mL) and H_2O (72 equiv, 0.65 mL) under argon atmosphere, resulting in the formation of a dark brown color of the SmI_2−Et_3N−H_2O complex. Then the reaction mixture was stirred for 24 h at room temperature. After the completion of reaction, the reaction mixture was diluted with CH_2Cl_2 and NaOH (1 N) solution. The aqueous layer was extracted with CH_2Cl_2 (3 × 30 mL), and the combined organic layers were dried over Na_2SO_4 and concentrated. The crude mixture was purified by silica gel column chromatography (230−400 mesh size) using CH_2Cl_2/MeOH as an eluting system.

3. Characterization Data of Compounds. *(E)-1-Methoxy-4-styrylbenzene (**3a**).*[18a] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. White solid. Yield: 84%, 176 mg. ^{1}H NMR (200 MHz, chloroform-*d*) δ = 7.51−7.44 (m, 4H), 7.35 (t, *J* = 7.0 Hz, 2H), 7.27−7.23 (m, 1H), 7.02 (d, *J* = 7.4 Hz, 2H), 6.90 (d, *J* = 9.1 Hz, 2H), 3.83 (s, 3H). ^{13}C{^{1}H} NMR (50 MHz, CHLOROFORM-d) δ = 159.2, 137.6, 130.1, 128.6, 128.1, 127.7, 127.1, 126.6, 126.2, 114.1, 55.3.

*(E)-1-Methyl-4-styrylbenzene (**3b**).*[18a] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. White solid. Yield: 72%, 139.7 mg. ^{1}H NMR (200 MHz, chloroform-*d*) δ = 7.42 (d, *J* = 7.7 Hz, 2H), 7.37−7.28 (m, 3H), 7.24−7.17 (m, 2H), 7.10 (d, *J* = 6.8 Hz, 2H), 7.01 (s, 2H), 2.29 (s, 3H). ^{13}C NMR{^{1}H} (101 MHz, chloroform-*d*) δ = 137.5, 134.5, 129.4, 128.7, 128.6, 127.7, 127.4, 126.4, 21.2.

*(E)-Methyl-(4-styrylphenyl)sulfane (**3c**).*[18c] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. White solid. Yield: 79%, 178.5 mg. ^{1}H NMR (200 MHz, chloroform-*d*) δ = 7.52−7.46 (m, 3H), 7.42−7.32 (m, 3H), 7.27−7.22 (m, 3H), 7.06 (s, 2H), 2.50 (s, 3H). ^{13}C NMR{^{1}H} (50 MHz, chloroform-*d*) δ = 137.8, 137.3, 134.3, 128.6, 128.0, 127.5, 126.8, 126.6, 126.3, 15.7.

*(E)-1,2-Diphenylethene (**3d**).*[18a] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. White solid. Yield: 71%, 127.8 mg. ^{1}H NMR (200 MHz, chloroform-*d*) δ = 7.52 (d, *J* = 7.1 Hz, 4H), 7.36 (t, *J* = 8.3 Hz, 4H), 7.29−7.25 (m, 2H), 7.11 (s, 2H). ^{13}C NMR{^{1}H} (50 MHz, chloroform-*d*) δ = 137.3, 128.7, 128.5, 128.4, 127.6, 126.5.

*(E)-1-Fluoro-4-styrylbenzene (**3e**).*[18a] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. White solid. Yield: 58%, 115 mg. ^{1}H NMR (200 MHz, chloroform-*d*) δ = 7.52−7.44 (m, 4H), 7.39−7.35 (m, 1H), 7.33−7.29 (m, 2H), 7.09−7.00 (m, 4H). ^{13}C NMR{^{1}H} (50 MHz, chloroform-*d*) δ = 164.8, 159.9, 137.2, 133.4, 128.7, 128.1, 127.9, 127.6, 127.4, 126.4, 115.8, 115.4.

*(E)-1-Chloro-4-styrylbenzene (**3f**).*[18a] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. White solid. Yield: 62%, 132 mg. ^{1}H NMR (200 MHz, chloroform-*d*) δ = 7.52 (d, *J* = 8.7 Hz, 4H), 7.41−7.30 (m, 5H), 7.12 (s, 2H). ^{13}C NMR{^{1}H} (50 MHz, chloroform-*d*) δ = 136.9, 136.1, 128.9, 128.8, 128.6, 127.6, 126.5.

*(E)-1-Bromo-4-styrylbenzene (**3g**).*[18b] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. White solid. Yield: 63%, 154 mg. ^{1}H NMR (200 MHz, chloroform-*d*) δ = 7.65−7.49 (m, 4H), 7.49−7.30 (m, 6H), 7.11 (d, *J* = 3.7 Hz, 2H). ^{13}C NMR{^{1}H} (50 MHz, chloroform-*d*) δ = 136.9, 136.3, 131.8, 129.4, 128.7, 127.9, 127.9, 127.4, 126.5, 121.3.

*(E)-4-Styryl-1,1′-biphenyl (**3h**).*[18b] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. White solid. Yield: 70%, 179 mg. ^{1}H NMR (200 MHz, chloroform-*d*) δ = 7.58−7.18 (m, 14H), 7.08 (s, 2H). ^{13}C NMR{^{1}H} (50 MHz, chloroform-*d*) δ = 140.7, 140.3, 137.3, 136.4, 128.8, 128.7, 128.2, 127.6, 127.3, 126.9, 126.5.

*(E)-4-Styrylbenzonitrile (**3i**).*[18a] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. White solid. Yield: 41%, 84 mg. ^{1}H NMR (200 MHz, chloroform-*d*) δ 7.59−7.44 (m, 6H), 7.35−7.24 (m, 3H), 7.15 (d, *J* = 14.7 Hz, 1H), 7.00 (d, *J* = 16.2 Hz, 1H). ^{13}C NMR{^{1}H} (50 MHz, chloroform-*d*) δ = 141.8, 136.2, 132.4, 128.8, 128.6, 126.9, 126.8, 126.7, 118.9, 110.5.

*(E)-Methyl 4-styrylbenzoate (**3j**).*[18a] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. White solid. Yield: 44%, 104 mg. ^{1}H NMR (500 MHz, chloroform-*d*) δ = 7.95 (d, *J* = 8.3 Hz, 2H), 7.49−7.45 (m, 4H), 7.31−7.28 (t, *J* = 7.6 Hz, 2H), 7.23−7.20 (m, 1H), 7.13 (d, *J* = 16.4 Hz, 1H), 7.04 (d, *J* = 16.4 Hz, 1H), 3.84 (s, 3H). ^{13}C NMR{^{1}H} (126 MHz, chloroform-*d*) δ = 166.9, 141.8, 136.7, 131.2, 130.0, 128.9, 128.7, 128.2, 127.5, 126.7, 126.3, 52.0.

*(E)-1-Methoxy-3-styrylbenzene (**3k**).*[18c] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. White solid. Yield: 83%, 174 mg. ^{1}H NMR (200 MHz, chloroform-*d*) δ = 7.52 (d, *J* = 8.9 Hz, 2H), 7.37 (t, *J* = 7.8 Hz, 2H), 7.29−7.24 (m, 2H), 7.14−7.06 (m, 4H), 6.83 (d, *J* = 7.8 Hz, 1H), 3.85 (s, 3H). ^{13}C NMR{^{1}H} (50 MHz, chloroform-*d*) δ = 159.9, 138.8, 137.2, 129.6, 128.9, 128.6, 128.5, 127.6, 126.5, 119.2, 113.3, 111.7, 55.2.

*(E)-1-Methyl-3-styrylbenzene (**3l**).*[18c] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. White solid. Yield: 75%, 145 mg. ^{1}H NMR (200 MHz, chloroform-*d*) δ = 7.41 (d, *J* = 7.7 Hz, 2H), 7.28−7.20 (m, 4H), 7.18−7.10 (m, 3H), 6.99 (s, 2H), 2.27 (s, 3H). ^{13}C NMR{^{1}H} (50 MHz, chloroform-*d*) δ = 138.1, 137.4, 137.2, 128.7, 128.6, 128.5, 128.4, 127.5, 127.2, 126.4, 123.7, 21.4.

*(E)-3-Styrylaniline (**3m**).*[18b] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. Brown solid. Yield: 76%, 148 mg. ^{1}H NMR (200 MHz, chloroform-*d*) δ = 7.43 (d, *J* = 9.4 Hz, 2H), 7.28 (t, *J* = 6.2 Hz, 2H), 7.19 (d, *J* = 6.2 Hz, 1H), 7.06 (d, *J* = 6.2 Hz, 1H), 6.97 (s, 2H), 6.86 (d, *J* = 9.4 Hz, 1H), 6.78 (s, 1H), 6.54 (d, *J* = 8.6 Hz, 1H), 3.61 (s, 2H). ^{13}C NMR{^{1}H} (50 MHz, chloroform-*d*) δ = 146.6, 138.4, 137.4, 129.6, 128.8, 128.6, 128.5, 127.5, 126.5, 117.3, 114.7, 112.9.

*(E)-N-Methyl-3-styrylaniline (**3n**).*[18d] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc

https://doi.org/10.1021/acs.joc.1c00592
J. Org. Chem. 2021, 86, 7552−7562

as an eluent. White solid. Yield: 86%, 179 mg. ^{1}H NMR (200 MHz, chloroform-*d*) δ = 7.50 (d, *J* = 7.4 Hz, 2H), 7.35 (t, *J* = 8.3 Hz, 2H), 7.25 (d, *J* = 8.3 Hz, 1H), 7.18 (t, *J* = 8.0 Hz, 1H), 7.06 (s, 2H), 6.89 (d, *J* = 7.1 Hz, 1H), 6.74 (s, 1H), 6.53 (d, *J* = 6.6 Hz, 1H), 2.86 (s, 3H). ^{13}C NMR{^{1}H} (50 MHz, chloroform-*d*) δ = 148.8, 138.3, 137.4, 129.5, 129.1, 128.6, 128.5, 127.5, 126.5, 116.6, 112.7, 110.8, 31.2.

*(E)-1-Chloro-3-styrylbenzene (**3o**).*[18a] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. White solid. Yield: 57%, 112.5 mg. ^{1}H NMR (200 MHz, chloroform-*d*) δ = 7.53−7.49 (m, 3H), 7.40−7.20 (m, 6H), 7.12 (d, *J* = 16.2 Hz, 1H), 7.01 (d, *J* = 16.4 Hz, 1H). ^{13}C NMR{^{1}H} (50 MHz, chloroform-*d*) δ = 139.2, 136.8, 134.6, 130.1, 129.7, 128.7, 128.0, 127.5, 127.2, 126.6, 126.3, 124.7.

*(E)-1-Methoxy-2-styrylbenzene (**3p**).*[18c] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. White solid. Yield: 69%, 145 mg. ^{1}H NMR (200 MHz, chloroform-*d*) δ = 7.54−7.38 (m, 4H), 7.27 (t, *J* = 7.2 Hz, 2H), 7.20−7.12 (m, 2H), 7.03 (d, *J* = 15.5 Hz, 1H), 6.93−6.80 (m, 2H), 3.80 (s, 3H). ^{13}C NMR{^{1}H} (50 MHz, chloroform-*d*) δ = 156.9, 137.9, 129.1, 128.6, 128.6, 127.3, 126.5, 126.4, 123.5, 120.7, 110.9, 55.5.

*(E)-1-Methyl-2-styrylbenzene (**3q**).*[18a] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. White solid. Yield: 62%, 120 mg. ^{1}H NMR (200 MHz, chloroform-*d*) δ = 7.61−7.51 (m, 3H), 7.37 (t, *J* = 6.1 Hz, 2H), 7.31−7.25 (m, 2H), 7.21−7.14 (m, 3H), 7.00 (d, *J* = 16.6 Hz, 1H), 2.43 (s, 3H). ^{13}C NMR{^{1}H} (50 MHz, chloroform-*d*) δ = 136.5, 135.8, 130.4, 129.9, 128.6, 127.6, 126.5, 126.2, 125.3, 19.9.

*(E)-1,3-Dimethyl-5-styrylbenzene (**3r**).*[18e] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. White solid. Yield: 68%, 141 mg. ^{1}H NMR (200 MHz, chloroform-*d*) δ = 7.51 (d, *J* = 7.7 Hz, 2H), 7.35 (t, *J* = 7.1 Hz, 2H), 7.28−7.22 (m, 1H), 7.19−7.14 (m, 2H), 7.07 (s, 2H), 6.88 (d, *J* = 14.8 Hz, 1H), 2.34 (s, 6H). ^{13}C NMR{^{1}H} (50 MHz, chloroform-*d*) δ = 138.1, 129.5, 128.8, 128.6, 128.3, 127.4, 126.4, 124.4, 21.3.

*(E)-1,2-Dimethoxy-4-styrylbenzene (**3s**).*[10e] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. White solid. Yield: 89%, 213.6 mg. ^{1}H NMR (400 MHz, chloroform-*d*) δ = 7.52 (d, *J* = 7.6 Hz, 2H), 7.37 (t, *J* = 8.0 Hz, 2H), 7.31−7.21 (m, 1H), 7.13−7.05 (m, 3H), 7.04−6.95 (m, 1H), 6.88 (d, *J* = 8.4 Hz, 1H), 3.97 (s, 3H), 3.92 (s, 3H). ^{13}C NMR{^{1}H} (100 MHz, chloroform-*d*) δ = 149.0, 148.9, 137.5, 130.4, 128.6, 128.4, 127.2, 126.7, 126.2, 119.8, 111.1, 108.7, 55.9, 55.8.

*(E)-5-Styrylbenzo[d][1,3]dioxole (**3t**).*[10e] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. Yellowish solid. Yield: 90%, 201.6 mg. ^{1}H NMR (200 MHz, chloroform-*d*) δ = 7.50−7.46 (m, 2H), 7.34−7.25 (m, 3H), 7.07 (d, *J* = 1.6 Hz, 1H), 7.00−6.93 (m, 3H), 6.80 (d, *J* = 8.0 Hz, 1H), 5.97 (s, 2H). ^{13}C NMR{^{1}H} (50 MHz, chloroform-*d*) δ = 148.1, 147.3, 137.4, 131.9, 128.6, 128.3, 127.3, 127.0, 126.3, 121.5, 108.4, 105.5, 101.1.

*(E)-1,2,3-Trimethoxy-5-styrylbenzene (**3u**).*[10e] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. White solid. Yield: 92%, 248 mg. ^{1}H NMR (200 MHz, chloroform-*d*) δ = 7.45−7.56 (m, 2H), 7.24−7.42 (m, 3H), 7.02 (s, 2H), 6.74 (s, 2H), 3.92 (s, 6H), 3.87 (s, 3H). ^{13}C NMR{^{1}H} (50 MHz, chloroform-*d*) δ = 153.4, 138.0, 137.2, 133.1, 128.7, 128.2, 127.6, 126.4, 103.6, 61.0, 56.1.

*(E)-1-Styrylnaphthalene (**3v**).*[10e] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. White solid. Yield: 78%, 179 mg. ^{1}H NMR (200 MHz, chloroform-*d*) δ = 8.15 (d, *J* = 8.0 Hz, 1H), 7.83−7.67 (m, 4H), 7.55−7.41 (m, 4H), 7.33 (t, *J* = 7.6 Hz, 2H), 7.28−7.22 (m, 1H), 7.18−7.01 (m, 2H). ^{13}C NMR{^{1}H} (126 MHz, chloroform-*d*) δ = 137.6, 135.0, 133.7, 131.7, 131.4, 129.0, 128.7, 128.6, 128.0, 127.8, 126.7, 126.1, 125.8, 125.7, 123.8, 123.6.

*(E)-2-Styrylnaphthalene (**3w**).*[10e] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. White solid. Yield: 72%, 165.5 mg. ^{1}H NMR (200 MHz, chloroform-*d*) δ = 7.77−7.68 (m, 5H), 7.48 (d, *J* = 8.8 Hz, 2H), 7.41−7.35 (m, 2H), 7.28 (d, *J* = 2H), 7.24−7.17 (m, 3H). ^{13}C NMR{^{1}H} (50 MHz, chloroform-*d*) δ = 137.37, 134.8, 133.7, 133.0, 129.0, 128.8, 128.7, 128.3, 127.9, 127.7, 126.6, 126.5, 126.3, 125.9, 123.5.

*(E)-2-Styrylpyridine (**3x**).*[18e] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. Light brown solid. Yield: 58%, 105 mg. ^{1}H NMR (400 MHz, chloroform-*d*): δ = 8.59−8.61 (m, 1H), 7.61−7.68 (m, 2H), 7.57−7.60 (m, 2H), 7.36−7.39 (m, 3H), 7.27−7.32 (m, 1H), 7.13−7.19 (m, 2H). ^{13}C NMR{^{1}H} (100 MHz, chloroform-*d*): δ = 155.7, 149.8, 136.7, 136.7, 132.8, 128.8, 128.4, 128.0, 127.2, 122.2.

*(E)-2-Styrylfuran (**3y**).*[10e] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. White solid. Yield: 61%, 103.5 mg. ^{1}H NMR (200 MHz, chloroform-*d*) δ = 7.51 (d, *J* = 7.3 Hz, 2H), 7.50−7.43 (m, 3H), 7.30 (d, *J* = 7.3 Hz, 1H), 7.09 (d, *J* = 15.9 Hz, 1H), 6.95 (d, *J* = 16.5 Hz, 1H), 6.59−6.43 (m, 1H), 6.40 (d, *J* = 3.1 Hz, 1H). ^{13}C NMR{^{1}H} (100 MHz, chloroform-*d*) δ = 153.3, 142.1, 137.0, 128.7, 127.6, 127.1, 126.3, 116.5, 111.6, 108.5.

*(E)-2-Styrylthiophene (**3z**).*[10e] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. Yellow solid. Yield: 53%, 98.5 mg. ^{1}H NMR (200 MHz, chloroform-*d*) δ = 7.51−7.46 (m, 2H), 7.39−7.29 (m, 3H), 7.26−7.19 (m, 2H), 7.08 (d, *J* = 2.9 Hz, 1H), 7.04−7.00 (m, 1H), 6.94 (d, *J* = 16.2 Hz, 1H). ^{13}C NMR{^{1}H} (50 MHz, chloroform-*d*) δ 142.9, 136.9, 128.7, 128.3, 127.6, 126.3, 126.1, 124.3, 121.8.

*2,6-Distyrylpyridine (**3za**).*[18e] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. White solid. Yield: 49%, 138.7 mg. ^{1}H NMR (400 MHz, chloroform-*d*) δ = 7.71 (d, *J* = 15.6 Hz, 2H), 7.65 (t, *J* = 7.8 Hz, 1H), 7.62 (d, *J* = 7.8 Hz, 3H), 7.39 (t, *J* = 7.8 Hz, 4H), 7.32−7.26 (m, 5H), 7.22 (d, *J* = 16.1 Hz, 2H). ^{13}C NMR{^{1}H} (100 MHz, chloroform-*d*) δ = 155.4, 136.9, 136.8, 132.9, 128.7, 128.3, 128.3, 127.1, 120.4.

*Heptylbenzene (**3zb**).*[18f] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. Sticky liquid. Yield: 52%, 91.5 mg. ^{1}H NMR (200 MHz, chloroform-*d*) δ = 7.26−7.09 (m, 5H), 2.53 (d, *J* = 6.2 Hz, 2H), 1.56−1.50 (m, 2H), 1.28−1.20 (m, 8H), 0.81 (t, *J* = 6.2 Hz, 3H). ^{13}C NMR{^{1}H} (50 MHz, chloroform-*d*) δ = 142.9, 128.4, 128.2, 125.9, 125.5, 36.0, 31.9, 31.5, 29.6, 29.5, 29.3, 22.7, 14.1.

*Undecylbenzene (**3zc**).*[18f] The title compound was synthesized according to the general procedure described in section 2A. The

https://doi.org/10.1021/acs.joc.1c00592
J. Org. Chem. 2021, 86, 7552−7562

product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. Sticky liquid. Yield: 63%, 144 mg. ^{1}H NMR (200 MHz, chloroform-*d*) δ = 7.24−7.08 (m, 5H), 2.52 (t, *J* = 6.9 Hz, 2H), 1.56−1.50 (m, 2H), 1.22−1.16 (m, 16H), 0.81 (t, *J* = 4 Hz, 3H).

Ethene-1,1,2-triyltribenzene (**3zd**).[18f] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. White solid. Yield: 81%, 207 mg. ^{1}H NMR (200 MHz, chloroform-*d*) δ = 7.32−7.29 (m, 8H), 7.23−7.18 (m, 2H), 7.11 (t, *J* = 5.5 Hz, 3H), 7.05−7.00 (m, 2H), 6.96 (s, 1H). ^{13}C NMR{^{1}H} (50 MHz, chloroform-*d*) δ = 143.4, 142.6, 140.3, 137.4, 130.4, 129.5, 128.6, 128.2, 127.9, 127.6, 127.5, 127.4, 126.7.

4,4′-(2-Phenylethene-1,1-diyl)bis(methoxybenzene) (**3ze**).[18f] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. White solid. Yield: 82%, 259 mg. ^{1}H NMR (200 MHz, chloroform-*d*) δ = 7.33−7.27 (m, 3H), 7.09 (d, *J* = 8.8 Hz, 6H), 6.87−6.80 (m, 5H), 3.78 (s, 6H). ^{13}C NMR{^{1}H} (50 MHz, chloroform-*d*) δ = 157.9, 133.7, 131.6, 129.7, 129.2, 128.8, 128.5, 127.9, 127.0, 113.8, 55.2.

(E)-1,2-Bis(4-methoxyphenyl)ethene (**4a**).[10e] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. White solid. Yield: 78%, 187 mg. ^{1}H NMR (200 MHz, chloroform-*d*) δ = 7.44 (d, *J* = 9.1 Hz, 4H), 6.94 (s, 2H), 6.90 (d, *J* = 9.1 Hz, 4H), 3.84 (s, 6H). ^{13}C NMR{^{1}H} (50 MHz, chloroform-*d*) δ = 159.0, 130.5, 127.4, 126.2, 114.1, 55.3.

(E)-1-Methoxy-4-(4-methylstyryl)benzene (**4b**).[18e] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. White solid. Yield: 67%, 150 mg. ^{1}H NMR (200 MHz, chloroform-*d*) δ = 7.45 (d, *J* = 9 Hz, 2H), 7.40 (d, *J* = 8.3 Hz, 2H), 7.17 (d, *J* = 7.1 Hz, 2H), 7.01 (s, 1H), 6.99 (s, 1H), 6.91 (d, *J* = 9 Hz, 2H). ^{13}C NMR{^{1}H} (50 MHz, chloroform-*d*) δ = 159.1, 137.0, 134.8, 130.3, 129.3, 127.6, 127.2, 126.6, 126.1, 114.1, 55.3, 21.2.

(E)-1-(4-Methoxystyryl)-3-methylbenzene (**4c**).[18h] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. White solid. Yield: 71%, 159 mg. ^{1}H NMR (200 MHz, chloroform-*d*) δ = 7.45 (d, *J* = 8.3 Hz, 2H), 7.31−7.28 (m, 2H), 7.23 (t, *J* = 6.7 Hz, 1H), 7.08−7.03 (m, 2H), 6.97 (s, 1H), 6.90 (d, *J* = 9.4 Hz, 2H), 3.83 (s, 3H), 2.37 (s, 3H). ^{13}C NMR{^{1}H} (50 MHz, chloroform-*d*) δ = 159.2, 138.1, 137.5, 130.2, 128.5, 128.0, 128.0, 127.6, 126.9, 126.7, 123.4, 114.1, 55.3, 21.4.

(E)-2-(4-Methoxystyryl)naphthalene (**4d**).[18i] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. White solid. Yield: 73%, 190 mg. ^{1}H NMR (200 MHz, chloroform-*d*) δ = 7.84−7.72 (m, 5H), 7.54−7.43 (m, 4H), 7.18 (s, 2H), 6.94 (d, *J* = 9.9 Hz, 2H), 3.86 (s, 3H). ^{13}C NMR{^{1}H} (50 MHz, chloroform-*d*) δ = 152.4, 133.8, 132.8, 130.2, 128.6, 127.9, 127.7, 126.7, 126.3, 126.1, 125.7, 123.5, 114.2, 55.3.

(E)-1,2,3-Trimethoxy-5-(4-methoxystyryl)benzene (**4e**).[10d] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. White solid. Yield: 83%, 249 mg. ^{1}H NMR (200 MHz, chloroform-*d*) δ = 7.46 (d, *J* = 8.8 Hz, 2H), 7.00−6.91 (m, 3H), 6.73 (s, 2H), 3.92 (s, 6H), 3.88 (s, 3H), 3.84 (s, 3H). ^{13}C NMR{^{1}H} (50 MHz, chloroform-*d*) δ = 159.3, 153.4, 137.7, 133.4, 130.0, 127.7, 127.6, 126.5, 114.1, 103.4, 60.9, 56.1, 55.3.

(E)-1,2-Dip-tolylethene (**4f**).[18e] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. White solid. Yield: 69%, 143.5 mg. ^{1}H NMR (200 MHz, chloroform-*d*) δ = 7.50 (d, *J* = 8.1 Hz, 4H), 7.23 (s, 4H), 7.13 (s, 2H), 2.45 (s, 6H). ^{13}C NMR{^{1}H} (50 MHz, chloroform-*d*) δ = 137.2, 134.7, 129.3, 127.6, 126.3, 21.2.

(E)-1,2-Bis(4-fluorophenyl)ethane (**4g**).[18j] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. White solid. Yield: 61%, 132 mg. ^{1}H NMR (200 MHz, chloroform-*d*) δ = 7.51−7.44 (m, 4H), 7.11−7.02 (m, 4H), 6.99 (s, 2H). ^{13}C NMR{^{1}H} (50 MHz, chloroform-*d*) δ = 164.8, 159.9, 133.4, 127.9, 127.8, 127.3, 115.8, 115.4.

(E)-2-(4-Methylstyryl)quinoline (**4h**).[18k] The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. Brown solid. Yield: 57%, 139.5 mg. ^{1}H NMR (500 MHz, chloroform-*d*) δ = 8.14 (d, *J* = 8.5 Hz, 1H), 8.08 (d, *J* = 8.5 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.71−7.65 (m, 3H), 7.56 (d, *J* = 8.0 Hz, 2H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.38 (d, *J* = 16.3 Hz, 1H), 7.22 (d, *J* = 7.5 Hz, 2H), 2.40 (s, 3H). ^{13}C NMR{^{1}H} (125 MHz, chloroform-*d*) δ 156.1, 148.2, 138.7, 136.3, 134.4, 133.7, 129.7, 129.5, 129.1, 127.9, 127.5, 127.2, 126.0, 119.1, 21.3.

(S)-2-(3,5-Bis(trifluoromethyl)phenyl)-3-(4-methoxyphenyl)-propanenitrile (**4i**). The title compound was synthesized according to the general procedure described in section 2A. The product was purified using silica gel (230−400 mesh) column chromatography using a mixture of petroleum ether/EtOAc as an eluent. White solid. Yield: 54%, 201 mg. ^{1}H NMR (200 MHz, chloroform-*d*) δ = 7.86 (s, 1H), 7.62 (s, 2H), 6.99 (d, *J* = 8.3 Hz, 2H), 6.83 (d, *J* = 8.3 Hz, 2H), 4.12 (t, *J* = 6.9 Hz, 1H), 3.79 (s, 3H), 3.26−3.05 (m, 2H). ^{13}C NMR{^{1}H} (50 MHz, chloroform-*d*) δ = 159.3, 137.6, 132.7, 130.3, 127.9, 126.6, 122.3, 118.9, 114.2, 55.2, 41.0, 39.6. HRMS (ESI) *m*/*z*: $[M + H]^+$ Calcd for $C_{18}H_{14}F_6NO$ 374.0974. Found: 374.0908.

(E)-1,3-Dimethoxy-5-(4-methoxystyryl)benzene (**5**).[19] White solid. Yield: 93%, 251 mg. ^{1}H NMR (200 MHz, chloroform-*d*) δ = 7.55−7.41 (m, 2H), 7.02 (s, 1H), 6.98−6.91 (m, 2H), 6.91−6.87 (m, 1H), 6.67 (d, *J* = 2.1 Hz, 2H), 6.39 (t, *J* = 2.2 Hz, 1H), 3.84 (s, 9H). ^{13}C NMR{^{1}H} (50 MHz, chloroform-*d*) δ = 161.0, 159.4, 139.7, 129.9, 128.7, 127.8, 126.6, 114.1, 104.3, 99.6, 55.3.

(E)-5-(4-Hydroxystyryl)benzene-1,3-diol (**6**).[19] Colorless liquid. Yield: 74%, 169 mg. ^{1}H NMR (200 MHz, DMSO-d_6) δ = 8.59 (s, 1H), 8.25 (s, 2H), 6.32 (d, *J* = 8.6 Hz, 2H), 5.89−5.61 (m, 4H), 5.33 (s, 2H), 5.17−4.95 (m, 1H). ^{13}C NMR{^{1}H} (50 MHz, DMSO-d_6) δ = 158.6, 157.3, 139.5, 128.3, 128.0, 125.8, 115.7, 104.5, 102.0.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c00592.

Experimental and spectroscopic data, copies of ^{1}H and ^{13}C NMR spectra, and HRMS (PDF)

FAIR data, including the primary NMR FID files, for compounds **3a**−**3d**, **3f**, **3k**−**3n**, **3p**−**3r**, **3w**, **3y**, **3za**−**3ze**, **4a**−**4d**, **4i**, and **7**−**8** (ZIP)

■ AUTHOR INFORMATION

Corresponding Author

Ekambaram Balaraman − *Department of Chemistry, Indian Institute of Science Education and Research (IISER)—Tirupati, Tirupati 517507, India;* orcid.org/0000-0001-9248-2809; Email: eb.raman@iisertirupati.ac.in

https://doi.org/10.1021/acs.joc.1c00592
J. Org. Chem. 2021, 86, 7552−7562

Authors

Siba P. Midya − *Department of Chemistry, Indian Institute of Science Education and Research (IISER)—Tirupati, Tirupati 517507, India*

Murugan Subaramanian − *Department of Chemistry, Indian Institute of Science Education and Research (IISER)—Tirupati, Tirupati 517507, India*

Reshma Babu − *Department of Chemistry, Indian Institute of Science Education and Research (IISER)—Tirupati, Tirupati 517507, India*

Vinita Yadav − *Organic Chemistry Division, CSIR-National Chemical Laboratory (CSIR-NCL), Pune 411008, India*

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.joc.1c00592

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work is supported by the SERB, India (No. CRG/2018/002480), and IISER-Tirupati. E.B. acknowledges the Swarna-Jayanti Fellowship grant (DST/SJF/CSA-04/2019-2020 and SERB/F/5892/2020-2021). R.B. thanks SERB-PMRF, India, for a fellowship. M.S. and V.Y. acknowledge the UGC, India, for their fellowships.

■ REFERENCES

(1) (a) Rychnovsky, S. D. Oxo Polyene Macrolide Antibiotics. *Chem. Rev.* **1995**, *95*, 2021−2040. (b) Dumeunie, R.; Marko, I. E. *Modern Carbonyl Olefination*; Takeda, T., Ed.; Wiley-VCH: Weinheim, 2004; p 104.

(2) Wittig, G.; Schollkopf, U. About Triphenylphosphine Methylene as an Olefin-forming Reagent (I. Part). *Chem. Ber.* **1954**, *87*, 1318−1330.

(3) Julia, M.; Paris, J. M. Synthesis Using v (+) Sulfones - General Synthesis Method of Double Bonds. *Tetrahedron Lett.* **1973**, *14*, 4833−4836.

(4) Peterson, D. J. Carbonyl Olefination Reaction using Silyl-substituted Organometallic Compounds. *J. Org. Chem.* **1968**, *33*, 780−784.

(5) Tebbe, F. N.; Parshall, G. W.; Reddy, G. S. Olefin Homologation with Titanium Methylene Compounds. *J. Am. Chem. Soc.* **1978**, *100*, 3611−3613.

(6) Grubbs, R. H. In *Handbook of Metathesis*; Grubbs, R. H., Eds.; Wiley: Weinheim, 2003; Vol. 2, pp 1−4.

(7) Beletskaya, I. P.; Cheprakov, A. V. The Heck Reaction as a Sharpening Stone of Palladium Catalysis. *Chem. Rev.* **2000**, *100*, 3009−3066.

(8) For selected examples of HA strategy, see: (a) Obora, Y. Recent Advances in α-Alkylation Reactions using Alcohols with Hydrogen Borrowing Methodologies. *ACS Catal.* **2014**, *4*, 3972−3981. (b) Huang, F.; Liu, Z.; Yu, Z. C-Alkylation of Ketones and Related Compounds by Alcohols: Transition-Metal-Catalyzed Dehydrogenation. *Angew. Chem., Int. Ed.* **2016**, *55*, 862−875. (c) Chelucci, G. Ruthenium and Osmium Complexes in C-C Bond-forming Reactions by Borrowing Hydrogen Catalysis. *Coord. Chem. Rev.* **2017**, *331*, 1−36. (d) Leonard, J.; Blacker, A. J.; Marsden, S. P.; Jones, M. F.; Mulholland, K. R.; Newton, R. A Survey of the Borrowing Hydrogen Approach to the Synthesis of some Pharmaceutically Relevant Intermediates. *Org. Process Res. Dev.* **2015**, *19*, 1400−1410. (e) Avelino, C.; Javier, N.; Maria, J.; Corma, S.; Navas, J.; Sabater, M. Advances in One-Pot Synthesis through Borrowing Hydrogen Catalysis. *Chem. Rev.* **2018**, *118*, 1410−1459. (f) Gunanathan, C.; Milstein, D. Bond Activation and Catalysis by Ruthenium Pincer Complexes. *Chem. Rev.* **2014**, *114*, 12024−12087. (g) Guillena, G.; Ramon, D. J.; Yus, M. Hydrogen Autotransfer in the N-alkylation of Amines and Related Compounds using Alcohols and Amines as Electrophiles. *Chem. Rev.* **2010**, *110*, 1611−1641.

(9) For selected reviews of AD strategy, see: (a) Gorgas, N.; Kirchner, K. Isoelectronic Manganese and Iron Hydrogenation/Dehydrogenation Catalysts: Similarities and Divergences. *Acc. Chem. Res.* **2018**, *51*, 1558−1569. (b) Sordakis, K.; Tang, C.; Vogt, L. K.; Junge, H.; Dyson, P. J.; Beller, M.; Laurenczy, G. Homogeneous Catalysis for Sustainable Hydrogen Storage in Formic Acid and Alcohols. *Chem. Rev.* **2018**, *118*, 372−382. (c) Crabtree, R. H. Homogeneous Transition Metal Catalysis of Acceptorless Dehydrogenative Alcohol Oxidation: Applications in Hydrogen Storage and to Heterocycle Synthesis. *Chem. Rev.* **2017**, *117*, 9228−9246. (d) Gunanathan, C.; Milstein, D. Applications of Acceptorless Dehydrogenation and Related Transformations in Chemical Synthesis. *Science* **2013**, *341*, 1229712. (e) Werkmeister, S.; Neumann, J.; Junge, K.; Beller, M. Pincer-Type Complexes for Catalytic (De)Hydrogenation and Transfer (De)Hydrogenation Reactions: Recent Progress. *Chem. - Eur. J.* **2015**, *21*, 12226−12250. (f) Balaraman, E.; Nandakumar, A.; Jaiswal, G.; Sahoo, M. K. Iron-Catalyzed Dehydrogenation Reactions and their Applications in Sustainable Energy and Catalysis. *Catal. Sci. Technol.* **2017**, *7*, 3177−3195. (g) Maji, B.; Barman, M. K. Recent Developments of Manganese Complexes for Catalytic Hydrogenation and Dehydrogenation Reactions. *Synthesis* **2017**, *49*, 3377−3393. (h) Kallmeier, F.; Kempe, R. Manganese Complexes for (De)-Hydrogenation Catalysis: A Comparison to Cobalt and Iron Catalysts. *Angew. Chem., Int. Ed.* **2018**, *57*, 46−60.

(10) (a) Srimani, D.; Leitus, G.; Ben-David, Y.; Milstein, D. Direct Catalytic Olefination of Alcohols with Sulfones. *Angew. Chem., Int. Ed.* **2014**, *53*, 11092−11095. (b) Khaskin, E.; Milstein, D. Catalytic, Oxidant-free, Direct Olefination of Alcohols using Wittig Reagents. *Chem. Commun.* **2015**, *51*, 9002−9005. (c) Siddiki, S. M. A. H.; Touchy, A. S.; Kon, K.; Shimizu, K.-I. Direct Olefination of Alcohols with Sulfones by Using Heterogeneous Platinum Catalysts. *Chem. - Eur. J.* **2016**, *22*, 6111−6119. (d) Yao, C.-Z.; Li, Q.-Q.; Wang, M.-M.; Ning, X.-S.; Kang, Y.-B. (*E*)-Specific Direct Julia-Olefination of Aryl Alcohols without Extra Reducing Agents Promoted by Bases. *Chem. Commun.* **2015**, *51*, 7729−7732. (e) Landge, V. G.; Yadav, V.; Subaramanian, M.; Dangarh, P.; Balaraman, E. Nickel(II)-Catalyzed Direct Olefination of Benzyl Alcohols with Sulfones with the Liberation of H_2. *Chem. Commun.* **2019**, *55*, 6130−6133.

(11) Das, U. K.; Chakraborty, S.; Diskin-Posner, Y.; Milstein, D. Direct Conversion of Alcohols into Alkenes by Dehydrogenative Coupling with Hydrazine/Hydrazone Catalyzed by Manganese. *Angew. Chem., Int. Ed.* **2018**, *57*, 13444−13448.

(12) For α-alkylation of nitriles, see: (a) Grigg, R.; Mitchell, T. R. B.; Sutthivaiyakit, S.; Tongpenyai, N. Oxidation of Alcohols by Transition Metal Complexes Part V. Selective Catalytic Monoalkylation of Arylacetonitriles by Alcohols. *Tetrahedron Lett.* **1981**, *22*, 4107−4110. (b) Anxionnat, B.; Gomez Pardo, D.; Ricci, G.; Cossy, J. Monoalkylation of Acetonitrile by Primary Alcohols Catalyzed by Iridium Complexes. *Org. Lett.* **2011**, *13*, 4084−4087. (c) Sawaguchi, T.; Obora, Y. Iridium-catalyzed α-Alkylation of Acetonitrile with Primary and Secondary Alcohols. *Chem. Lett.* **2011**, *40*, 1055−1057. (d) Morita, M.; Obora, Y.; Ishii, Y. Alkylation of Active Methylene Compounds with Alcohols Catalyzed by an Iridium Complex. *Chem. Commun.* **2007**, 2850−2852. (e) Thiyagarajan, S.; Gunanathan, C. Facile Ruthenium(II)-Catalyzed α-Alkylation of Arylmethyl Nitriles using Alcohols Enabled by Metal−Ligand Cooperation. *ACS Catal.* **2017**, *7*, 5483−5490. (f) Borghs, J. C.; Tran, M. A.; Sklyaruk, J.; Rueping, M.; El-Sepelgy, O. Sustainable Alkylation of Nitriles with Alcohols by Manganese Catalysis. *J. Org. Chem.* **2019**, *84*, 7927−7935. For α-alkenylation of nitriles, see: (g) Thiyagarajan, S.; Gunanathan, C. Ruthenium-Catalyzed α-Olefination of Nitriles using Secondary Alcohols. *ACS Catal.* **2018**, *8*, 2473−2478. (h) Chakraborty, S.; Das, U. K.; Ben-David, Y.; Milstein, D. Manganese Catalyzed α-Olefination of Nitriles by Primary Alcohols. *J. Am. Chem. Soc.* **2017**, *139*, 11710−11713. (i) Yadav, V.; Landge, V. G.; Subaramanian, M.; Balaraman, E. Manganese-Catalyzed α-Olefination of Nitriles with Secondary Alcohols. *ACS Catal.* **2020**, *10*, 947−954.

(13) Li, F.; Zou, X.; Wang, N. Direct Coupling of Arylacetonitriles and Primary Alcohols to α-Alkylated Arylacetamides with Complete Atom Economy Catalyzed by a Rhodium Complex-Triphenylphosphine-Potassium Hydroxide System. *Adv. Synth. Catal.* **2015**, *357*, 1405−141.
(14) For a recent review on nickel-catalyzed ADC and HA reactions, see: Subaramanian, M.; Sivakumar, G.; Balaraman, E. Recent Advances in Nickel-Catalyzed C-C and C-N Bond Formation via ADC and HA Reactions. *Org. Biomol. Chem.* **2021**, *19*, 4213−4277 and references cited therein..
(15) For decyanation reactions, see: (a) Ding, Y.; Luo, S.; Ma, L.; An, J. Reductive Cleavage of Unactivated Carbon-Cyano Bonds under Ammonia-Free Birch Conditions. *J. Org. Chem.* **2019**, *84*, 15827−15833. (b) Mattalia, J-M. R. The Reductive Decyanation Reaction: An Overview and Recent Developments. *Beilstein J. Org. Chem.* **2017**, *13*, 267−284.
(16) Maeda, K.; Morioka, K.; Yashima, E. Synthesis and Chirality Sensing Properties of Poly[(phenyleneethynylene)-alt-(carboxybiphenyleneethynylene)]s. *Macromolecules* **2007**, *40*, 1349−1352.
(17) Armarego, W. L. F.; Perrin, D. D. *Purification of Laboratory Chemicals*, ed. 3; Pergamon Press: Oxford, 1988.
(18) (a) Fu, S.; Chen, N. Y.; Liu, X.; Shao, Z.; Luo, S. P.; Liu, Q. Ligand-Controlled Cobalt-Catalyzed Transfer Hydrogenation of Alkynes: Stereodivergent Synthesis of *Z*- and *E*-Alkenes. *J. Am. Chem. Soc.* **2016**, *138*, 8588−8594. (b) Luo, X.; Chen, X.; Chen, L.; Zhang, K.; Li, Y. Xanthate-mediated Synthesis of (E)-Alkenes by Semi-hydrogenation of Alkynes using Water as the Hydrogen Donor. *Chem. Commun.* **2019**, *55*, 2170−2173. (c) Keesara, S.; Parvathaneni, S.; Mandapati, M. R. N,N′-Mono Substituted Acyclic Thioureas: Efficient Ligands for the Palladium Catalyzed Heck Reaction of Deactivated Aryl Bromides. *Tetrahedron Lett.* **2014**, *55*, 6769−6772. (d) Wang, L.; Neumann, H.; Beller, M. Palladium-Catalyzed Methylation of Nitroarenes with Methanol. *Angew. Chem., Int. Ed.* **2019**, *58*, 5417−5421. (e) Loska, R.; Volla, C. M. R.; Vogel, P. Iron-Catalyzed Mizoroki−Heck Cross-Coupling Reaction with Styrenes. *Adv. Synth. Catal.* **2008**, *350*, 2859−2864. (f) Han, M.; Cui, Z.; Xu, C.; Chen, W.; Jin, Y. Synthesis of Linear Alkylbenzene Catalyzed by Hβ-Zeolite. *Appl. Catal., A* **2003**, *238*, 99−107. (g) Xue, F.; Zhao, J.; Hor, T. S. A. Ambient Arylmagnesiation of Alkynes Catalysed by Ligandless Nickel(II). *Chem. Commun.* **2013**, *49*, 10121−10123. (h) Schmidt, B.; Elizarov, N.; Berger, R.; Hölter, F. Scope and Limitations of the Heck−Matsuda-coupling of Phenol Diazonium Salts and Styrenes: A Protecting-group Economic Synthesis of Phenolic Stilbenes. *Org. Biomol. Chem.* **2013**, *11*, 3674−3691. (i) Ehle, A. R.; Zhou, Q.; Watson, M. P. Nickel(0)-Catalyzed Heck Cross-Coupling via Activation of Aryl C−O Piv Bonds. *Org. Lett.* **2012**, *14* (5), 1202−1205. (j) Huang, T.; Chen, T.; Han, L.-B. Oxidative Dephosphorylation of Benzylic Phosphonates with Dioxygen Generating Symmetrical trans-Stilbenes. *J. Org. Chem.* **2018**, *83*, 2959−2965. (k) Zhang, G.; Irrgang, T.; Dietel, T.; Kallmeier, F.; Kempe, R. Manganese-Catalyzed Dehydrogenative Alkylation or α-Olefination of Alkyl-Substituted N-Heteroarenes with Alcohols. *Angew. Chem., Int. Ed.* **2018**, *57*, 9131−9135.
(19) Yao, C.-Z.; Li, Q.-Q.; Wang, M.-M.; Ning, X.-S.; Kang, Y.-B. (E)-Specific Direct Julia-olefination of Aryl Alcohols without Extra Reducing Agents Promoted by Bases. *Chem. Commun.* **2015**, *51*, 7729−7732.

https://doi.org/10.1021/acs.joc.1c00592
J. Org. Chem. 2021, 86, 7552−7562