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NOTE

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[3,3]-Sigmatropic Rearrangement/5-*exo-dig* Cyclization Reactions of Benzyl Alkynyl Ethers: Synthesis of Substituted 2-Indanones and Indenes

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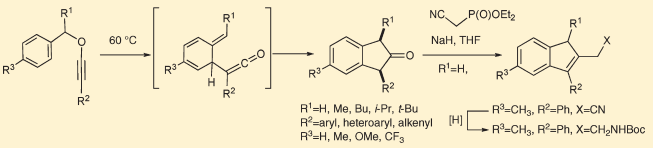
Supporting Information

ABSTRACT: Substituted benzyl alkynyl ethers, prepared from the corresponding α-alkoxy ketones in a two-step sequence involving enol triflate formation and KO*t*Bu-induced E2 elimination, undergo [3,3]-sigmatropic rearrangement/intramolecular 5-*exo-dig* cyclization at 60 °C to form substituted 2-indanones in good overall yields. 1,3-*cis*-Disubstituted-2-indanones are formed preferentially when the benzylic substituent R^1 is bulky. Substituted indenes may be prepared from 2-indanones in high yields by Horner−Wadsworth−Emmons reaction.



Ynol ethers are functional groups that possess significant potential in organic chemistry for the formation of carbon−carbon bonds.[1−3] Due to their linear geometry, alkynyl ethers are relatively unhindered to approach by functional groups present in the same or different molecules; furthermore, alkynyl ethers can prospectively form up to three new bonds in a single reaction.[4]

We have recently uncovered a straightforward methodology for the preparation of alkynyl ethers (Scheme 1)[2] involving the coupling of alcohols **2** with diazoketones **1** in the presence of indium triflate as a catalyst; the α-alkoxy ketone product **3** is readily transformed into the enol triflate or phosphate at low temperatures, which then undergoes base-induced elimination.[3] Allyl-1-alkynyl ethers **7** are thermally unstable and undergo a rapid [3,3]-sigmatropic rearrangement[5] upon generation at −78 °C to form allyl ketene intermediate **8**, which is subsequently trapped by an alcohol or amine to form γ,δ-unsaturated carboxylic acid derivatives **9** in high yields.[4]

Guided by the pioneering studies of Arens[6] and Schmidt,[7] we have also shown that benzyl-1-alkynyl ether **12**, which is stable at ambient temperatures, undergoes sigmatropic rearrangement and intramolecular cyclization at 60 °C to form 1-phenyl-2-indanone **13** in 98% yield. Due to the efficiency of this process, we decided to further explore its scope and utility, and in this Note we report our findings on the diastereoselectivity of the benzyl alkynyl ether sigmatropic rearrangement/intramolecular cyclization reaction and its applicability to the preparation of substituted 2-indanones and indenes.

The α-alkoxy ketones **3** (Scheme 2 and Table 1) necessary for the synthesis of benzyl alkynyl ethers **12** were prepared either by coupling of the appropriate diazoketones **1**[8] with benzyl alcohol **2** in the presence of 10 mol % $In(OTf)_3$ (path **A**, Scheme 2; Table 1, entries 1, 2, and 5)[9] or by reaction of aryloxyacetic acid[10] derived Weinreb amide[11] **10** with the appropriate organolithium or Grignard reagent (path **B**, Scheme 2; Table 1, entries 3−4 and 6−10). Pathway **B** proved to be more general for the synthesis of α-alkoxy ketones; indeed, attempted synthesis of electron-rich substrates **3g** and **3i** by diazoketone-alcohol coupling led to extensive decomposition and minimal yields of the desired products.

Treatment of α-alkoxy ketones **3** with LHMDS at −78 °C, followed by addition of $NPhTf_2$ in THF/DMPU, led to enol triflates **11a**−**j**, which were sensitive to trace amounts of acid and heat. After rapid filtration of the crude reaction mixture through silica gel, the enol triflates were immediately treated with potassium *tert*-butoxide (1 M in THF) at −78 °C to effect elimination of triflate ion, affording benzyl alkynyl ethers **12a**−**i**. The crude benzyl alkynyl ethers were also sensitive to heat and silica gel chromatography, so they were directly warmed to 60 °C in toluene to effect [3,3]-sigmatropic rearrangement/5-*exo-dig* cyclization to provide the substituted indanones **13a**−**i** in good overall yields. This process was successfully employed for alkynyl ether substrates derived from electron-rich (Table 1, entries 2 and 3) and electron-deficient (entry 4) benzylic alcohols and electron-rich (entries 6 and 7) and electron-deficient (entry 8) aryl ketones.

Alkynyl ethers derived from α,β-unsaturated ketones (entry 5) and heteroaryl ketones (entry 9) also smoothly underwent the rearrangement/cyclization process, furnishing indanones **13e** and **13i** in 95% and 62% yields, respectively. However, attempted elimination and thermolysis of alkyne-substituted enol triflate **11j** (entry 10) led to a complex mixture of products, likely arising

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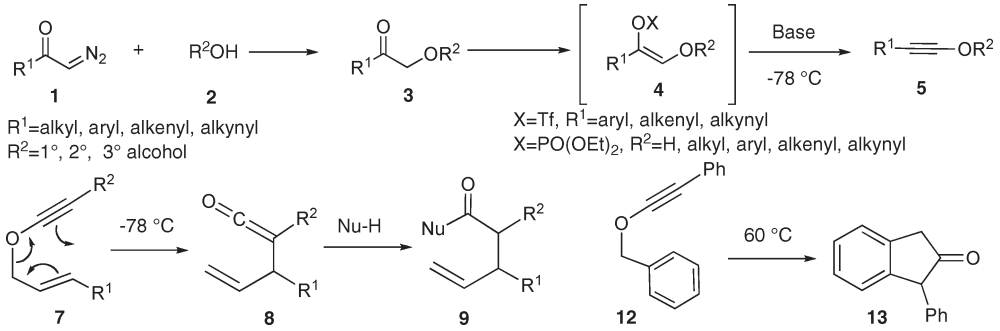
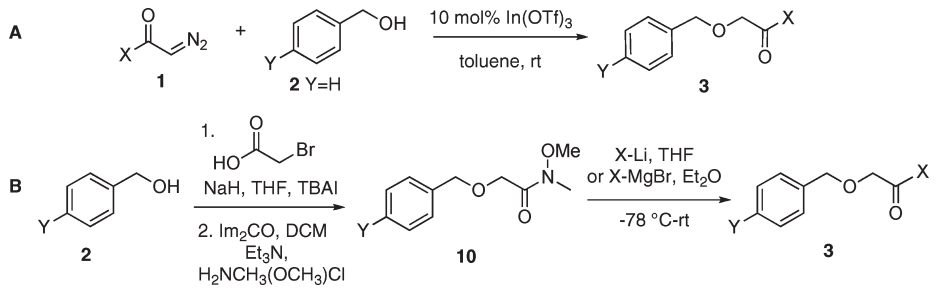
Scheme 1. 1-Alkynyl Ether Synthesis and [3,3]-Sigmatropy



Scheme 2. Two Methods for the Synthesis of Ketones 3



from the intermediacy of various allenic species[3] under the basic conditions employed for elimination.

Monitoring the rates of rearrangement/cyclization[12] for alkynyl ether substrates **12a**−**d** by ^{1}H NMR spectroscopy revealed interesting trends (Table 2). Whereas unsubstituted parent compound **12a** underwent first-order decay to **13a** at 57 °C in $CDCl_3$ with a half-life of 4.8 min, alkynyl ether **12b** under the same conditions displayed a half-life of only 0.8 min, and methoxy-substituted substrate **12c** could not be isolated at room temperature, having completely rearranged to indanone **13c** upon warming the KO*t*Bu elimination reaction of **11c** from −78 °C to ambient. In contrast, CF_3-substituted alkynyl ether **12d** displayed a half-life of 13.3 min at 57 °C. Assuming that the rate-determining step of the transformation **12**→**13** is the [3,3]-sigmatropic rearrangement, the rate acceleration observed for substrates bearing electron-donating substituents (**Y**) on the benzyl moiety suggests the development of charge deficiency (either a radical or cationic intermediate)[13] at the benzylic carbon atom during the transition state for sigmatropic rearrangement.

A similar analysis of the rates of rearrangement of **12f**−**h** compared to **12a** revealed again that electron-donating substituents accelerated the rearrangement/cyclization process: whereas **12f** displayed a half-life of 3.6 min at 57 °C, substrate **12g** had completely rearranged to **13g** upon reaching room temperature after generation at −78 °C. Intriguingly, however, it was found that CF_3-substituted alkynyl ether **12h** underwent first-order decay slightly *faster* than **12a**, displaying a half-life of 4.6 min at 57 °C. These observations are consistent with a change in mechanism[14] upon proceeding from electron-donating to electron-withdrawing substituents on the aromatic moiety **X**, with a radical mechanism (pathway **A**, Figure 1) likely operative for the former and a polar mechanism (pathway **B**, Figure 1) for the latter.

Next, we sought to examine the stereoselectivity of the rearrangement/cyclization reaction when α-substituted benzyl ethers are employed. Ketones **14a**−**e** were prepared by protocol **A** (Scheme 2) and subjected to enol triflate formation, *tert*-butoxide induced triflate elimination, and thermal rearrangement/cyclization to furnish 1,3-disubstituted-2-indanones **15** (Table 3). Only in the case of the phenyl-substituted ketone **14e** did the reaction sequence fail to afford the desired indanone product; enol triflate formation from **14e** led to complicated mixtures due to the heightened acidity of the benzylic proton and the basic conditions involved.

Low to moderate diastereoselectivity was observed for methyl-, butyl-, and isopropyl-substituted indanones **15a**−**c**; however, excellent diastereoselectivity (>95:5) was obtained for 1-*tert*-butyl-3-phenyl-indanone **15d**. The presence of crosspeaks between the C.1 and C.3 protons (H_b and H_a, respectively) observed in the NOESY spectrum of **15d** (as well as correlations between H_a and H_c, H_c and H_d, and H_d and H_b) confirmed the *cis* stereochemistry (Scheme 3). Mechanistically, we propose that the large *tert*-butyl substituent prefers to be oriented *trans* to the ketene in the nonaromatic intermediate **16**[a];[15] 5-*exo*-*dig* cyclization, followed by a *syn*-1,2-proton migration to the enolate carbon atom, would give rise to the product with the observed stereochemistry.

Finally, we sought to transform our 2-indanone products **13** into synthetically useful substituted indenes. Indenes are building blocks in the synthesis of biologically active pharmaceutical agents[16] and are often used as ligands in olefin polymerization catalysts.[17] Addition of indanone **13b** to a solution of diethyl(cyanomethyl)phosphonoacetate and NaH in THF and stirring for 4 h at room temperature resulted in clean transformation to indene **18b** (91% isolated yield), arising from carbonyl olefination and base-mediated isomerization (Scheme 4). Reduction of the nitrile functional group and *in situ* primary amine protection as a *tert*-butyl carbamate was accomplished in a single step by

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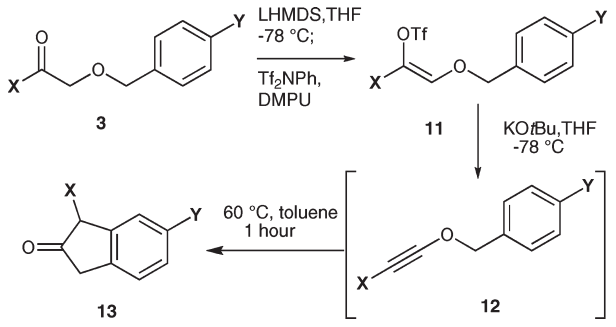
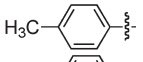
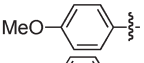
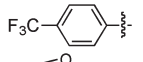
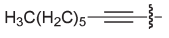
Table 1. Scope of Benzyl Alkynyl Ether [3,3]-Sigmatropy/ 5-*exo-dig* Cyclization



entry	X	Y	3	% yield 11[d]	% yield 13[e]
1		H	a[a]	75	98
2		CH_3	b[a]	73	93
3		OCH_3	c[b]	68	65
4		CF_3	d[b]	81	72
5		H	e[a]	85	95
6		H	f[b]	68	90
7		H	g[b]	81	88
8		H	h[b]	78	91
9		H	i[b]	67	62
10		H	j[b]	82	—[c]

[a] α-Alkoxy ketone **3** prepared by method **A** (Scheme 2). [b] α-Alkoxy ketone **3** prepared by method **B** (Scheme 2). [c] A complex mixture of products was formed. [d] Yield (from **3**) based on weight obtained after rapid filtration of the crude triflation reaction mixture through silica gel (see text). [e] Isolated yield (from **11**) after silica gel chromatography.

Table 2. Kinetic Data for the First-Order Decay of 12 to 13 at 57 °C in $CDCl_3$

substrate	$t_{1/2}$(min)	k (min^{-1})
12a	4.8	0.145
12b	0.8	0.905
12d	13.3	0.052
12f	3.6	0.191
12h	4.6	0.149

employing Caddick's protocol[18] (cat. $NiCl_2 \cdot H_2O$, $NaBH_4$, Boc_2O, MeOH) to afford indene **19b** in 60% yield.

In conclusion, we have shown that the [3,3]-sigmatropic rearrangement of benzyl alkynyl ethers may be successfully employed for a variety of substrates bearing electron- deficient and electron-rich aromatic and heteroaromatic ring systems, and the rates of rearrangement vary depending upon the electronic nature of the aromatic substituents. Furthermore, 1,3-*cis*-disubstituted-2-indanones are formed in excess when α-substituted

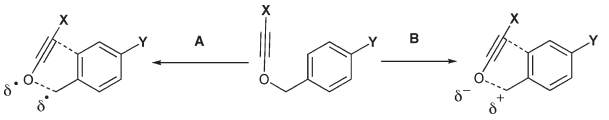
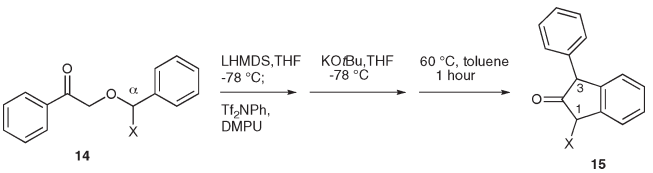


Figure 1. Possible TS charge development for benzyl alkynyl ether sigmatropy.

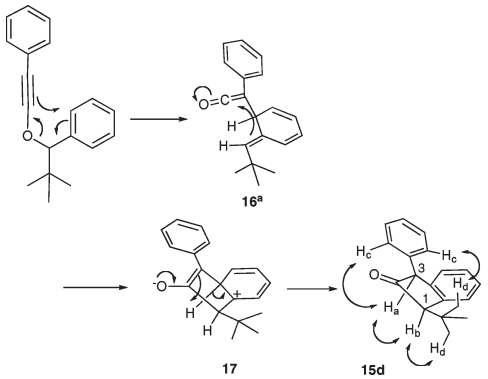
Table 3. Rearrangement/Cyclization of α-Substituted Benzyl Alkynyl Ethers[a]



entry	X	14	% yield 15 (from 14)[b]	d.r.
1	CH_3	a	61	1:1
2	$CH_3(CH_2)_3$	b	53	4:1
3	$(CH_3)_2CH$	c	48	2:1
4	$(CH_3)_3C$	d	69	>95:5
5		e	—	—

[a] Ketones **14** prepared by method A (Scheme 2). [b] Isolated yields.

Scheme 3. Mechanistic Proposal for the Formation of Indanone 15d



benzyl alkynyl ethers are employed as substrates. The 2-indanones obtained by this method may be easily transformed into useful substituted indene products.

EXPERIMENTAL SECTION

Representative Procedure for the Synthesis of Ketones 3a, 3b, 3e, and 14a–e. *2-(Benzyloxy)-1-phenylethanone* ***3a***. A mixture of the diazoacetophenone (136 mg, 1 mmol) and benzyl alcohol (162 mg, 1.5 mmol) was dissolved in dry toluene (4 mL) under argon and stirred at room temperature for 2 min. Indium(III) trifluoromethanesulfonate (56.2 mg, 0.1 mmol, 10 mol %) was added, and a rapid evolution of nitrogen gas was observed. The reaction was monitored by TLC, and when complete consumption of the starting material was observed, saturated $NaHCO_3$ (10 mL) was added, and the reaction mixture was diluted with ether (20 mL). The phases were

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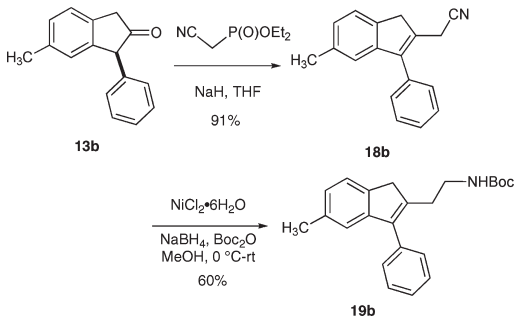
Scheme 4. Transformation of 2-Indanones into Substituted Indenes



13b 18b 19b

separated, and the aqueous phase was back-extracted with ether (1 × 20 mL). The combined organic extracts were then dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification of the residue by flash chromatography (SiO_2) afforded α-alkoxyketone **3a**.

3a[3] (87%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 7.6 Hz, 2H), 7.57 (t, J = 7.6 Hz, 1H), 7.46 (t, J = 8.0 Hz, 2H), 7.40- 7.27 (m, 5H), 4.82 (s, 2H), 4.70 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.2, 136.9, 134.6, 133.9, 129.4, 128.8, 128.6, 128.2, 127.9, 127.1, 123.6, 73.4, 72.4; HRMS (ESI) calculated for $C_{15}H_{14}NaO_2$ 249.0892, found 249.0854 $(M + Na)^+$.

3b (82%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 7.6 Hz, 2H), 7.51 (t, J = 7.6 Hz, 1H), 7.46−7.27 (m, 6H), 4.72 (s, 2H), 4.65 (s, 2H), 2.34 (s, 3H); ^{13}C NMR: (100 MHz, $CDCl_3$) δ 196.3, 137.6, 135.0, 134.4, 133.5, 129.2, 128.7, 128.2, 128.0, 73.2, 72.5, 21.2; HRMS (ESI) calculated for $C_{16}H_{16}NaO_2$ 263.1048, found 263.1107 $(M + Na)^+$.

3e (61%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (dd, J = 8.4, 1.2 Hz, 2H), 7.45−7.25 (m, 5H), 6.83 (d, J = 8.8 Hz, 2H), 4.62 (s, 2H), 4.54 (s, 2H), 3.67 (s, 3H); 13C NMR (100 MHz, $CDCl_3$) δ 196.3, 159.4, 134.9, 133.4, 129.7, 129.4, 128.6, 128.3, 127.8, 113.8, 72.9, 72.2, 55.1; HRMS (ESI) calculated for $C_{16}H_{16}NaO_3$ 279.0997, found 279.1098 $(M + Na)^+$.

14a (75%):^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 7.6 Hz, 2H), 7.46 (t, J = 7.6 Hz, 1H), 7.36−7.25 (m, 7H), 4.65 (d, J = 16.8 Hz, 1H), 4.54 (q, J = 6.4 Hz, 1H), 4.52 (d, J = 16.8 Hz, 1H), 1.54 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.9, 142.9, 135.0, 131.1, 128.6, 128.5, 128.2, 127.8, 127.7, 126.3, 78.3, 77.9, 71.2, 24.0, 23.9; HRMS (ESI) calculated for $C_{16}H_{16}NaO_2$ 263.1048 found 263.1632 $(M + Na)^+$.

14b (78%): ^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.84 (d, J = 8.4 Hz, 2H), 7.50 (t, J = 7.6 Hz, 1H), 7.40−7.25 (m, 7H), 4.63 (d, J = 16.8 Hz, 1H), 4.49 (d, J = 16.8 Hz, 1H), 4.40 (t, J = 6.8 Hz, 1H), 1.97 (m, 1H), 1.72 (m, 1H), 1.43 (m, 1H), 1.30 (m, 1H), 0.86 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.4, 141.7, 135.1, 133.3, 128.6, 128.5, 128.3, 127.9, 127.0, 83.1, 71.3, 37.9, 28.0, 22.6, 14.0; HRMS (ESI) calculated for $C_{19}H_{22}NaO_2$ 305.1517, found 305.1343 $(M + Na)^+$.

14c (73%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 8.0 Hz, 2H), 7.43 (t, J = 7.8 Hz, 1H), 7.33−7.21 (m, 7H), 4.52 (d, J = 16.0 Hz, 1H); 4.35 (d, J = 16.0 Hz, 1H); 3.97 (d, J = 8.0 Hz, 1H); 1.96 (m, J = 8.0 Hz, 1H); 0.98 (d, J = 8.0 Hz, 3H); 0.65 (d, J = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.6, 140.3, 135.2, 133.3, 128.6, 128.5, 128.2, 128.0, 127.8, 127.7, 88.6, 71.6, 34.8, 19.2, 19.0; HRMS (ESI) calculated for $C_{18}H_{20}NaO_2$ 291.1361, found 291.1440 $(M + Na)^+$.

14d (66%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 8.0 Hz, 2H), 7.49 (t, J = 7.8 Hz, 1H); 7.37 (t, J = 7.8 Hz, 2H). 7.32−7.25 (m, 5H), 4.62 (d, J = 16.0 Hz, 1H), 4.41 (d, J = 16.0 Hz, 1H), 4.15 (s, 1H), 0.96 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.5, 138.8, 135.3, 133.3, 128.6, 128.5, 128.0, 127.7, 127.6, 90.6, 71.9, 35.8; 26.4; HRMS (ESI) calculated for $C_{19}H_{22}NaO_2$ 305.1517, found 305.1962 $(M + Na)^+$.

14e (71%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 7.6 Hz, 2H), 7.55 (t, J = 7.4 Hz, 1H), 7.46−7.41 (m, 6H), 7.35 (t, J = 7.6 Hz, 4H), 7.28 (t, J = 7.8 Hz, 2H), 5.64 (s, 1H), 4.77 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.3, 141.3, 135.1, 133.5, 128.7, 128.5, 128.0, 127.8, 127.4, 83.8, 77.4, 77.1, 76.8, 71.4; HRMS (ESI) calculated for $C_{21}H_{18}NaO_2$ 325.1204, found 325.1541 $(M + Na)^+$.

Representative Procedure for the Synthesis of Ketones 3c, 3d, and 3f−j. To a solution of the aryloxy acetic acid[10] (1 g, 6 mmol) in 11 mL dichloromethane at 0 °C was added 1,1′-carbonyl diimidazole (1.26 g, 7.82 mmol) at 0 °C. The solution bubbled, and upon completion it was warmed to room temperature for 30 min. The solution was cooled to 0 °C, and triethylamine (1.1 mL, 8.4 mmol) was added, followed by the Weinreb amine hydrochloride salt (0.82 g, 8.4 mmol). The solution was allowed to warm to room temperature and was stirred overnight. The mixture was diluted with 1 M HCl (10 mL) and EtOAc (20 mL). The phases were separated, and the aqueous phase was back-extracted with EtOAc (1 × 20 mL). The combined organic extracts were then dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Crude amide **10** was taken directly to the next step without further purification.

To a solution of Weinreb amide **10** (5 mmol) in THF (5 mL) at −78 °C under argon was added a solution of aryllithium reagent (generated from the corresponding aryl bromide 1 M in THF by the addition of 0.95 equiv *n*-BuLi) dropwise. Upon completion of the addition, TLC indicated complete conversion to the aryl ketone. The mixture was allowed to warm to −20 °C and was quenched with saturated NH_4Cl solution (10 mL). The mixture was diluted with ether (3 mL) and was allowed to stir at room temperature for one hour. The phases were separated, and the aqueous phase was back-extracted with EtOAc (1 × 20 mL). The combined organic extracts were then dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification of the residue by flash chromatography (SiO_2) afforded α-alkoxyketones **3**.

3c (71%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (dd, J = 8.4, 1.2 Hz, 2H), 7.45−7.25 (m, 5H), 6.83 (d, J = 8.8 Hz, 2H), 4.62 (s, 2H), 4.54 (s, 2H), 3.67 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.3, 159.4, 134.9, 133.4, 129.7, 129.4, 128.6, 128.3, 127.8, 113.8, 72.9, 72.2, 55.1; HRMS (ESI) calculated for $C_{16}H_{16}NaO_3$ 279.0997, found 279.1098 $(M + Na)^+$.

3d (68%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (dd, J = 9.6 Hz, 2H), 7.61−7.42 (m, 7H), 4.81 (s, 2H), 4.72 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.0, 141.6, 134.7, 133.7, 129.5, 128.8, 127.9, 127.8, 125.4, 125.3, 115.4, 72.8, 72.5; HRMS (ESI) calculated for $C_{16}H_{13}F_3NaO_2$ 317.0765, found 317.0852 $(M + Na)^+$.

3f (69%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83−7.80 (d, J = 8.4 Hz, 2H), 7.41−7.23 (m, 7H), 4.73 (s, 2H), 4.68 (s, 2H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.9, 144.4, 137.4, 132.4, 129.3, 128.5, 128.1, 128.0, 73.3, 72.5, 21.7; HRMS (ESI) calculated for $C_{16}H_{16}NaO_2$ 263.1048, found 263.1055 $(M + Na)^+$.

3g (82%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, J = 8.8 Hz, 2H), 7.40−7.32 (m, 5H), 6.88 (d, J = 8.8 Hz, 2H), 4.69 (s, 2H), 4.66 (s, 2H), 3.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.9, 163.8, 150.6, 137.5, 130.3, 128.5, 128.0, 127.9, 116.2, 114.7, 113.9, 73.3, 72.5, 55.4; HRMS (ESI) calculated for $C_{16}H_{16}NaO_3$ 279.0997, found 279.0780 $(M + Na)^+$.

3h (73%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 8.0 Hz, 2H), 7.74 (d, J = 8.4 Hz, 2H), 7.39−7.33 (m, 5H), 4.76 (s, 2H), 4.70 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.6, 137.5, 136.9, 134.8, 128.6, 128.4, 128.2, 128.1, 125.7, 73.5, 72.8; HRMS (ESI) calculated for $C_{16}H_{13}F_3NaO_2$ 317.0765, found 317.0923 $(M + Na)^+$.

3i (85%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (s, 1H), 7.52−7.24 (m, 6H), 6.47 (m, 1H), 4.63 (s, 2H), 4.54 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.5, 150.9, 146.7, 137.3, 128.5, 128.3, 128.0, 127.9, 118.2, 112.3, 73.4, 72.2; HRMS (ESI) calculated for $C_{13}H_{12}NaO_3$ 239.0684, found 239.0717 $(M + Na)^+$.

3j (92%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.25 (m, 5H), 4.62 (s, 2H), 4.19 (s, 2H), 2.37 (t, J = 6.8 Hz, 2H), 1.56 (m, J = 7.2 Hz, 2H), 1.38−1.26 (m, 5H), 0.89 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz,

$CDCl_3$) δ 185.0, 137.1, 128.4, 127.9, 97.5, 82.7, 75.8, 73.3, 31.2, 28.5, 27.5, 22.5, 22.4, 19.0, 14.0; HRMS (ESI) calculated for $C_{17}H_{22}NaO_2$ 281.1517, found 281.1582 $(M + Na)^+$.

Representative Procedure for Enol Triflate (11a−i) Formation. Hexamethyldisilazane (0.29 mL, 2.5 mmol) dissolved in dry THF (1 mL) under argon was cooled to 0 °C in an ice bath, and *n*-BuLi (0.75 mL), 2 M in cyclohexane, 1.5 mmol) was added dropwise. After 10 min, the mixture was cooled to −78 °C and a solution of α-alkoxyketone (1 mmol) in THF (1 mL) was added dropwise. The reaction mixture was stirred for 1 h at −78 °C, and then a solution of *N*-phenyl triflimide (1.5 mmol) in 1:1 THF/DMPU (1 mL) was added rapidly (1 s). The mixture was allowed to warm to room temperature and then was stirred for 1 h, at which time TLC indicated >90% consumption of starting material. The phases were separated, and the aqueous phase was back-extracted with ether (1 × 20 mL). The combined organic extracts were then dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude enol triflate was filtered over silica gel employing 1% Et_3N in the eluant (95:5 hexanes/ether), and the material obtained was used directly in the next reaction.

Representative Procedure for Alkynyl Ether (12a−i) Formation and Sigmatropic Rearrangement/Cyclization to Indanones 13a−i and 15a−d. The enol triflate obtained from the above procedure (∼1 mmol) was dissolved in THF (1 mL) under argon and cooled to −78 °C. A solution of potassium *tert*-butoxide (1 M in THF, 3.0 mL, 3.0 mmol) was added dropwise, and the reaction mixture darkened in color. After 20 min, a solution of saturated $NaHCO_3$ (10 mL) was added, and the mixture was allowed to warm to room temperature with stirring. Ether (10 mL) was added, and the phases were separated. The aqueous later was back-extracted with ether (1 × 20 mL), and the combined organic extracts were then dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude alkynyl ether was then dissolved in toluene (2 mL) and heated on an oil bath under argon for 1 h, at which time TLC indicated complete conversion to the indanone product. Concentration *in vacuo* and purification of the residue by flash chromatography (SiO_2) afforded indanones **13a−i** and **15a−d**.

13a[3] (98%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43−7.22 (m, 7H), 7.17 (d, J = 7.6 Hz, 2H), 4.71 (s, 1H), 3.68 (s, 2H); ^{13}C NMR (100 MHz, C_6D_6) δ 213.8, 141.4, 138.2, 137.3, 128.8, 128.5, 128.0, 127.9, 127.3, 126.0, 124.9, 59.8, 43.0; HRMS (ESI) calculated for $C_{15}H_{12}NaO$ 231.0786, found 231.0777 $(M + Na)^+$.

13b (93%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.24 (m, 3H), 7.17−7.10 (m, 3H), 7.01 (s, 1H), 4.63 (s, 1H), 3.62 (s, 2H), 2.33 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 216.8, 143.3, 140.0, 137.7, 128.8, 128.5, 128.0, 127.9, 126.7, 124.3, 123.1, 60.2, 47.1, 23.5; HRMS (ESI) calculated for $C_{16}H_{14}NaO$ 245.0942, found 245.1399 $(M + Na)^+$.

13c (65%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.27 (m, 4H), 7.15 (d, J = 7.6 Hz, 2H), 6.93 (m, 1H), 6.74 (m, 1H), 4.66 (s, 1H), 3.78 (s, 3H), 3.62 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 214.2, 159.5, 142.4, 138.0, 129.1, 128.8, 128.4, 127.3, 125.7, 114.7, 110.7, 60.2, 55.4, 42.3; HRMS (ESI) calculated for $C_{16}H_{14}NaO_2$ 261.0891, found 261.0922 $(M + Na)^+$.

13d (72%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63−7.26 (m, 7H), 7.11 (dd, J = 9.2 Hz, 1H), 4.75 (m, 1H), 3.72 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.3, 142.2, 137.2, 130.5, 130.2, 129.0, 128.4, 128.1, 127.2, 126.4, 125.0, 123.0, 122.9, 122.7, 59.6, 42.8; HRMS (ESI) calculated for $C_{16}H_{11}F_3NaO$ 299.0660, found 299.0598 $(M + Na)^+$.

13e (95%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30−7.24 (m, 4H), 5.54 (s, 1H), 3.98 (s, 1H), 3.53 (s, 2H), 1.67−1.49 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 215.8; 141.3; 137.3; 134.7; 127.6; 127.5; 127.0; 125.3; 124.7; 62.3; 43.4; 26.1; 25.4; 22.7; 22.1; HRMS (ESI) calculated for $C_{15}H_{16}NaO$ 235.1099, found 235.1174 $(M + Na)^+$.

13f (90%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.30 (m, 3H), 7.21 (d, J = 7.2 Hz, 1H), 7.14 (d, J = 7.6 Hz, 2H), 7.02 (d, J = 8.0 Hz, 2H), 4.63 (s, 1H), 3.65 (s, 2H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 214.2, 141.5, 137.2, 137.0, 135.2, 129.5, 128.5, 128.3, 127.9, 127.8, 126.0, 124.8, 59.4, 42.9, 21.1; HRMS (ESI) calculated for $C_{16}H_{14}NaO$ 245.0942, found 245.0921 $(M + Na)^+$.

13g (88%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.20 (m, 5H), 7.05 (d, J = 6.4 Hz, 2H), 6.87 (d, J = 6.4 Hz, 2H), 4.63 (s, 1H), 3.78 (s, 3H), 3.66 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 214.4, 158.9, 141.6, 137.2, 130.3, 129.5, 128.3, 127.9, 127.8, 126.0, 124.8, 114.2, 58.9, 55.2, 42.8; HRMS (ESI) calculated for $C_{16}H_{14}NaO_2$ 261.0891, found 261.0664 $(M + Na)^+$.

13h (91%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 8.0 Hz, 1H), 7.75 (d, J = 8.4 Hz, 2H), 7.61 (d, J = 8.0 Hz, 2H), 7.45−7.18 (m, 5H), 4.71 (s, 1H), 3.73 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.9, 140.2, 136.7, 129.8, 129.4, 128.9, 128.5, 128.2, 126.9, 125.9, 125.7, 125.6, 125.4, 59.4, 42.8; HRMS (ESI) calculated for $C_{16}H_{11}F_3NaO$ 299.0659, found 299.0721 $(M + Na)^+$.

13i (62%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39−7.27 (m, 5H), 6.35 (m, 1H), 6.16 (m, 1H), 4.82 (s, 1H), 3.72 (d, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.4, 150.5, 142.7, 136.9, 128.3, 127.8, 125.6, 124.9, 110.4, 107.8, 53.3, 42.9; HRMS (ESI) calculated for $C_{13}H_{10}NaO_2$ 221.0578, found 221.0842 $(M + Na)^+$.

15a (61%; dr = 1:1): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41−7.26 (m, 6H); 7.18−7.10 (m, 3H); 4.70 (s, 1H); 3.61 (q, J = 4.2 Hz, 1H); 1.48 (d, J = 5.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 216.4, 143.2, 140.1, 138.3, 128.9, 128.6, 128.0, 127.6, 126.0, 124.2, 59.0, 46.7, 15.8; HRMS (ESI) calculated for $C_{16}H_{14}NaO$ 245.0942, found 245.4017 $(M + Na)^+$.

15b (53%; dr = 4:1): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33−7.21 (m, 9H), 4.42 (s, 1H), 3.34 (t, J = 5.4 Hz, 1H), 1.86 (m, 2H), 1.41−1.19 (m, 4H), 0.80 (t, J = 6.0, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 214.2, 142.3, 141.0, 128.9, 128.5, 128.0, 127.7, 127.5, 58.9, 52.0, 31.2, 28.8, 22.7, 19.6; HRMS (ESI) calculated for $C_{19}H_{20}NaO$ 287.1412, found 287.1361 $(M + Na)^+$.

15c (48%; dr = 2:1): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24−7.01 (m, 9H), 4.38 (s, 1H), 3.25 (d, J = 3.6 Hz, 1H), 2.29 (m, J = 4.0 Hz, 1H), 1.01 (d, J = 6.4 Hz, 3H), 0.89 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 213.8, 141.3, 140.9, 138.0, 128.9, 128.4, 128.0, 127.7, 127.5, 126.9, 126.1, 124.7, 58.9, 58.0, 31.2, 19.9, 19.6; HRMS (ESI) calculated for $C_{18}H_{18}NaO$ 273.1255, found 273.1271 $(M + Na)^+$.

15d (69%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, J = 10.0 Hz, 2H); 7.31 (m, 1H); 7.20−7.09 (m, 6H); 4.40 (s, 1H), 3.09 (s, 1H), 0.99 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 213.3, 141.3, 140.7, 138.6, 128.5, 128.0, 127.9, 127.6, 127.3, 126.6, 62.3, 58.6, 35.0; 30.5, 28.6; HRMS (ESI) calculated for $C_{19}H_{20}NaO$ 287.1412, found 287.1438 $(M + Na)^+$.

Synthesis of 2-(5-Methyl-3-phenyl-1*H*-inden-2-yl)ethanenitrile 18b. To a solution of diethyl(cyanomethyl)phosphonate (531 mg, 3.0 mmol) in THF (1 mL) was added NaH (100 mg, 2.5 mmol) at 0 °C, and the solution was allowed to stir for 30 min. Then a solution of 2-indanone **13b** (100 mg, 0.45 mmol) in THF (1 mL) was added, and the mixture was allowed to stir for 4 h at room temperature. The mixture was diluted with saturated $NaHCO_3$ (10 mL). Ether (20 mL) was added, and the phases were separated. The aqueous later was back-extracted with ether (1 × 20 mL), and the combined organic extracts were then dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification of the residue by flash chromatography (SiO_2) afforded indene **18b**.

18b (91%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53−7.35 (m, 6H), 7.09−7.05 (m, 2H), 3.63 (s, 2H), 3.55 (s, 2H), 2.35 (s, 3H); ^{13}C NMR: (100 MHz, $CDCl_3$) δ 144.8, 139.1, 136.4, 133.6, 130.5, 128.9, 128.8, 128.1, 126.5, 123.6, 121.2, 40.2, 21.5, 17.9; HRMS (ESI) calculated for $C_{18}H_{15}NNa$ 268.1102, found 268.1099 $(M + Na)^+$.

Synthesis of *tert*-Butyl 2-(5-methyl-3-phenyl-1*H*-inden-2-yl)ethylcarbamate 19b. To a solution of nitrile **18b** (35.0 mg, 0.142 mmol) in methanol (1.2 mL) at 0 °C were added Boc_2O (69.0 mg, 0.32

mmol) and $NiCl_2 \cdot 6H_2O$ (3.8 mg, 0.016 mmol). Then $NaBH_4$ (42.4 mg, 1.12 mmol) was added in small portions over 30 min. After warming to room temperature and stirring for 2 h, the mixture was diluted with saturated $NaHCO_3$ (10 mL) and concentrated *in vacuo* to remove methanol. Ethyl acetate (10 mL) was added and the phases were separated. The aqueous later was back-extracted with ethyl acetate (1×10 mL), and the combined organic extracts were then dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification of the residue by flash chromatography (SiO_2) afforded indene **19b**.

19b (60%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49−7.35 (m, 6H), 7.00 (m, 2H), 3.47 (s, 2H), 3.35 (m, 2H), 2.71 (t, J = 6.8 Hz, 2H) 2.34 (s, 3H), 1.41 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.7, 146.3, 141.1, 138.0, 135.2, 129.1, 128.5, 128.3, 127.3, 125.3, 123.3, 120.4, 100.0, 79.2, 40.2, 40.0, 29.4, 28.3, 21.5; HRMS (ESI) calculated for $C_{23}H_{27}NNaO_2$ 372.1939, found 372.1763 $(M + Na)^+$.

■ ASSOCIATED CONTENT

Supporting Information. Experimental details, characterization data, ^{1}H, ^{13}C spectra of all products, and ^{1}H NMR kinetic data at 330 K. This material is available free of charge via the Internet at http://pubs.acs.org.

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(13) A Hammett plot of $\ln(k/k_0)$ vs σ for the data for substrates **12a**,**b**, and **d** shows a break in slope at the data point for **12a**, with a strongly negative slope ($\rho = -10.5$) to **12b** and a moderately negative slope ($\rho = -1.9$) to **12d**. The break in slope is suggestive of a change in mechanism upon proceeding from substrates bearing electron-donating substituents (**12b**) to substrates bearing electron-withdrawing subsituents (**12d**). SeeRitchie, C. D.; Sager, W. F. *Prog. Phys. Org. Chem.* **1964**, *2*, 323. See Supporting Information for data graphs.

(14) A Hammett plot of $\ln(k/k_0)$ vs σ for the data for substrates **12a**, **f**, and **h** shows a break in slope at the data point for **12a**, with a negative slope ($\rho = -1.62$) to **12f** and a slightly positive slope ($\rho = +0.05$) to **12h**. Again, the break in slope is suggestive of a change in mechanism upon proceeding from substrates bearing electron-donating substituents (**12f**) to substrates bearing electron-withdrawing subsituents (**12h**). See Supporting Information for data graphs.

(15) (a) We thank a reviewer for mentioning the allylic strain apparent in the *anti* disposition of the *tert*-butyl group in structure **16**^{a}. We believe that steric interactions between the *tert*-butyl group and the phenyl-substituted ketene in the corresponding *syn* form (**16**^{s}, see Supporting Information) hinder alignment of the ketene carbonyl carbon with the benzylic carbon atom (which is necessary for 5-*exo-dig* cyclization to occur) by favoring rotamers in which the ketene is directed away from the benzylic carbon atom. Thus, despite the allylic strain present in **16**^{a}, it appears that the reaction proceeds preferentially through **16**^{a} to **15d**. (b) To assess if the product ratios obtained for **15a**−**c** represent an equilibrium mixture arising from a reversible process, we have attempted to obtain pure major or minor isomer from these reactions and resubject them individually to the reaction conditions. Chromatographic separation of the *cis* and *trans* indanone products has proven quite difficult since the diastereomers co-elute in most solvent systems. Thus, a mixture enriched in the major isomer of indanone **15c** (dr = >2:1) was heated to 57°C in an NMR tube ($CDCl_3$ as solvent) for 30 minutes, and essentially no change in the isomer ratio was observed. This suggests that the 5-*exo-dig* cyclization is irreversible under these reaction conditions and that the isomer distributions are under kinetic control.

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