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Electronic Regioselectivity of Diarylalkynes in Cobalt-Mediated Pauson–Khand Reaction: An Experimental and Computational Study with Para- and Meta-Substituted Diarylalkynes and Norbornene

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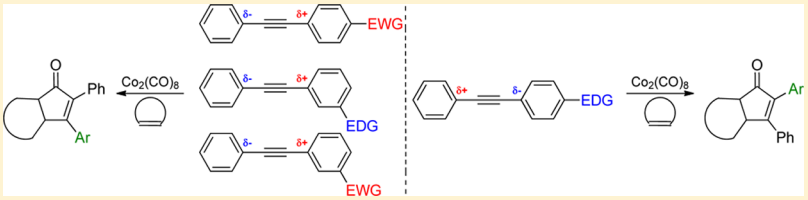
Supporting Information



ABSTRACT: Both steric and electronic factors of substituted alkynes are known to guide α/β-cyclopentenone regioselectivity in the cobalt-mediated Pauson–Khand reaction (PKR). In synthetic applications of the PKR, the steric factors can often override or render possible electronic effects. This study examined alkyne-dependent electronic regioselectivity of cyclopentenone formation in PKR with norbornene and sterically equivalent, but electronically unsymmetrical, meta- and para-substituted diarylethynyls to unveil the role of electronic effects alone. In agreement with the literature reports, EDG para-substituted aryls, to some extent, favored the cyclopentenone α-regioisomer, while the EWG-substituted aryls correspondingly preferred the β-regioisomer. The cooperation of EGW and EDG in diaryl-substituted alkynes did not lead to any increased regioselectivities that could be expected by a "push–pull" effect. Both EWG and EDG meta-substituted aryls preferred the β-regioisomer, which was demonstrated by 3,5-dimethoxy- and 3,5-bis(trifluoromethyl)-1-phenylethynyls that yielded 1/1.6 and 1/2.0 α/β-regioselectivities, respectively. Theoretically, inspection of Hammett values of α-alkyne carbons gave qualitatively satisfactory prediction for para-substituted aryls but correlated only weakly with meta-substituted effects. Computational investigations at the DFT level revealed a correlation between NBO charges and the regioselectivity. Overall, the results suggest that the polarity of an alkyne, also designated by the relative polarization of aryl α-carbons, dictates the regioselectivity in the absence of steric effects.

INTRODUCTION

The Pauson–Khand reaction (PKR),[1] i.e., a formal [2 + 2 + 1] cycloaddition of an alkyne, alkene, and a carbonyl unit, is a powerful and versatile tool in the synthesis of substituted cyclopentenones.[2] Nevertheless, as a drawback, the intermolecular PKR chemist is often challenged with an issue of somewhat undefined regiochemical selectivity, which is inherent especially for the alkynes equipped with sterically similar substituents. It has been established that the regiochemistry is controlled by both steric and electronic factors; large and electron-donating groups (EDG) tend to favor a cyclopentenone α-position, while small and electron-withdrawing groups (EWG) tend to favor the β-position. The rationale for the α-position-directing steric effects is explained by Magnus, who proposed the PKR mechanism (Figure 1),[3] which illustrates that the alkene approaches from the less crowded side for bond formation.

However, the electronic effects are a more obscure issue, while steric effects tend to predominate in the selectivity. Even so, there are examples of purely electronic selectivity in the cobalt-catalyzed PKR. For instance, the β-selectivity in the PKR of ethyl butynoate with norbornene has been shown to proceed by electronic guidance of the EWG, the ester group.[4] The related computational studies at the DFT level, carried out by Gimbert, Milet, and co-workers, suggested that, out of several possible pseudorotamers, the axial rotamer ($\mathbf{ax_b}$) has a local minimum energy conformer that leads to the lowest energy transition state (**TS1**) and subsequently to the formation of an intermediate with defined β-regiochemistry (Figure 2).[5] Interestingly, the inspection of the relative NBO charges of the alkyne carbons of the axial conformers ($\mathbf{ax_a}$ and $\mathbf{ax_b}$) revealed that the alkyne carbon bearing higher electron density leads to formation of a lower energy transition state (**TS1**) and subsequent formation of an intermediate leading to β-regiochemistry. Overall, the authors suggested that the polarization of the acetylenic bond dictates the regioselectivity. The inconsistency that a seemingly similar reaction of the

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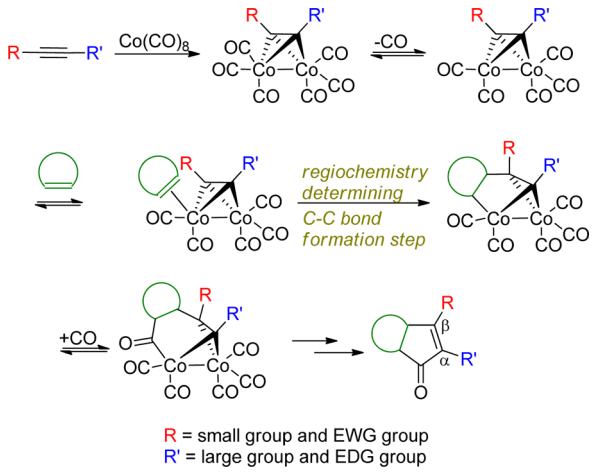

Figure 1. Postulated Magnus mechanism for PKR.[3]

terminal alkyne, ethyl propiolate, and norbornene gives the α-position as the major isomer can be explained by the similar polarities of the alkyne carbons and thus decisive steric guidance.[6] However, a recent result reported by Riera and co-workers, that ethyl 4,4,4-trifluorobutynoate PKR with norbornadiene gives the same regiochemical outcome as the corresponding reaction of norbornene with the nonfluorinated ethyl butynoate, implies that electronic effects influence the regiochemistry determination only slightly.[7]

A couple of engaging cases have been reported for cobalt-catalyzed PKR with sterically equivalent alkynes equipped with both EDG and EWG substituents (Scheme 1). For the reaction of ethyl 4-(4′-methylphenylethynyl)benzoate **1a** and norbornene, only cyclopentenone **2a*β***, with ethyl benzoate at the β-position, was isolated from the reaction mixture in 65% yield.[8] Meanwhile, for the reaction of methyl 4-(4′-methoxyphenylethynyl)benzoate **1b** with norbornadiene, a 1/2.5 α/β-regioisomer mixture of cyclopentenones **2b*α*** and **2b*β*** was obtained, in 67% combined yield.[9] It has been suggested that the cooperation of EWG and EDG alkyne substituents (4-benzoate and 4-methylphenyl/4-methoxyphenyl, respectively) produces a "push−pull" polarization effect for the alkyne, which would explain the dominance of one regioisomer.[10]

Recently, Fairlamb and co-workers highlighted the possibility of a "push−pull" effect with several sterically equivalent, or near-equivalent, heteroaromatic-substituted alkynes.[10,11] For the PKR of norbornene and (2-phenylethynyl) heteroaromatic compounds, "π-deficient" (e.g., pyrones, 2- and 3-pyridyls) and some "π-excessive" (e.g., 2- and 3-thiophene and 2-furan) compounds led to an excess of the β-regioisomer, while certain "π-excessive" heteroaromatics (e.g., 2-pyrrole or 2-indole) favored the α-position. Overall, the obtained regioisomer populations could not be fully explained by the electronic factors alone, because, for example, the β-regioisomer was predominate in the case of "π-excessive" furans and thiophenes violating the rule that the EDG substituent would favor the α-regioisomer. However, in this respect, the set of studied compounds was not entirely sterically equivalent and possible interfering coordinative interactions by these heteroaromatics also could not be excluded. In the present study, we decided to investigate the PKR with a series of sterically equivalent, but electronically unequal, aromatic alkynes, to obtain further understanding regarding electronically guided regioselectivity.

RESULTS AND DISCUSSION

Initially, electronic effects were varied by altering one functional group in the para-position of alkynes (Table 1). The dimethylamine, methoxy, and methyl substituents were representative EDGs, while dimethylaminium, trifluoromethyl, ethyl carboxylate, acetyl, and fluoro substituents represented EWGs, with each series following a decreasing order of the Hammett σ_p values. In the case of aryl alkynes with one para substituent, expectedly, the EDG-substituted aryls favored α-regioisomer in most cases, while the EWGs favored the β-regioisomer. However, the magnitude of these preferences did not correlate fully with the Hammett values, as shown in Figure

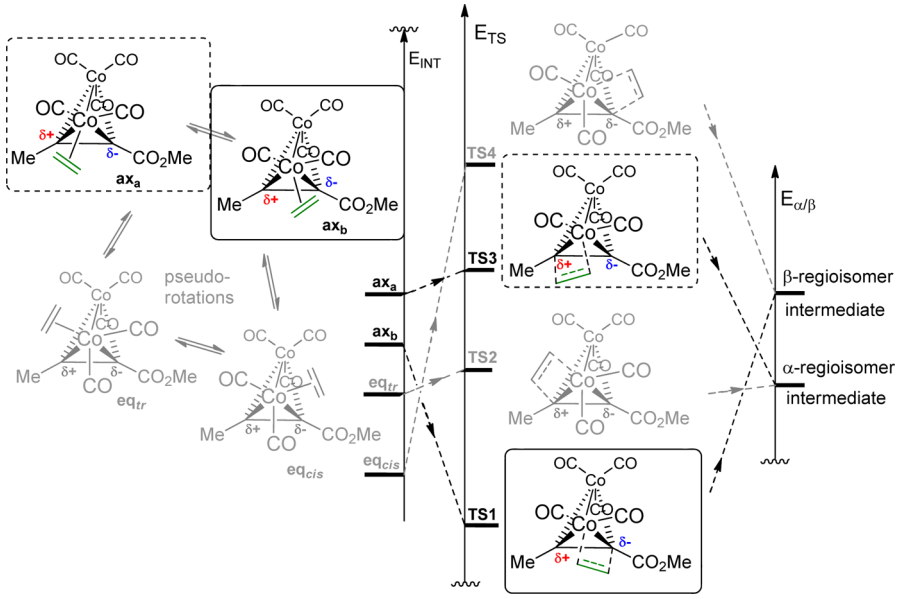

Figure 2. Computational insight into the 2-methyl butynoate−ethylene dicobalt pentacarbonyl complex regiochemistry-determining step ($\pm\delta$ is the relative NBO charge). The lowest energy pathway $\mathbf{ax_b}$-**TS1** to the β-regioisomer and the energetically unfavorable pathway $\mathbf{ax_a}$-**TS3** to the α-regioisomer is framed with solid and broken lines, respectively.[5]

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Scheme 1. Suggested "Push-Pull" Effect by EWG and EDG Substituents, Leading to Higher Regioselectivity

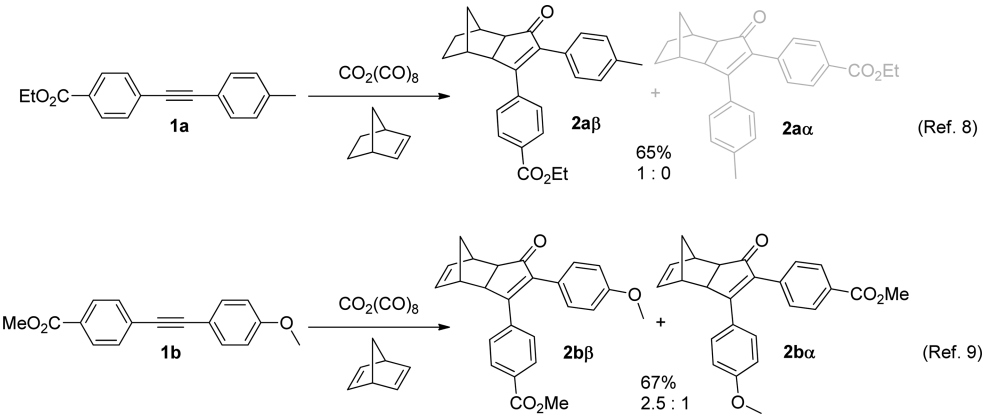
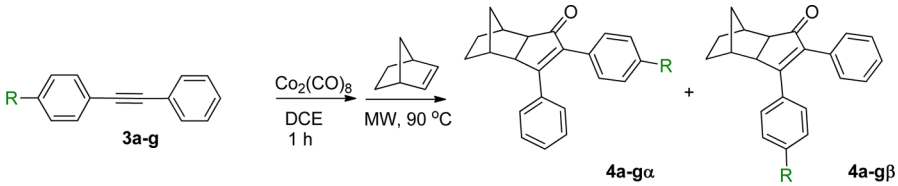


Table 1. Regiochemical Outcomes of PK Reactions with an EDG or EWG Group at Individual Para-Positions[a]



entry	alkyne		α : β[b]	combined yield
1	MeO	**3a**	1.6 : 1	97%
2[c]	Me_2N	**3b**	1.3 : 1	55%
3	Me_2N	**3b**	1 : 1	70%
4	$H-N^{\oplus}$ $\ominus BF_4$	**3c**	1 : 1.3	100%
5	Me	**3d**	1.2 : 1	73%
6	F	**3e**	1 : 1	80%
7	O	**3f**	1 : 1.25	100%
8	F_3C	**3g**	1 : 1.3	95%

[a]Reaction conditions: (i) $Co_2(CO)_8$ (1 equiv), alkyne (1 equiv, **3a**–**g**), DCE, room temperature, 1 h; (ii) norbornene (5 equiv added, MW 90 °C. [b]Regiochemistry relative to the substituted phenyl-position in the cycloadduct. The isomer ratio is determined by the ^{1}H NMR integrals of characteristic protons. [c]The reaction was carried out with 1 equiv of triethylamine in the reaction mixture.

3. The best α/β-regioselectivity, 1.6/1, was obtained with the methoxy group (entry 1), even though dimethylamine is the most electron-donating and polarizing group of the series and should thus give the highest α-regiopreference. Some other factors might also be involved in the PKR. For instance, under standard conditions (entry 3), no regioselectivity was observed in the PKR of dimethylamine **3b**. Meanwhile, with a base additive, 1 equiv of triethylamine, the α-regioisomer clearly predominated, with a 1.3/1 α/β ratio. We think that the Lewis acidity of the cobalt species may interfere with the selectivity by its amine coordination affinity. The conversion of amines into aminium salts has been shown to facilitate their PKR.[12] Pleasingly, when we converted the dimethylamine **3b** into the corresponding BF_4^- salt **3c** (entry 4), the β-regioisomer **4b*β*** turned out to be more favored with a 1/1.3 α/β ratio. Again this was qualitatively satisfactory but not in full quantitative agreement with the pertinent Hammett values.

Among EWG substituents, acetate **3f** and trifluoromethyl **3g** regioselectivity followed their Hammett values (entries 7 and 8).[13] Obviously, the 4-fluorine substituent in **3e** alone was too weak of an EWG to give an experimentally detectable product regioisomer distribution. For the rest of the compounds that were equipped with one para substituent, the isomer ratio correlates qualitatively well. By excluding the anilines, the Hammett value fit is quantitatively satisfactory (Figure 3).

In another set of compounds, each aryl group was functionalized either with an EDG or EWG (Table 2) to probe possible "push–pull" effects in the PKR. For the MW reaction of ethyl 4-(4′-methylphenylethynyl)benzoate **1a** (entry 2), an excess 1/1.3 of β-regioisomer **2a*β*** was obtained. However, the ratio was less than expected, while the β-

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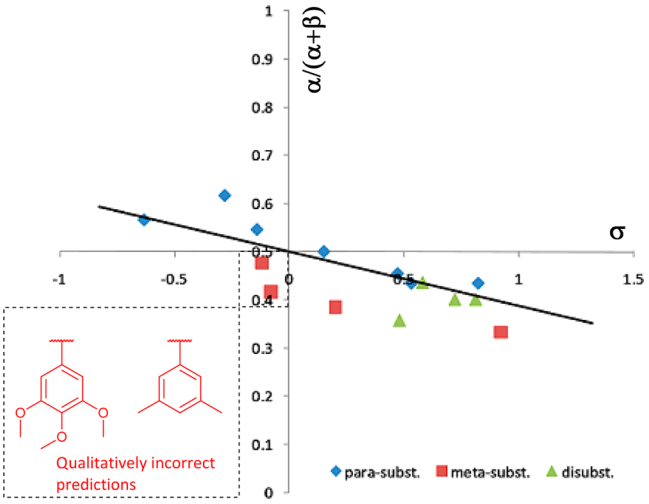


Figure 3. Correlations of Hammett $\sigma_{p/m}$ values (on the *x*-axis) to the regioisomer outcome of the reactions ($\alpha/(\alpha + \beta)$ on the *y*-axis). The linear fitting is forced via the origin (0.0, 0.5).

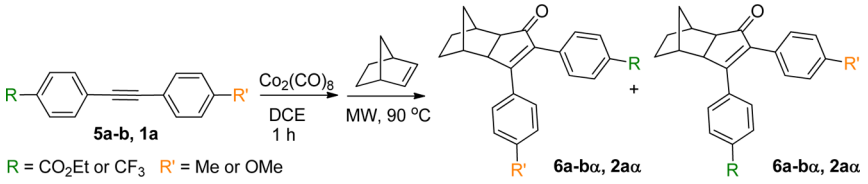
regioisomer **2a*β*** was obtained exclusively for the same substrate by Gimbert, Greene, and co-workers when the reaction was carried out thermally in toluene.[8] When we performed our reaction thermally in toluene at 80 °C, the yield dropped from quantitative to 76%, but the regioisomer ratio remained identical (entry 1). There was, in any case, one technical difference in our thermal reaction in comparison to the literature example; we prepared the cobalt−alkyne complex in a standard manner in situ, while in the reported reaction, the cobalt complex was isolated prior to the PKR. Nonetheless, the reported complete regioselectivity by purely electronic factors is an exceptional case and also, based on our results, is likely an overstatement possibly due to an erroneous or inadequate regioisomer analysis.

The change of 4-methylphenyl into a stronger EDG, 4-methoxyphenyl, for the ethyl 4-(ethynyl)benzoate partner (**1a** to **5a**) increased the excess of the *β*-regioisomer only slightly, up to 1/1.5 (entry 3), which was less than that obtained for 4-methoxyphenyl without the EWG partner group **3a** (Table 1, entry 1). In fact, this comparison suggests a negative cooperation in regioselectivity, indicating a depressing "push−pull" effect. In contrast to this, Li et al. have reported a higher *β*-regioselectivity (1/2.5) for the similar alkyne **1b** in its PKR with norbornadiene in hexane under thermal activation at 60 °C.[9] The higher selectivity might originate from the use of a more active alkene, lower temperature, and nonpolar conditions.

To confirm this effect, 4-ethylbenzoate was replaced with a slightly stronger EWG, 4-(trifluoromethyl)phenyl, in **5b**. However, the change did not affect the regioselectivity (1/1.5), even though a higher yield of cyclopentenone isomers **6bα** and **6bβ** was obtained (entry 4). Overall, the MW PKRs of para-substituted alkynes carried out in DCE at 90 °C did not show any increased regioselectivity by the functional groups attached to the adjacent ethynyl phenyl rings. Thus, under these conditions, the PKRs for the para-substituted aryls did not cooperate to show any "push−pull" effect in the regioselectivity.

Encouraged by the good matches for Hammett values of the single para-substituted aryls, we prepared a set of meta-substituted aryls with EDGs and EWG to probe whether these values would have wider applicability in the PKR (Table 3). In the case when two methoxy groups were added to compound **3a** (Table 1, entry 1) in the meta-positions (Table 3, entry 2), the regioselectivity was flipped and a 1/1.4 excess of *β*-regioisomer **8aβ** was obtained. Without the 4-methoxy group, the 3,5-dimethoxy substituents fully inverted the regioisomer ratio 1/1.6 (entry 3) compared to the para-substituted methoxy compound **3a**. This indicates that the polarizing effect of the *m*-methoxy substituent was stronger than predicted by the Hammett values (Figure 3). Moreover, when one phenyl was 4-methoxy- and another 3,5-dimethoxy-substituted (**7c**), the guidance effect was to some extent additive (entry 4), while the combined polarization yielded an 1/1.8 excess of *β*-regioisomer **8cβ**. The 3,5-dimethyl-substituted compound **7d** (entry 6) indicates that a similar meta regioguidance trend also applies for a weaker EDG; polarization leads to a small excess of *β*-regioisomer **8dβ** (1/1.1). Finally, the 3,5-bis(trifluoromethyl)-substituted compound **7e** (entry 8) gives an intuitively unexpected result; the *β*-regioisomer **8eβ** clearly predominates with a 1/2 ratio, indicating that an EWG in the meta-position leads to a *β*-regioisomer-directing effect. However, this is also in qualitative agreement with the Hammett values (Figure 3). Overall, these values give poor correlations for the meta

Table 2. Regiochemical Outcomes of Diphenylacetylene PKRs with EDG or EWG Para Substituents in Each Aryl Ring[a]



entry	alkyne		α : β[b]	combined yield
1[c]	EtO_2C—≡—Me	**1a**	1 : 1.3	76%
2	EtO_2C—≡—Me	**1a**	1 : 1.3	100%
3	EtO_2C—≡—OMe	**5a**	1 : 1.5	73%
4	F_3C—≡—OMe	**5b**	1 : 1.5	91%

[a]Reaction conditions: (i) $Co_2(CO)_8$ (1 equiv), alkyne (1 equiv, **1a**, **5a**,**b**), DCE, room temperature, 1 h; (ii) norbornene (5 equiv) added, MW 90 °C. [b]Regiochemistry relative to the EWG-position in the cycloadduct. The isomer ratio is determined by ^{1}H NMR integrals of corresponding protons. [c]Thermal reaction in toluene at 80 °C.

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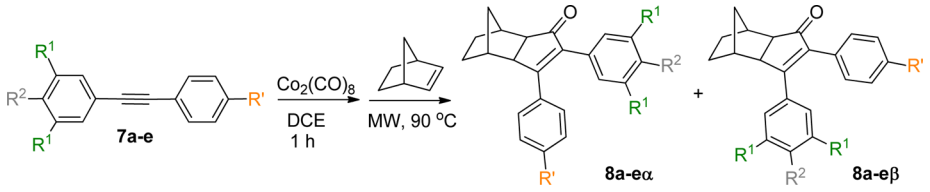
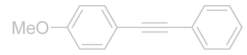
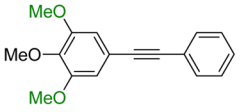
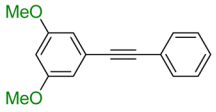
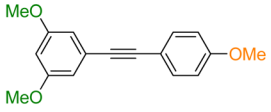
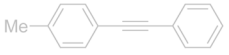
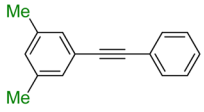
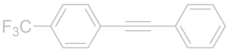
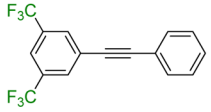
Table 3. Regiochemical Outcomes of Diphenylacetylenes PKRs with Unsymmetrical Electronic EWD and EDG Substitutions in Meta-Positions[a,b]



entry	alkyne		α : β[c]	combined yield
1		3a	1.6 : 1	97%
2		7a	1 : 1.4	89%
3		7b	1 : 1.6	67%
4		7c	1:1.8[d]	62%
5		3d	1.2 : 1	73%
6		7d	1 : 1.1	85%
7		3g	1 : 1.3	95%
8		7e	1 : 2	100%

[a]Reactions with gray coloring are also presented in Table 1. [b]Reaction conditions: (i) $Co_2(CO)_8$ (1 equiv), alkyne (1 equiv, **7a**–**e**), DCE, room temperature, 1 h; (ii) norbornene (5 equiv) added, MW 90 °C. [c]Regiochemistry relative to the substituted phenyl-position in the cycloadduct. The regioisomer ratio is determined by ^{1}H NMR integrals of characteristic protons. [d]Regiochemistry relative to 3,5-dimethoxyphenyl.

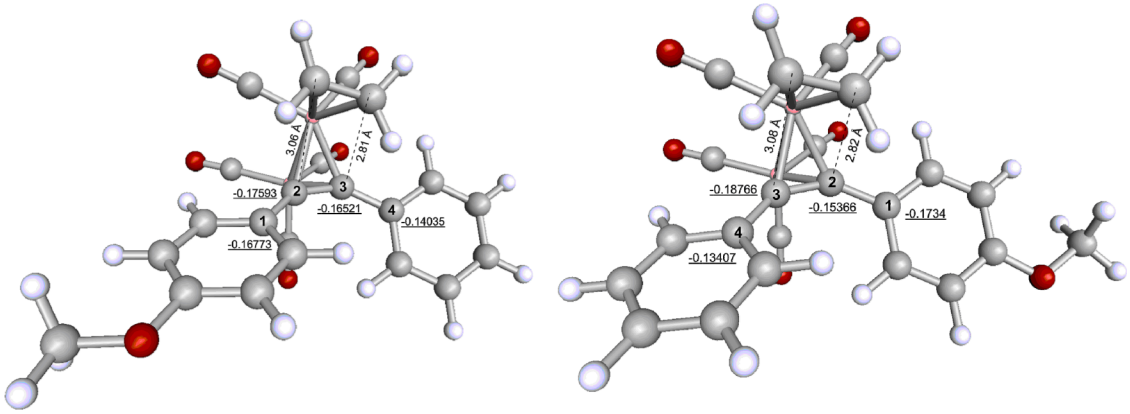


Figure 4. Gas-phase-optimized ethene-coordinated pentacarbonyl–alkyne dicobalt complexes **3a-int*α*** and **3a-int*β***, based on TPSS-D3/def2-TZVPP. Ethene–ethyne C–C distances are given in angstroms, and NBO charges are listed for alkyne and *α*-alkyne carbons (underlined).

substituents, also giving a qualitative inaccuracy for compounds **7a** and **7d**. This led us to perform computational studies to obtain a deeper theoretical insight into the electronic affects in the regioselectivity. Previous computations of dicobalt-mediated PKRs at the DFT level have enlightened us regarding mechanistic details and have successfully predicted regio- and stereochemical outcomes.[5,8,14]

Computational Studies. Following the study of Gimbert, Milet, and co-workers,[5] we initiated a computational study with ethene-coordinated pentacarbonyl–alkyne complexes of methoxy-substituted phenyls **3a**, **7a**, and **7b** . The complexes were

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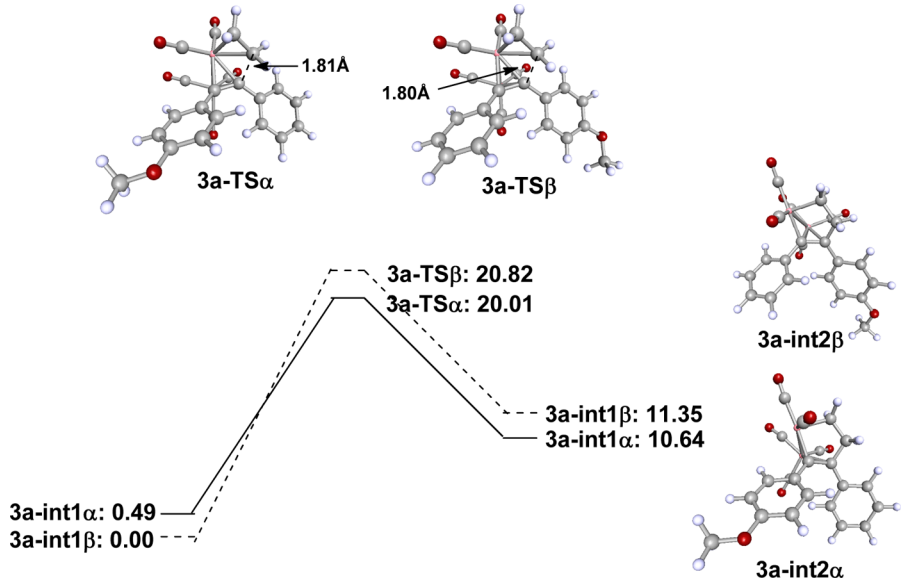
Table 4. NBO Charges on Complexes 3a-, 7a-, and 7b-int1-α/β, Based on TPSS-D3/def2-TZVPP Gas-Phase Calculations[a]

	C_1	C_2	C_3	C_4	$\Delta(C_2 - C_3) \times 10^{-2}$	$\Delta(C_1 - C_4) \times 10^{-2}$
3a-int1-α	−0.16773	−0.17593	−0.16521	−0.14035	−1.07	−2.74
3a-int1-β	−0.1734	−0.15366	−0.18766	−0.13407	3.40	−3.93
7a-int1-α	−0.12008	−0.17651	−0.16078	−0.14164	−1.57	2.16
7a-int1-β	−0.12545	−0.15472	−0.18282	−0.13472	2.81	0.93
7b-int1-α	−0.10139	−0.17927	−0.16314	−0.14157	−1.61	4.02
7b-int1-β	−0.10732	−0.15849	−0.18413	−0.13569	2.56	2.84

[a]Numbering of the carbons is shown in Figure 4.

Table 5. Computed Activation Energies Leading to Different Regioisomers (reaction scheme presented is for substrate 3a)[a]



substrate	α/β	$\triangle G$(**int1**)	$\triangle G$(**TS**)	$\triangle G^{\ddagger}$	$\triangle G$(**int2**)
3a	α	0.49	20.01	19.52	10.64
3a	β	0.00	20.82	20.82	11.35
7a	α	0.34	20.20	19.85	10.63
7a	β	0.00	22.39	22.38	12.19
7b	α	0.00	18.55	18.55	8.78
7b	β	0.12	19.83	19.70	9.64

[a]Computations were carried out in the gas phase at the TPSS-D3/def2-SVP level. Energies are in kcal/mol.

optimized in the gas phase, using the TPSS-D3 functional with a triple-ζ basis set, namely def2-TZVPP.[15−17] The multipole-accelerated resolution of the identity approximation, MARI-J, was used with a suitable fitting basis set.[18,19] We have previously determined that this method gives good correlation between experimental and computational results.[20]

Because the alkene can be either equatorially or axially coordinated to the cobalt (Figure 2),[5] we began our study with the intermediates and transition states most likely to be involved in the reaction pathway, i.e., the axially coordinated complexes on three different methoxy-substituted substrates **3a**, **7a**, and **7b** in two conformations **int1-α/β**, depending upon which alkyne carbon is closer to the alkene (Figure 4).

The conformation **int-α** represents a structure where the alkene is closer to the alkyne carbon C_3 (Figure 4), bearing the closest alkene−alkyne C−C distance of 2.80−2.82 Å, depending on the substrate **3a**, **7a**,**b**. Formation of a C−C bond between these carbons would lead to the α-regioisomer. A slight rotation of conformer **int1-α** leads to conformer **int1-β**, in which the related alkene−alkyne distance of 2.80−2.82 Å is attributed to alkyne carbon C_2. Correspondingly, formation of a C−C bond between these carbons would lead to the β-regioisomer.

Having in mind that the C−C bond has been suggested to form more preferably with the alkyne carbon carrying higher electronic density,[5] we decided to test whether this applies to our set of compounds. According to our experimental results on regioselectivity, the higher electronic density for the complex **3a-int1** should be associated with carbon C_3, while for complexes **7a-int1** and **7b-int1** it should be located in carbon C_2. In fact, such results can be obtained, but a change in the conformation from α to β will affect the results (Table 4). As the differences in the NBO charges in our systems are very small, they are susceptible to the conformational changes.

Next, we had a look at the NBO charges of the C_1 and C_4 carbons in the α-position to the alkyne carbons. These values are not as prone to conformational changes (Table 4). The polarization of these carbons should have a direct impact on the polarization of the alkyne and therefore also on the regioselectivity, as suggested by the Hammett value analysis vide supra. The $\Delta(C_1 - C_4)$ values give qualitative correlation in all complexes **3a-**, **7a-**, and **7b-int1-α/β**, indicating that the

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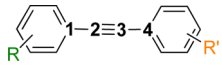
Table 6. The NBO Charges for Experimentally Studied Alkynes Based on TPSS-D3/def2-TZVPP in the Gas Phase[a]



entry	experimental α/β-distribution	substrate	C_1	C_2	C_3	C_4	$\Delta(C_2 - C_3) \times 10^{-2}$	$\Delta(C_1 - C_4) \times 10^{-2}$
1	1/1.3	**1a**	−0.10193	−0.00157	0.02603	−0.13628	−2.76	3.44
2	1.6/1	**3a**	−0.152	0.01302	−0.00287	−0.12099	1.59	−3.10
3	1.3/1	**3b**	−0.16753	0.01798	−0.0144	−0.11816	3.24	−4.94
4	1.2/1	**3d**	−0.1325	0.01149	0.00437	−0.12263	0.712	−0.987
5	1/1	**3e**	−0.13661	0.00453	0.01184	−0.12469	−0.731	−1.192
6	1/1.2	**3f**	−0.10042	0.00115	0.02759	−0.12885	−2.64	2.84
7	1/1.3	**3g**	−0.10588	−0.00224	0.02903	−0.12922	−3.13	2.33
8	1/1.5	**5a**	−0.10043	−0.00875	−0.02773	−0.15581	1.898	5.538
9	1/1.5	**5b**	−0.10288	−0.01356	0.03208	−0.1576	−4.564	5.472
10	1/1.4	**7a**	−0.11305	0.01324	0.00407	−0.12239	0.917	0.934
11	1/1.6	**7b**	−0.0923	0.01659	0.00516	−0.12235	1.143	3.01
12	1/1.8	**7c**	−0.08913	0.00429	0.00933	−0.15043	−0.504	6.13
13	1/1.1	**7d**	−0.11186	0.01472	0.00255	−0.12246	1.22	1.06
14	1/2	**7e**	−0.10645	−0.01172	0.04369	−0.1331	−5.541	2.67

[a]Numbering of the carbons is shown below, substituents according to Tables 1–3.

C–C bond would be formed with the alkyne carbon that has lower electron density on its aromatic α-carbon.

To gain a deeper insight into these systems, we optimized the transition states from complexes **3a-**, **7a-**, and **7b-int1-*α*/*β***, leading to either the α- or β-regioisomer through intermediate **int2-*α*/*β*** (Table 5). As described previously, the TPSS-D3 functional was used. Instead of a triple-ζ basis set, a double-ζ quality basis set (def2-SVP) was employed.[17] The α/β conformations of ethane-coordinated alkyne–cobalt complexes (**int1**) are very close to each other in energies. Notably, the C–C bond formation step is computed to be endothermic for all of the studied systems. Disappointingly, the differences in the activation energies suggest that the transition state leading to the α-regioisomer would be more favored in all of the complexes. Moreover, the differences are small and inside the error bars of even highly accurate DFT methods.[21] One major limitation in our approach was that only the two possible axial pathways were studied. For a complete picture, a comprehensive transition state search should be performed, including both the axial and equatorial coordination of alkene to cobalt. However, this would be time-consuming and rather impractical for the purpose of finding out electronic rules for the regioselectivity of the experimental set of compounds.

Encouraged by the qualitative correlation between electronic density differences on the aryl carbons C_1 and C_4 (Table 5) and the experimentally observed regioselectivity, we studied whether these differences can be obtained for the plain alkynes. All experimentally studied alkynes were optimized in the gas phase, as previously described, employing the def2-TZVPP basis set, and their NBO charges were calculated. The results are presented in Table 6.

The electronic density differences between aryl carbons C_1 and C_4 correlate well with the experimental results qualitatively (Tables 1–3 and 6). The only exception is the *p*-fluoro-substituted substrate (**3e**), for which a slight selectivity toward the α-regioisomer is predicted. Experimentally, no selectivity was observed for this substrate. Overall, simple para-substituted substrates seem to correlate well with the observations made by Gimbert, Milet, and co-workers, where the C–C bond is formed with the more electron-rich alkyne carbon.[5] However, as pointed out above, for the aryl rings equipped with electron-donating substituents in the meta-position, the charge difference of the alkyne carbons do not correlate soundly with the experimentally observed regioselectivity. Instead, when the charge differences of aryl carbons C_1 and C_4 are inspected, the correlation is quantitatively satisfactory. Figure 5 illustrates that

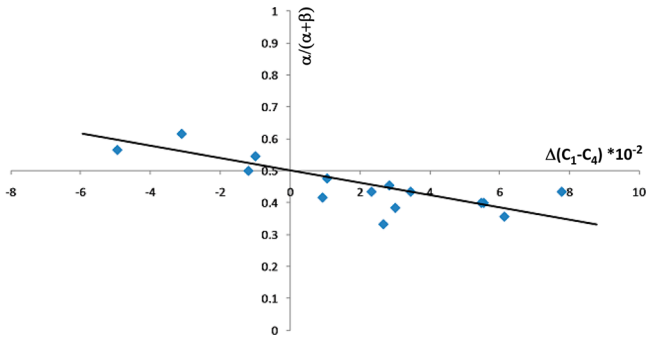


Figure 5. Correlation of regioselectivity and NBO charges on TPSS-D3/def2-TZVPP. The linear fitting is forced via the origin (0.0, 0.5).

the correlation of the computed density differences ($\Delta(C_1 - C_4) \times 10^{-2}$ values) against the regioselectivity is of high degree and largely independent of the specific type and positions of the substituent(s).

In contrast to our experimental observations, the computational $\Delta(C_1–C_4)$ charge density differences favor a "push–pull" effect. For instance, the difference is nearly additive when the value 5.4×10^{-2} of ethyne **5b** equipped with 4-methoxyphenyl and 4-trifluorophenyl groups is compared with the values of ethynes equipped with either one of these functional groups; 3.4×10^{-2} and 2.3×10^{-2} for 4-methoxy **3a** and 4-trifluoromethyl group **3g**, respectively. Similarly, a comparison of the values 4-methyl **3d** vs 4-methoxy **3a** substituent effects gives a value for ΔΔ of 2.1×10^{-2}. This value matches perfectly with the ΔΔ value obtained between the ethyl benzoates **1a** and **5a** (2.1×10^{-2}), when the same alteration of 4-methyl to 4-methoxy groups has taken place.

To check for problems related to the basis set superposition error (BSSE), we also calculated NBO charges using the double-ζ quality basis set (def2-SVP). Some slight changes in the NBO charges were observed, but the nature of the Δ value was the same in all cases. Solvating effects were included in

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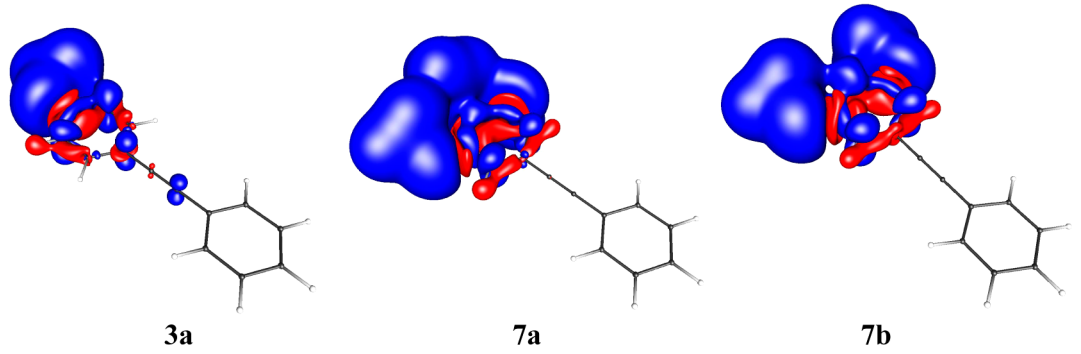

Figure 6. The relative electronic density of substrates 4-methoxyphenyl-, 3,4,5-trimethylphenyl-, and 3,5-dimethylphenyl-ethylnylbenzenes **3a**, **7a**, and **7b**, respectively, compared to 1,2-diphenylethylene electron density.

single-point calculations using the COSMO approach, with an ε value of 10.3 (dichloroethane).[22] The hybrid functional TPSSh was also used for NBO analysis as a single-point calculation.[23] None of these approaches changed the nature of the results, indicating that our choice of the method was justified (see Supporting Information).

As the correlation between the carbon C_1 and C_4 NBO charges and the regioselectivity was found to be qualitative, and within certain limits quantitative, we wondered whether this polarization effect could be visualized. To answer this question, we calculated the differences between the electronic densities of nonsubstituted and substituted phenyls. All figures are based on TPSS-D3/def2-TZVPP calculations and were produced using the same isovalue and can therefore be easily compared.

Figure 6 shows how the density differences are affected by the position of the methoxy substituents. The blue color indicates a higher electronic density of the substituted phenyl compared to that of the nonsubstituted phenyl, while the red color indicates a lower density. These can also be expressed as blue to indicate negative polarization and red to indicate positive.

The electron-donating methoxy group at the para-position brings more electron density to the C_1 carbon, polarizing the p-type orbital negatively (Figure 6, **3a**). Addition of two methoxy groups to the meta-positions causes the ortho-positions to gain strong negative polarization, and the negative p-orbital polarization of C_1 is therefore decreased (**7a**). The 3,5-dimethoxy substitution, to some extent, produces positive polarization for the C_1 carbon. Notably, the polarization is extended into the C_2 and C_3 alkyne carbons only in the para-substituted aryl alkyne **3a**.

Weaker polarization effects were expected for the methyl substituents (**3d**, **7d**). For the para-methyl-substituted aryl alkyne **3d**, the C_1-position is negatively polarized (Figure 7). Overall, this effect is similar but weaker, compared to *p*-methoxy-substituted phenyl (Figure 6). In the case of 3,5-dimethyl-substituted phenyl, the polarization becomes inversed, as already noted for the methoxy-substituted substrates. Overall, with the methyl groups, the polarization is weaker and not visible in the alkyne carbons (C_2–C_3), even on the para-substituted substrate **3d**.

The experimental results presented above (Tables 1–3) suggest that electron-withdrawing groups direct the regiochemistry into the β-conformer, despite the position of the substituent. The inversion of the regioselectivity was not observed when the electron-withdrawing trifluoromethyl substituent was changed from the para- to meta-position, in

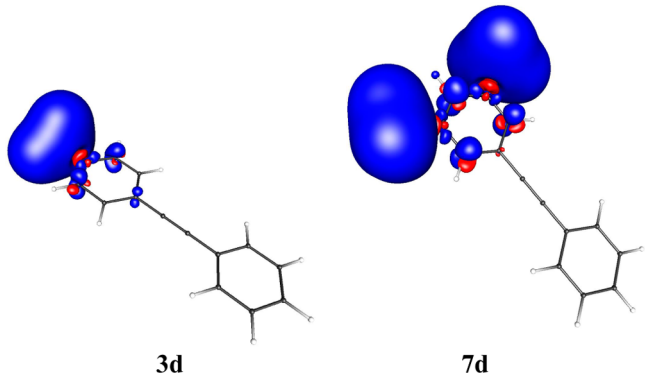

Figure 7. The relative electronic density of 4-methylphenyl- and 3,5-dimethylphenyl-ethylnylbenzenes, **3d** and **7d**, respectively, compared to 1,2-diphenylethylene electron density.

contrast to the case with electron-donating substituents. The polarization effect is increased from trifluoromethyl para-substitution (**3g**) to 3,5-disubstition (**7e**); the experimentally observed α/β-regiodistribution changed from 1/1.3 to 1/2 in going from the para to meta substitution, respectively. This is well visualized by the density difference plots (Figure 8). The p-orbitals of carbons C_1 and C_3 are positively polarized in both cases; additionally, the alkyne carbons (C_2 and C_3) are clearly more strongly polarized for the meta-disubstituted compound **7e**. Interestingly, for this compound, the s-type orbitals of

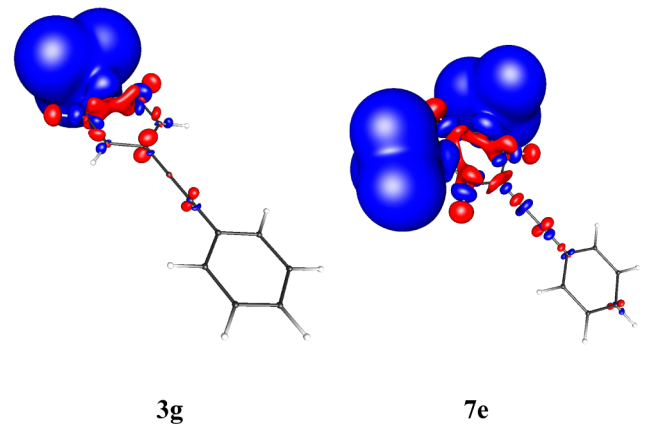

Figure 8. The relative electronic density of 4-(trifluoromethyl)phenyl- and 3,5-bis(trifluoromethyl)-ethylnylbenzenes, **3g** and **7e**, respectively, compared to 1,2-diphenylethylene electron density.

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alkyne carbons are also polarized with an opposed phase to the p-type orbitals.

To visualize the so-called "push−pull" effect, the similarly calculated relative electron densities are illustrated for 3,5-dimethoxyphenyl and 4-(trifluoromethyl)phenyl, **7c** and **5b**, respectively, in Figure 9. For **7c**, the polarization of the alkyne

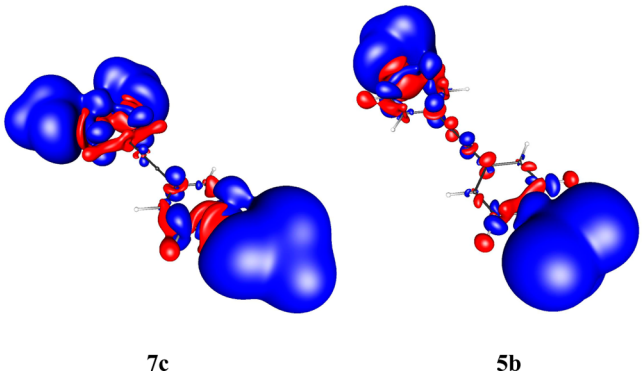


Figure 9. The relative electron densities of 4-methoxyphenyl-ethynyl to 3,5-dimethoxyphenyl and 4-(trifluoromethyl)phenyl, **7c** and **5b** (compared to 1,2-diphenylethylene electron density).

C_2-C_3 carbons is less prominent than for 4-methoxyphenyl ethynylbenzene **3a** (Figure 6). Instead, a clearly stronger p-type polarization of the alkyne carbons can be observed for **5b**, indicating a concerted polarization effect by the 4-methoxy and 4-trifluoromethoxy groups. In both cases, the same trend could be observed in the NBO charge densities (Table 6). Overall, the localization of charge density in the p-type orbitals can be expected to correlate with the PKR.

Finally, to discover an easily accessible and computationally affordable method for predicting the regioselectivity, the studied alkynes were optimized using a semiempirical PM6 method.[24] When electrostatic potential charges were plotted against the regiochemical outcome, the PM6 produced qualitatively well-correlated results, with one noteworthy exception, 3,5-bis(trifluoromethyl)-disubstituted phenyl **7e**, as presented in Figure 10 (for numerical values, see Supporting Information). In fact, apart from this exception, the correlation of the experimental values was even better with the PM6 method than with the DFT method (Figures 5 and 10). Thus, the semiempirical method seems to provide a simple prediction method for a range of compounds which are well parametrized

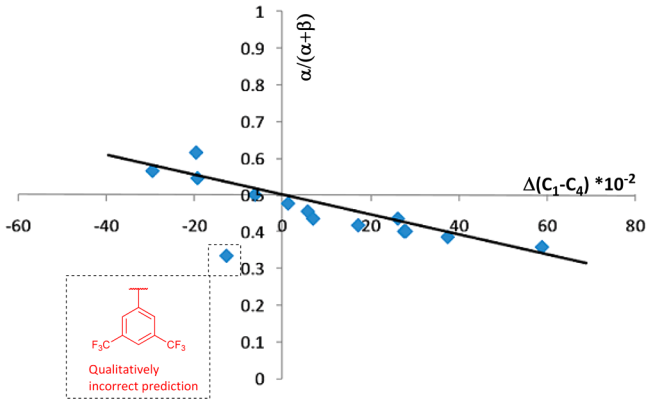


Figure 10. Correlation of regioselectivity and electrostatic potential charges on PM6. The linear fitting is forced via the origin (0.0, 0.5).

in the method, but it should be used with these restrictions in mind.

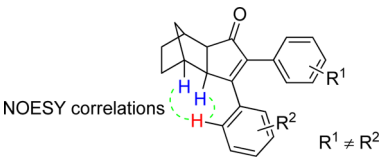
CONCLUSIONS

The performed experimental PKRs with sterically equivalent and electronically differently substituted diarylalkynes confirm the general assumption that the alkyne bond polarization dictates the α/β-regioselectivity of the formed cyclopentenones. For the studied diarylalkynes, the relative polarities of aryl carbons at α-alkyne-positions show a correlation with the regioselectivity. The Hammett values of aryl substituents provide good regioselectivity correlation for the diarylethynes with a single para substituent. As a general approach, the NBO charges of the α-alkyne carbons calculated at the DFT level give good correlation for diarylalkynes with several substitutions at the meta- and para-positions.

Experimentally, under the studied reaction conditions, we were not able to observe any "push−pull" effect in PKR α/β-regioselectivity for diarylethynes functionalized in one aryl with an EDG and in the other aryl with an EWG substituent. In fact, the only additive regioguidance effect was observed with EDG substituents for the compound where one phenyl was functionalized with a 4-methoxy group and another one was 3,5-dimethoxy-substituted. Apart from this, the relative computational charge densities of aryl carbons at the α-alkyne-positions support the "push−pull" theory. Plots of relative charge densities illustrate that the charge polarities of the ethyne moieties are associated with p-type orbitals, which are essentially involved in the PKRs.

EXPERIMENTAL SECTION

Microwave reactions were performed using a Biotage Initiator 2.0 (400 W) and sealed vials. Temperatures were monitored by an external surface sensor. Reaction conditions (including reaction times) were not optimized, and shorter reaction times would have been sufficient in many cases. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ at room temperature (rt). ^{1}H spectra were referenced to tetramethylsilane (TMS, 0 ppm), and ^{13}C spectra were referenced to solvent carbon (77.0 ppm). Regiochemistry of the products was determined by NMR with NOESY experiments in combination with ^{1}H, ^{13}C, gCOSY, gHSQC, and gHMBC experiments. ^{1}H and ^{13}C spectra of all new compounds and NOESY spectra of the PK products are available in the Supporting Information.



All geometry optimizations and NBO charge and electronic density calculations were performed using the Turbomole 6.4 program package.[25,26] Electronic densities were calculated on a 350 × 350 × 350 grid. The pictures of optimized complexes were made using the TmoleX GUI, and the pictures of density differences were made with gOpenMol.[27] All semiempirical calculations were performed with the MOPAC2009 package.[28] Vibrational calculations were performed on all DFT-optimized structures to ascertain that they presented minima or saddle points in the potential energy hypersurface.

General Procedure for Sonogashira Couplings. Aryl iodide (2.5 mmol, 1 equiv), $PdCl_2(PPh_3)_2$ (35 mg, 0.05 mmol, 0.02 equiv), and CuI (10 mg, 0.05 mmol, 0.02 equiv) were dissolved in degassed solvent (triethylamine or 1:1 mixture of triethylamine and THF). The mixture was stirred for 30 min at rt, followed by addition of an aromatic alkyne (2.75 mmol, 1.1 equiv). The reaction mixture was

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stirred overnight at rt, adsorbed onto a small amount of silica, and purified by silica column chromatography.

General Method for PKRs. Alkyne (0.25 mmol, 1 equiv) and $Co_2(CO)_8$ (0.25 mmol, 1 equiv) were placed in Biotage microwave tube, dissolved in DCE, and stirred under argon over 30 min at rt. Thereafter, norbornene (118 mg, 1.25 mmol, 5 equiv) was added, the tube was sealed, and the reaction mixture was heated for 2.5−6.5 h under MW at 90 °C. During the heating, pressure was released from the tube between every 10 min during the first 30 min. After the reaction was completed, the reaction mixture was adsorbed onto a small amount of silica and purified by silica column chromatography.

1-Methoxy-4-(phenylethynyl)benzene ***3a***. was prepared according to the general method in a TEA/THF 1:1 mixture in 81% yield (419 mg) after column chromatography (hexane−EtOAc 40:1). HRMS (EI) m/z calcd for $C_{15}H_{12}O$ 208.0888, found 208.0897. ^{1}H NMR and ^{13}C NMR spectra were found to match with published data.[29,30]

N,N-Dimethyl-4-(phenylethynyl)aniline ***3b***. was prepared according to the general method on a 5 mmol scale in TEA with 97% yield (1076 mg) after column chromatography (hexane−EtOAc 40:1 → 20:1). HRMS (EI) m/z calcd for $C_{16}H_{15}N$ 221.1204, found 221.1210. ^{1}H NMR and ^{13}C NMR spectra were found to match with published data.[31]

N,N-Dimethyl-4-(phenylethynyl)benzenaminium tetrafluoroborate ***3c***. was prepared by making a suspension of *N,N*-dimethyl-4-(phenylethynyl)aniline (1 mmol, 221 mg, 1 equiv) in dry Et_2O (4 mL) and adding $HBF_4{\cdot}Et_2O$ (1.1 mmol, 150 μL, 1.1 equiv) at 0 °C. The reaction mixture was stirred at 0 °C for 5 min, and the precipitate was filtered and washed with Et_2O. The salt was collected as a white powder in quantitative yield (308 mg). Mp 122−160 °C (decomp) Anal. Calcd for $C_{16}H_{16}BF_4N$: C, 62.17; H, 5.22; N, 4.53. Found: C, 62.36; H, 5.33; N, 4.51. ^{1}H NMR (500 MHz, $CD_3OD/CDCl_3$) δ 7.71 (d, J = 7.7 Hz, 2H), 7.58 (d, J = 7.7 Hz, 2H), 7.53 (m, 2H), 7.38 (m, 3H), 3.31 (s, 6H). ^{13}C NMR (126 MHz, $CD_3OD/CDCl_3$) δ 143.8, 135.2 (2C), 133.2 (2C), 130.5, 130.1 (2C), 127.0, 124.1, 121.9 (2C), 93.2, 88.7, 47.70, 47.66.

4-Phenylethynyltoluene ***3d***. was prepared according to the general method in TEA at 50 °C in 94% yield (453 mg) after column chromatography (hexane−EtOAc 1:0 → 40:1). HRMS (EI) m/z calcd for $C_{15}H_{12}$ 192.0939, found 192.0923. ^{1}H NMR and ^{13}C NMR spectra were found to match with published data.[32]

4-(Fluorophenyl)phenylacetylene ***3e***. was prepared according to the general method in TEA at 50 °C in 88% yield (431 mg) after column chromatography (hexane). HRMS (EI) m/z calcd for $C_{14}H_9F$ 196.0688, found 196.0695. ^{1}H NMR and ^{13}C NMR spectra were found close to published data.[32] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54−7.47 (m, 4H), 7.37−7.30 (m, 3H), 7.03 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.5 (d, J = 249.5 Hz), 133.5 (d, J = 8.3 Hz, 2C), 131.5, 128.4, 128.3, 123.1, 119.4 (d, J = 3.5 Hz), 115.6 (d, J = 22.1 Hz, 2C), 89.0 (d, J = 1.4 Hz), 88.28.

1-(4-(Phenylethynyl)phenyl)ethanone ***3f***. was prepared according to the general method on a 1.25 mmol scale in a TEA/THF 1:1 mixture in 90% yield (250 mg) after column chromatography (hexane−EtOAc 40:1 → 20:1). HRMS (EI) m/z calcd for $C_{16}H_{12}O$ 220.0888, found 220.0886. ^{1}H NMR and ^{13}C NMR spectra were found to match with published data.[33]

1-(Phenylethynyl)-4-(trifluoromethyl)benzene ***3g***. was prepared according to the general method on a 1.25 mmol scale in a TEA/THF 1:1 mixture in 70% yield (215 mg) after the column chromatography (hexane−EtOAc 60:1 → 20:1). HRMS (EI) m/z calcd for $C_{15}H_9F_3$ 246.0656, found 246.0647. ^{1}H NMR and ^{13}C NMR spectra were found to match with published data.[34]

Ethyl 4-(p-tolylethynyl)benzoate ***1a***. was prepared according to the general method in a TEA/THF 1:1 mixture in 95% yield (630 mg) after column chromatography (hexane−EtOAc 40:1 → 20:1). HRMS (EI) m/z calcd for $C_{18}H_{16}O_2$ 264.1150, found 264.1149. ^{1}H NMR and ^{13}C NMR spectra were found to match with published data.[35]

Ethyl 4-(4-methoxybenzylethynyl)benzoate ***5a***. was prepared according to the general method in TEA at 50 °C in 100% yield (419 mg) after column chromatography (hexane−EtOAc 20:1). HRMS (EI) m/z calcd for $C_{18}H_{16}O_3$ 280.1099, found 280.1097. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, J = 8.5 Hz, 2H), 7.55 (d, J = 8.5 Hz, 2H), 7.48 (d, J = 8.9 Hz, 2H), 6.89 (d, J = 8.9 Hz, 2H), 4.38 (q, J = 7.1 Hz, 2H), 3.83 (s, 3H), 1.40 (t, J = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.1, 160.0, 133.2 (2C), 131.2 (2C), 129.5, 129.4 (2C), 128.2, 114.8, 114.1 (2C), 92.5, 87.5, 61.1, 55.3, 14.3.

1-Trifluoromethyl-4-((4-methoxyphenyl)ethynyl)benzene ***5b***. was prepared according to the general method in TEA at 50 °C in 85% yield (351 mg) after column chromatography (hexane−EtOAc 40:1). HRMS (EI) m/z calcd for $C_{16}H_{11}F_3O$ 276.0762, found 276.0762. ^{1}H NMR and ^{13}C NMR spectra were found close to published data.[36] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61−7.55 (m, 4H), 7.48 (d, J = 8.8 Hz, 2H), 6.89 (d, J = 8.8 Hz, 2H), 3.82 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.1, 133.3 (2C), 131.6 (2C), 129.5 (q, J = 32.7 Hz), 127.5 (q, J = 1.3 Hz), 125.2 (q, J = 3.8 Hz, 2C), 124.2 (q, J = 272 Hz), 114.6, 114.1 (2C), 91.9, 86.8, 55.3.

1,2,3-Trimethoxy-5-(phenylethynyl)benzene ***7a***. was prepared according to the general method on a 1.5 mmol scale in a TEA/THF 1:1 mixture in 93% yield (374 mg) after column chromatography (hexane−EtOAc 10:1 → 5:1). HRMS (EI) m/z calcd for $C_{17}H_{16}O_3$ 268.1099, found 268.1106. ^{1}H NMR and ^{13}C NMR spectra were found close to published data.[37] ^{1}H NMR (300 MHz, $CDCl_3$) 7.55−7.50 (m, 2H), 7.36−7.32 (m, 3H), 6.78 (s, 2H), 3.88 (s, 6H), 3.87 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.0 (2C), 138.8, 131.5 (2C), 128.3 (2C), 128.2, 123.1, 118.2, 108.8 (2C), 89.4, 88.4, 60.9, 56.1 (2C).

1,3-Dimethoxy-5-((4-methoxyphenyl)ethynyl)benzene ***7c***. was prepared according to the general method in TEA in 25% yield (167 mg) after column chromatography (hexane−EtOAc 20:1). HRMS (EI) m/z calcd for $C_{17}H_{16}O_3$ 268.1099, found 268.1089. ^{1}H NMR and ^{13}C NMR spectra were found to match with published data.[38]

4-Phenylethynylxylene ***7d***. was prepared according to the general method in TEA at 50 °C in 71% yield (367 mg) after column chromatography (hexane). HRMS (EI) m/z calcd for $C_{16}H_{14}$ 206.1096, found 206.1083. ^{1}H NMR and ^{13}C NMR spectra were found to match with published data.[39]

1,3-Trifluoromethyl-5-(phenylethynyl)benzene ***7e***. was prepared according to the general method in TEA in 81% (633 mg) yield after column chromatography (hexane). HRMS (EI) m/z calcd for $C_{16}H_8F_6$ 314.0530, found 314.0530. ^{1}H NMR and ^{13}C NMR spectra were found close to published data.[40] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (s (br.), 2H), 7.81 (s (br.), 1H), 7.58−7.53 (m, 2H), 7.41−7.35 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 132.0 (q, J = 33.7 Hz, 2C), 131.8 (2C), 131.4 (q, J = 2.7 Hz, 2C), 129.3, 128.6 (2C), 125.7, 123.0 (q, J = 273 Hz, 2C), 121.5 (m, 1C), 92.8, 86.3.

4aα and 4aβ. PKR of 1-methoxy-4-(phenylethynyl)benzene **3a** was performed according to the general method (5 h heating) in combined 97% yield (80 mg) after column chromatography (hexane−EtOAc 1:0 → 10:1). Isomers **4aα** and **4aβ** were formed in 1/1.3 ratio. 3a,4,5,6,7,7a-Hexahydro-3-phenyl-2-(4-methoxyphenyl)-4,7-methano-1*H*-inden-1-one **4aα**, off-white amorphous solid. HRMS (EI) m/z calcd for $C_{23}H_{22}O_2$ 330.1620, found 330.1635. ^{1}H NMR (300 MHz, $CDCl_3$) 7.35−7.27 (m, 5H), 7.14 (d, 8.0 Hz, 2H), 6.83 (d, 8.0 Hz, 2H), 3.79 (s, 3H), 3.17 (m, 1H), 2.60 (m, 1H), 2.48 (m, 1H), 2.09 (m, 1H), 1.65 (m, 2H), 1.40 (m, 2H), 1.22 (d, 10.0 Hz, 1H), 1.00 (d, 10.0 Hz, 1H). ^{13}C NMH (126 MHz, $CDCl_3$) 208.9, 169.0, 159.2, 142.0, 135.5, 130.6, 129.3, 128.5, 128.4, 124.3, 113.9, 55.2, 54.1, 50.7, 39.5, 38.3, 31.6, 29.0, 28.9. 3a,4,5,6,7,7a-Hexahydro-2-phenyl-3-(4-methoxyphenyl)-4,7-methano-1*H*-inden-1-one **4aβ**, off-white amorphous solid. HRMS (EI) m/z calcd for $C_{23}H_{22}O_2$ 330.1620, found 330.1636. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36−7.25 (m, 5H), 7.23−7.18 (m, 2H), 6.82−6.77 (m, 2H), 3.80 (s, 3H), 3.19 (d, J = 5.5 Hz, 1H), 2.60 (br, 1H), 2.48 (d, J = 5.5 Hz, 1H), 2.15 (br, 1H), 1.70−1.64 (m, 2H), 1.45−1.40 (m, 2H), 1.22 (d, J = 10.5 Hz, 1H), 1.01 (d, J = 10.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 208.5, 169.1, 160.7, 141.3, 132.9, 130.5, 129.3, 128.5, 127.6, 127.2, 113.8, 55.3, 54.0, 50.4, 39.4, 38.8, 31.7, 29.1, 28.9.

4bα and 4bβ. PKR of 1-*N,N*-dimethylamine-4-(phenylethynyl)-benzene **3b** was performed according to the general method (4 h 30 min heating) in combined 70% yield (60 mg) after column

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chromatography (hexane−EtOAc 10:1 → 5:1). Isomers **4bα** and **4bβ** were formed in 1/1 ratio. The reaction was repeated according to the general method (3 h 30 min heating) with 1 equiv (0.25 mmol, 32 μL) of triethylamine added to the reaction mixture together with norbornene. Combined yield after column chromatography (hexane−EtOAc 10:1 → 5:1) was 55% (47 mg), and the isomers **4bα** and **4bβ** were formed in 1/1.3 ratio. 3a,4,5,6,7,7a-Hexahydro-3-phenyl-2-(4-*N*,*N*-dimethylaniline)-4,7-methano-1*H*-inden-1-one **4bα** HRMS (ESI-TOF) *m*/*z* calcd for $[C_{24}H_{26}NO]^+$ 344.2009, found 344.2024. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (m, 2H), 7.31−7.28 (m, 3H), 7.11 (d, *J* = 8.9 Hz, 2H), 6.63 (d, *J* = 8.9 Hz, 2H), 3.14 (d, *J* = 5.5 Hz, 1H), 2.93 (s, 6H), 2.58 (s, 1H), 2.46 (d, *J* = 5.5 Hz, 1H), 2.08 (s, 1H), 1.67−1.62 (m, 2H), 1.41 - 1.36 (m, 2H), 1.22 (d, *J* = 10.5 Hz, 1H), 0.98 (d, *J* = 10.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 209.3, 167.6, 150.0, 142.2, 136.0, 130.1 (2C), 129.0, 128.5 (2C), 128.3 (2C), 119.6, 112.1 (2C), 54.1, 50.7, 40.4 (2C), 39.4, 38.2, 31.6, 29.0, 28.9. 3a,4,5,6,7,7a-Hexahydro-2-phenyl-3-(4-*N*,*N*-dimethylaniline)-4,7-methano-1*H*-inden-1-one **4bβ** HRMS (ESI-TOF) *m*/*z* calcd for $[C_{24}H_{26}NO]^+$ 344.2009, found 344.2005. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (m, 2H), 7.30−7.22 (m, 5H), 6.54 (d, *J* = 9.1 Hz, 2H), 3.20 (d, *J* = 5.6 Hz, 1H), 2.97 (s, 5H), 2.57 (s, 1H), 2.46 (d, *J* = 5.6 Hz, 1H), 2.22 (s, 1H), 1.67 (m, 2H), 1.44 (m, 2H), 1.24 (d, *J* = 10.5 Hz, 1H), 1.00 (d, *J* = 10.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 208.3, 169.4, 151.1, 139.3, 134.0, 130.7 (2C), 129.4 (2C), 128.5 (2C), 127.3, 121.7, 111.1 (2C), 54.0, 49.9, 40.0 (2C), 39.4, 39.3, 31.8, 29.1, 29.0.

PKR of *N*,*N*-dimethyl-4-(phenylethynyl)benzenaminium tetrafluoroborate **3c** was performed according to the general method (3 h 30 min heating) in combined 100% yield (86 mg) in 1/1.3 of **4bα**:**4bβ** after column chromatography (hexane−EtOAc 20:1 → 5:1). The product was isolated as an amine. ^{1}H and ^{13}C NMR spectra were found to match with those of **4bα** and **4bβ**.

4dα* and *4dβ. PKR of 1-methyl-4-(phenylethynyl)benzene **3d** was performed according to the general method (3 h heating) in combined 73% yield (57 mg) after column chromatography (hexane−EtOAc 20:1 → 10:1). We were unable to separate the isomers by column chromatography; based on ^{1}H NMR integrals, isomers **4dα** and **4dβ** were formed in 1.2/1 ratio. HRMS (EI) *m*/*z* calcd for $C_{23}H_{22}O$ 314.1671, found 314.1671. ^{1}H NMR for 3a,4,5,6,7,7a-hexahydro-3-phenyl-2-tolyl-4,7-methano-1*H*-inden-1-one **4dα** (500 MHz, $CDCl_3$) δ 7.33−7.26 (m, 4H), 7.22−7.18 (m, 2H), 7.12−7.06 (m, 3H), 3.18 (d, *J* = 5.4 Hz, 1H), 2.60 (s, 1H), 2.49 (d, *J* = 5.4 Hz, 1H), 2.32 (s, 3H), 2.10 (s, 1H), 1.68−1.63 (m, 2H), 1.44−1.38 (m, 2H), 1.25−1.20 (m, 1H), 1.00 (d, *J* = 10.5 Hz, 1H). ^{1}H NMR for 3a,4,5,6,7,7a-hexahydro-2-phenyl-3-tolyl-4,7-methano-1*H*-inden-1-one **4dβ** (500 MHz, $CDCl_3$) δ 7.33−7.26 (m, 4H), 7.22−7.18 (m, 2H), 7.12−7.06 (m, 3H), 3.20 (d, *J* = 5.4 Hz, 1H), 2.60 (s, 1H), 2.49 (d, *J* = 5.4 Hz, 1H), 2.33 (s, 3H), 2.11 (s, 1H), 1.68−1.63 (m, 2H), 1.44−1.38 (m, 2H), 1.25−1.20 (m, 1H), 1.00 (d, *J* = 10.5 Hz, 1H).

4eα* and *4eβ. PKR of 1-fluoro-4-(phenylethynyl)benzene **3e** was performed according to the general method (3 h heating) in combined 71% yield (57 mg) after column chromatography (hexane−EtOAc 1:0 → 10:1). Isomers **4eα** and **4eβ** were in 1/1 ratio and easy to separate (hexane−EtOAc 1:0 → 10:1), but we were unable to determine the regiochemistry. **4eα** and **4eβ**, for the isomer moving faster on silica: HRMS (EI) *m*/*z* calcd for $C_{22}H_{19}FO$ 318.1420, found 318.1438. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36−7.26 (m, 5H), 7.20−7.16 (m, 2H), 6.98 (m, 2H), 3.19 (d, *J* = 5.4 Hz, 1H), 2.60 (s, 1H), 2.50 (d, *J* = 5.4 Hz, 1H), 2.10 (s, 1H), 1.67 (m, 2H), 1.41 (m, 2H), 1.21 (d, *J* = 10.5 Hz, 1H), 1.02 (d, *J* = 10.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 208.5, 170.2, 162.3 (d, *J* = 247.2 Hz), 141.5, 135.1, 131.1 (d, *J* = 8.0 Hz, 2C), 129.6, 128.5 (2C), 128.4 (2C), 128.0 (d, *J* = 3.4 Hz), 115.4 (d, *J* = 21.4 Hz, 2C), 54.1, 50.8, 39.5, 38.3, 31.6, 29.0, 28.8. For the isomer moving slower on silica: HRMS (EI) *m*/*z* calcd for $C_{22}H_{19}FO$ 318.1420, found 318.1409. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34−7.27 (m, 5H), 7.19−7.16 (m, 2H), 6.97 (m, 2H), 3.17 (d, *J* = 5.5 Hz, 1H), 2.61 (s, 1H), 2.50 (d, *J* = 5.5 Hz, 1H), 2.10 (s, 1H), 1.70−1.64 (m, 2H), 1.44−1.40 (m, 2H), 1.22 (d, *J* = 10.6 Hz, 1H), 1.03 (d, *J* = 10.6 Hz, 1H). ^{13}C NMR (126 MHz, $CDCL_3$) δ 208.3, 168.3, 163.2 (d, *J* = 251.1 Hz), 142.7, 132.1, 131.1 (d, *J* = 3.4 Hz), 130.6 (d, *J* = 8.35 Hz, 2C), 129.3 (2C), 128.5 (2C), 127.9, 115.6 (d, *J* = 21.6 Hz, 2C), 54.1, 50.7, 39.5, 38.4, 31.6, 29.0, 28.8.

4fα* and *4fβ. PKR of 1-(4-(phenylethynyl)phenyl)ethanone **3f** was performed according to the general method (5 h heating) in combined 100% yield (86 mg) after column chromatography (hexane−EtOAc 10:1 → 3:1). We were unable to separate the isomer by column chromatography. On the basis of ^{1}H NMR integrals, the isomers **4fα** and **4fβ** were formed in 1/1.25 ratio. HRMS (EI) *m*/*z* calcd for $C_{24}H_{22}O_2$ 342.1620, found 342.1628. ^{1}H NMR for 3a,4,5,6,7,7a-hexahydro-3-phenyl-2-(4-acetylphenyl)-4,7-methano-1*H*-inden-1-one **4fα** (500 MHz, $CDCL_3$) δ 7.88 (m, 2H), 7.36−7.15 (m, 7H), 3.24 (m, 1H), 2.66−2.50 (m, 5H), 2.12 (br, 1H), 1.70−1.65 (m, 2H), 1.45−1.40 (m, 2H), 1.24 (d, *J* = 10.6 Hz, 1H), 1.04 (d, *J* = 10.6 Hz, 1H). ^{1}H NMR for 3a,4,5,6,7,7a-hexahydro-2-phenyl-3-(4-acetylphenyl)-4,7-methano-1*H*-inden-1-one **4fβ** (500 MHz, $CDCL_3$) δ 7.87 (m, 2H), 7.38(m, 2H), 7.36−7.15 (m, 5H), 3.22 (m, 1H), 2.66−2.50 (m, 5H), 2.07 (br, 1H), 1.70−1.65 (m, 2H), 1.45−1.40 (m, 2H), 1.24 (d, *J* = 10.6 Hz, 1H), 1.04 (d, *J* = 10.6 Hz, 1H).

4gα* and *4gβ. PKR of 1-(phenylethynyl)-4-(trifluoromethyl)-benzene **3g** was performed according to the general method (5 h heating) in combined 95% yield (88 mg) after column chromatography (hexane−EtOAc 1:0 → 10:1). Isomers **4gα** and **4gβ** were in 1/1.3 ratio. 3a,4,5,6,7,7a-Hexahydro-3-phenyl-2-(4-(trifluoromethyl)-phenyl)-4,7-methano-1*H*-inden-1-one **4gα**, white amorphous solid. HRMS (EI) *m*/*z* calcd for $C_{23}H_{19}F_3O$ 368.1388, found 368.1389. ^{1}H NMR (300 MHz, $CDCl_3$) 7.55 (m, 2H), 7.38−7.29 (m, 5H), 7.27 (m, 2H), 3.23 (d, 5.3 Hz, 1H), 2.62 (m, 1H), 2.53 (d, 5.3 Hz, 1H), 2.12 (m, 1H), 1.68 (m, 2H), 1.42 (m, 2H), 1.23 (d, 10.6 Hz, 1H), 1.04 (d, 10.6 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) 207.9, 171.6, 141.3, 136.0, 134.7, 129.9, 129.7, 128.7, 128.4, 125.3 (q, 3.4 Hz, 2C), 124.1 (q, 272.1 Hz, 1C), 54.2, 51.1, 39.6, 38.3, 31.6, 29.0, 28.8. One carbon ($C-CF_3$) overlaps with other signals at 130 ppm region and is therefore missing. ^{1}H NMR (500 MHz, DMSO) δ 7.65 (d, *J* = 8.1 Hz, 2H), 7.39−7.29 (m, 7H), 3.38 (d, *J* = 5.4 Hz, 1H), 2.48 (s, 1H), 2.43 (s, 1H), 1.97 (s, 1H), 1.65−1.55 (m, 2H), 1.46−1.36 (m, 2H), 1.16 (d, *J* = 10.4 Hz, 1H), 0.99 (d, *J* = 10.4 Hz, 1H). ^{13}C NMR (126 MHz, DMSO) δ 206.7, 171.4, 140.5, 136.5, 134.3, 129.9, 129.8, 128.5, 128.2, 128.2 (q, *J* = 31.9 Hz, 1C), 124.9 (q, *J* = 3.7 Hz, 2C), 124.3 (q, *J* = 272 Hz, 1C), 53.4, 50.1, 39.0, 37.8, 31.2, 28.2, 28.1. 3a,4,5,6,7,7a-Hexahydro-2-phenyl-3-(4-(trifluoromethyl)phenyl)-4,7-methano-1*H*-inden-1-one **4gβ**, white amorphous solid. HRMS (EI) *m*/*z* calcd for $C_{23}H_{19}F_3O$ 368.1388, found 368.1395. ^{1}H NMR (300 MHz, $CDCl_3$) 7.54 (d, 8.2 Hz, 2H), 7.40 (d, 8.2 Hz, 2H), 7.34−7.27 (m, 3H), 7.19−7.15 (m, 2H), 3.22 (d, 5.3 Hz, 1H), 2.63 (m, 1H), 2.53 (d, 5.3 Hz, 1H), 2.07 (m, 1H), 1.68 (m, 2H), 1.42 (m, 2H), 1.23 (d, 10.6 Hz, 1H), 1.05 (d, 10.6 Hz, 1H). ^{13}C NMH (126 MHz, $CDCl_3$) 208.2, 167.7, 144.0, 138.9, 131.4, 131.0 (q, 32.6 Hz, 1C), 129.2, 128.8, 128.5, 128.2, 125.4 (q, 3.7 Hz, 2C), 124.0 (q, 272.2 Hz, 1C), 54.1, 50.8, 39.6, 38.1, 31.6, 28.9, 28.8.

2aα* and *2aβ. PKR of ethyl 4-(*p*-tolylethynyl)benzoate **1a** was performed according to the general method (4 h 30 min heating) in combined 100% yield (97 mg) after column chromatography (hexane−EtOAc 10:1 → 5:1). Isomers **2aα** and **2aβ** were formed in 1/1.3 ratio. Column chromatography (hexane−Et_2O 6:1) separated isomers. 3a,4,5,6,7,7a-Hexahydro-2-(4-(ethoxycarbonyl)phenyl)-3-(*p*-tolyl)-4,7-methano-1*H*-inden-1-one **2aα** HRMS (EI) *m*/*z* calcd for $C_{26}H_{26}O_3$ 386.1882, found 386.1898. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.3 Hz, 2H), 7.28 (d, *J* = 8.3 Hz, 2H), 7.17 (d, *J* = 8.1 Hz, 2H), 7.09 (d, *J* = 8.1 Hz, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 3.21 (d, *J* = 5.4 Hz, 1H), 2.61 (br, 1H), 2.50 (d, *J* = 5.4 Hz, 1H), 2.33 (s, 3H), 2.12 (br, 1H), 1.67 (m, 2H), 1.42 (m, 2H), 1.38 (t, *J* = 7.1 Hz, 3H), 1.22 (d, *J* = 10.5 Hz, 1H), 1.02 (d, *J* = 10.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 208.0, 171.2, 166.5, 141.2, 140.3, 137.4, 131.7, 129.5 (2C), 129.4 (2C), 129.3 (2C), 128.6 (2C), 60.9, 54.2, 50.8, 39.5, 38.5, 31.7, 29.0, 28.8, 21.4, 14.3. 3a,4,5,6,7,7a-Hexahydro-3-(4-(ethoxycarbonyl)-phenyl)-2-(*p*-tolyl)-4,7-methano-1*H*-inden-1-one **2aβ** HRMS (EI) *m*/*z* calcd for $C_{26}H_{26}O_3$ 386.1882, found 386.1894. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.3 Hz, 2H), 7.36 (d, *J* = 8.3 Hz, 2H), 7.10 (d, *J* = 8.1 Hz, 2H), 7.06 (d, *J* = 8.1 Hz, 2H), 4.37 (q, *J* = 7.1 Hz, 2H), 3.19 (d, *J* = 5.4 Hz, 1H), 2.61 (br, 1H), 2.51 (d, *J* = 5.4 Hz, 1H), 2.32 (s,

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3H), 2.06 (br, 1H), 1.70−1.64 (m, 2H), 1.43−1.36 (m, 5H), 1.23 (d, J = 10.5 Hz, 1H), 1.02 (d, J = 10.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 208.8, 168.2, 166.2, 144.0, 140.2, 138.2, 131.2, 129.8 (2C), 129.42 (2C), 129.36 (2C), 128.7, 128.6 (2C), 61.4, 54.3, 51.0, 39.8, 38.4, 31.8, 29.2, 29.1, 21.6, 14.5.

PKR of ethyl 4-(*p*-tolylethynyl)benzoate **1a** was also performed under conventional heating. Alkyne (0.25 mmol, 1 equiv) and $Co_2(CO)_8$ (0.25 mmol, 1equiv) were placed in Schlenk tube, dissolved in toluene (4 mL), and stirred under argon at rt for 30 min. Norbornene (118 mg, 1.25 mmol, 5 equiv) was added, and the reaction mixture was heated overnight in an oil bath at 80 °C. The reaction mixture was adsorbed on silica and purified by column chromatography (hexane−EtOAc 10:1 → 5:1), yielding a 1/1.3 mixture of **2a*α*** and **2a*β*** in combined 76% yield (74 mg).

6aα *and* ***6aβ***. PKR of ethyl 4-(4-methoxyphenylethynyl)benzoate **5a** was performed according to the general method (4 h heating) in combined 73% yield (73 mg) after column chromatography (hexane−EtOAc 10:1 → 5:1). Isomers **6a*α*** and **6a*β*** were formed in 1/1.5 ratio. 3a,4,5,6,7,7a-Hexahydro-3-(4-methoxyphenyl)-2-(4-(ethoxycarbonyl)-phenyl)-4,7-methano-1*H*-inden-1-one **6a*α***, yellow amorphous solid. HRMS (EI) m/z calcd for $C_{26}H_{26}O_4$ 402.1831, found 402.1845. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, J = 8.3 Hz, 2H), 7.29 (d, J = 8.3 Hz, 2H), 7.25 (d, J = 8.8 Hz, 2H), 6.80 (d, J = 8.8 Hz, 2H), 4.37 (q, J = 7.1 Hz, 2H), 3.80 (s, 3H), 3.21 (d, J = 5.5 Hz, 1H), 2.60 (s, 1H), 2.50 (d, J = 5.5 Hz, 1H), 2.15 (s, 1H), 1.72−1.64 (m, 2H), 1.43 (m, 2H), 1.39 (t, J = 7.1 Hz, 3H), 1.21 (d, J = 10.6 Hz, 1H), 1.03 (d, J = 10.6 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 207.9, 170.4, 166.5, 161.0, 140.4, 137.8, 130.5 (2C), 129.7 (2C), 129.5, 129.4 (2C), 126.7, 113.9 (2C), 60.9, 55.3, 54.2, 50.5, 39.4, 38.8, 31.7, 29.0, 28.9, 14.3. 3a,4,5,6,7,7a-Hexahydro-2-(4-methoxyphenyl)-3-(4-(ethoxycarbonyl)-phenyl)-4,7-methano-1*H*-inden-1-one **6a*β***, yellow amorphous solid. HRMS (EI) m/z calcd for $C_{26}H_{26}O_4$ 402.1831, found 402.1813. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, J = 8.3 Hz, 2H), 7.37 (d, J = 8.3 Hz, 2H), 7.12 (d, J = 8.6 Hz, 2H), 6.82 (d, J = 8.6 Hz, 2H), 4.37 (q, J = 7.1 Hz, 2H), 3.79 (s, 3H), 3.17 (d, J = 5.4 Hz, 1H), 2.61 (s, 1H), 2.50 (d, J = 5.4 Hz, 1H), 2.05 (s, 1H), 1.66 (d, J = 7.3 Hz, 2H), 1.43−1.35 (m,5H), 1.21 (d, J = 10.5 Hz, 1H), 1.02 (d, J = 10.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 208.6, 167.5, 166.0, 159.4, 143.1, 140.1, 130.9, 130.5 (2C), 129.6 (2C), 128.4 (2C), 123.6, 113.9 (2C), 61.1, 55.2, 54.1, 50.7, 39.5, 38.1, 31.6, 28.9, 28.8, 14.3.

6bα *and* ***6bβ***. PKR of 1-(trifluoromethyl)-4-(4-methoxyphenylethynyl)benzene **5b** was performed according to the general method (4 h heating) in combined 91% yield (91 mg) after column chromatography (hexane−EtOAc 10:1 → 5:1). We were unable to separate the regioisomers by column chromatography. On the basis of ^{1}H NMR integrals, the isomers **6b*α*** and **6b*β*** were formed in 1/1.5 ratio. HRMS (EI) m/z calcd for $C_{24}H_{21}F_3O_2$ 398.1494, found 398.1491. ^{1}H NMR for 3a,4,5,6,7,7a-hexahydro-3-(4-methoxyphenyl)-2-(4-(trifluoromethyl)phenyl)-4,7-methano-1*H*-inden-1-one **6b*α*** (500 MHz, $CDCl_3$) δ 7.58 (d, J = 8.1 Hz, 2H), 7.34 (d, J = 8.1 Hz, 2H), 7.26 (d, J = 8.8 Hz, 2H), 6.82 (m, 2H), 3.81 (s, 3H), 3.22 (d, J = 5.4 Hz, 1H), 2.61 (s, 1H), 2.51 (d, J = 5.4 Hz, 1H), 2.15 (s, 1H), 1.67 (m, 2H), 1.42 (m, 2H), 1.21 (d, J = 10.5 Hz, 1H), 1.03 (d, J = 10.5 Hz, 1H). ^{1}H NMR for 3a,4,5,6,7,7a-hexahydro-2-(4-methoxyphenyl)-3-(4-(trifluoromethyl)phenyl)-4,7-methano-1*H*-inden-1-one **6b*β*** (500 MHz, $CDCl_3$) δ 7.56 (d, J = 8.2 Hz, 2H), 7.42 (d, J = 8.2 Hz, 2H), 7.12 (d, J = 8.7 Hz, 2H), 6.84 (m, 2H), 3.79 (s, 3H), 3.17 (d, J = 5.4 Hz, 1H), 2.61 (s, 1H), 2.51 (d, J = 5.4 Hz, 1H), 2.05 (s, 1H), 1.67 (m, 2H), 1.42 (m, 2H), 1.21 (d, J = 10.5 Hz, 1H), 1.03 (d, J = 10.5 Hz, 1H).

8aα *and* ***8aβ***. PKR of 1,2,3-trimethoxy-5-(phenylethynyl)benzene **7a** was performed according to the general method (2 h 30 min heating) in combined 89% yield (87 mg) after column chromatography (hexane−EtOAc 10:1 → 3:1). We were unable to separate the isomer by column chromatography. On the basis of ^{1}H NMR integrals, the isomers **8a*α*** and **8a*β*** were formed in 1/1.4 ratio and HRMS (EI) m/z calcd for $C_{25}H_{26}O_4$ 390.1831, found 390.1825. ^{1}H NMR for 3a,4,5,6,7,7a-hexahydro-3-phenyl-2-(3,4,5-trimethoxyphenyl)-4,7-methano-1*H*-inden-1-one **8a*α*** (500 MHz, $CDCl_3$) δ 7.37−7.18 (m, 5H), 6.44 (s, 2H), 3.83 (s, 3H), 3.59 (s, 6H), 3.18 (d, J = 5.6 Hz, 1H), 2.61 (s, 1H), 2.50 (m, 1H), 2.13 (s, 1H), 1.75−1.64 (m, 2H), 1.50−1.38 (m, 2H), 1.25 (m, 1H), 1.04 (m, 1H). ^{1}H NMR for 3a,4,5,6,7,7a-hexahydro-2-phenyl-3-(3,4,5-trimethoxyphenyl)-4,7-methano-1*H*-inden-1-one **8a*β*** (500 MHz, $CDCL_3$) δ 7.37−7.18 (m, 5H), 6.56 (s, 2H), 3.85 (s, 3H), 3.59 (s, 6H), 3.20 (d, J = 5.5 Hz, 1H), 2.61 (s, 1H), 2.50 (m, 1H), 2.23 (s, 1H), 1.75−1.64 (m, 2H), 1.50−1.38 (m, 2H), 1.25 (m, 1H), 1.04 (m, 1H).

8bα *and* ***8bβ***. PKR of 1,3-dimethoxy-5-(phenylethynyl)benzene **7b**: **7b** was prepared according to the general method in a TEA/THF 1:1 mixture. We were not able to separate **7b** from 1,3-dimethoxy-5-bromobenzene by column chromatography; the corresponding $Co_2(CO)_6$ complex of **7b** was prepared in the mixture, isolated, and used as starting material in the PK reaction. A mixture of **7b** and 1,3-dimethoxy-5-bromobenzene was dissolved in DCM, and 300 mg of $Co_2(CO)_8$ was added. The reaction mixture was stirred over 2 h at rt, adsorbed on silica, and purified by column chromatography (hexane−EtOAc 20:1) yielding 111 mg (0.21 mmol) of the complex. This complex was used as such in the following PK reaction. The complex was placed in Biotage microwave tube and dissolved in DCE (1 mL). Norbornene (100 mg, 1.06 mmol, 5 equiv) was added, and the reaction was continued according to the general method (4 h 30 min heating) in combined 67% yield (51 mg) after column chromatography (hexane−EtOAc 10:1 → 3:1). Isomers **8b*α*** and **8b*β*** were received in 1/1.6 ratio. Column chromatography (hexane−EtOAc 5% → 9%) separated the isomers. 3a,4,5,6,7,7a-Hexahydro-2-(3,5-dimethoxyphenyl)-3-phenyl-4,7-methano-1*H*-inden-1-one **8b*α***, yellow amorphous solid. HRMS (EI) m/z calcd for $C_{24}H_{24}O_3$ 360.1725, found 360.1720. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35−7.29 (m, 5H), 6.38 (t, J = 2.2 Hz, 1H), 6.34 (d, J = 2.2 Hz, 2H), 3.67 (s, 6H), 3.19 (d, J = 5.3 Hz, 1H), 2.60 (br, 1H), 2.49 (d, J = 5.3 Hz, 1H), 2.13 (br, 1H), 1.69−1.64 (m, 2H), 1.44−1.39 (m, 2H), 1.24 (d, J = 10.5 Hz, 1H), 1.02 (d, J = 10.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 208.3, 170.1, 160.7, 142.6, 135.1, 134.1, 129.5, 128.5, 128.4, 107.2, 100.5, 55.3, 54.1, 50.7, 39.5, 38.4, 31.7, 29.0, 28.9. 3a,4,5,6,7,7a-Hexahydro-3-(3,5-dimethoxyphenyl)-2-phenyl-4,7-methano-1*H*-inden-1-one **8b*β***, yellow amorphous solid. HRMS (EI) m/z calcd for $C_{24}H_{24}O_3$ 360.1725, found 360.1733. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34−7.29 (m, 2H), 7.28−7.24 (m, 1H), 7.22−7.18 (m, 2H), 6.43 (m, 2H), 6.41 (m, 1H), 3.59 (s, 6H), 3.15 (d, J = 5.4 Hz, 1H), 2.61 (br, 1H), 2.49 (d, J = 5.4 Hz, 1H), 2.19 (br, 1H), 1.70−1.64 (m, 2H), 1.44−1.39 (m, 2H), 1.24 (d, J = 10.5 Hz, 1H), 1.03 (d, J = 10.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 208.6, 169.6, 160.5, 143.1, 136.8, 132.5, 129.3, 128.4, 127.8, 106.8, 101.6, 55.2, 54.1, 50.7, 39.5, 38.5, 31.7, 29.1, 28.8.

8cα *and* ***8cβ***. PKR of 1,3-dimethoxy-5-((4-methoxyphenyl)-ethynyl)benzene **7c** was performed according to the general method (6 h 30 min heating) in combined 62% yield (61 mg) after column chromatography (hexane−EtOAc 5:1). Isomers **8c*α*** and **8c*β*** were formed in 1/1.8 ratio. 3a,4,5,6,7,7a-Hexahydro-2-(3,5-dimethoxyphenyl)-3-(4-methoxyphenyl)-4,7-methano-1*H*-inden-1-one **8c*α***, yellow amorphous solid. HRMS (EI) m/z calcd for $C_{25}H_{26}O_4$ 390.1831, found 390.1839. ^{1}H NMR (500 MHz, $CDCL_3$) δ 7.33 (d, J = 8.5 Hz, 2H), 6.80 (d, J = 8.5 Hz, 3H), 6.41 (br, 2H), 6.35 (m, 2H), 3.80 (s, 3H), 3.71 (s, 6H), 3.18 (d, J = 5.4 Hz, 1H), 2.58 (br, 1H), 2.47 (d, J = 5.4 Hz, 1H), 2.16 (br, 1H), 1.67 (m, 2H), 1.42 (m, 2H), 1.22 (d, J = 10.5 Hz, 1H), 1.01 (d, J = 10.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCL_3$) δ 208.2, 169.1, 160.9, 160.8, 141.3, 135.0, 130.6 (2C), 127.0, 113.8 (2C), 107.2 (2C), 100.4, 55.31 (2C), 55.27, 54.0, 50.2, 39.3, 38.9, 31.7, 29.1, 28.9. 3a,4,5,6,7,7a-Hexahydro-3-(3,5-dimethoxyphenyl)-2-(4-methoxyphenyl)-4,7-methano-1*H*-inden-1-one **8c*β***, light brown amorphous solid. HRMS (EI) m/z calcd for $C_{25}H_{26}O_4$ 390.1831, found 390.1833. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.16 (m, 2H), 6.84 (m, 2H), 6.45 (d, J = 2.3 Hz, 2H), 6.43−6.39 (m, 1H), 3.78 (s, 3H), 3.63 (s, 6H), 3.11 (d, J = 5.5 Hz, 1H), 2.59 (br, 1H), 2.47 (d, J = 5.5 Hz, 1H), 2.16 (br, 1H) 1.66 (m, 2H), 1.40 (m, 2H), 1.29−1.21 (m, 1H), 1.01 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 209.2, 169.1, 160.8, 159.5, 142.7, 137.5, 130.8, 124.7, 114.1, 106.9, 101.5, 55.48, 55.45, 54.3, 51.0, 39.7, 38.6, 31.9, 29.3, 29.1.

8dα *and* ***8dβ***. PKR of 1,3-dimethyl-5-(phenylethynyl)benzene **7d** was performed according to the general method (4 h heating) in

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combined 85% yield (70 mg) after column chromatography (hexane−EtOAc 40:1 → 10:1). We were unable to separate the isomers by column chromatography. On the basis of ^{1}H NMR integrals, the isomers **8dα** and **8dβ** were formed in 1/1.1 ratio. HRMS (EI) *m*/*z* calcd for $C_{24}H_{24}O$ 328.1827, found 328.1841. ^{1}H NMR for 3a,4,5,6,7,7a-hexahydro-3-phenyl-2-(3,5-dimethylphenyl)-4,7-methano-1*H*-inden-1-one **8dα** (500 MHz, $CDCl_3$) δ 7.34−7.17 (m, 5H), 6.90 (s, 1H), 6.78 (s, 2H), 3.20 (d, *J* = 5.4 Hz, 1H), 2.60 (s, 1H), 2.48 (d, *J* = 5.4 Hz, 1H), 2.23 (s, 6H), 2.12 (s, 1H), 1.66 (m, 2H), 1.41 (m, 2H), 1.28−1.21 (m, 1H), 1.01 (m, 1H). ^{1}H NMR for 3a,4,5,6,7,7a-hexahydro-2-phenyl-3-(3,5-dimethylphenyl)-4,7-methano-1*H*-inden-1-one **8dβ** (500 MHz, $CDCl_3$) δ 7.34−7.17 (m, 5H), 6.94 (s, 1H), 6.87 (s, 2H), 3.17 (d, *J* = 5.4 Hz, 1H), 2.60 (s, 1H), 2.48 (d, *J* = 5.4 Hz, 1H), 2.21 (s, 6H), 2.12 (s, 1H), 1.66 (m, 2H), 1.41 (m, 2H), 1.28−1.21 (m, 1H), 1.01 (m, 1H).

8eα* and *8eβ. PKR of 1-(phenylethynyl)-3,5-bis(trifluoromethyl)-benzene **7e** was performed according to the general method (5 h heating) in combined 100% yield (109 mg) after column chromatography (hexane−EtOAc 1:0 → 20:1). Isomers **8eα** and **8eβ** were isolated in 1/2 ratio. 3a,4,5,6,7,7a-Hexahydro-3-phenyl-2-(3,5-bis(trifluoromethyl)phenyl)-4,7-methano-1*H*-inden-1-one **8eα**, white amorphous solid. HRMS (EI) *m*/*z* calcd for $C_{24}H_{18}F_6O$ 436.1262, found 436.1255. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (s, 1H), 7.68 (s, 2H), 7.42−7.31 (m, 3H), 7.25−7.22 (m, 2H), 3.25 (d, *J* = 5.5 Hz, 1H), 2.64 (s, 1H), 2.55 (d, *J* = 5.5 Hz, 1H), 2.15 (s, 1H), 1.69 (m, 2H), 1.43 (m, 2H), 1.22 (d, *J* = 10.7 Hz, 1H), 1.07 (d, *J* = 10.7 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 207.2, 173.1, 139.5, 134.2, 134.1, 131.5 (q, *J* = 33.3 Hz, 2C), 130.3, 129.7 (m, 2C), 128.9 (2C), 128.2 (2C), 123.2 (q, *J* = 273 Hz, 2C), 121.4 (m, 1C), 54.2, 51.3, 39.6, 38.3, 31.7, 29.0, 28.8. 3a,4,5,6,7,7a-Hexahydro-2-phenyl-3-(3,5-bis(trifluoromethyl)phenyl)-4,7-methano-1*H*-inden-1-one **8eβ**, white amorphous solid. HRMS (EI) *m*/*z* calcd for $C_{24}H_{18}F_6O$ 436.1262, found 436.1264. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (s, 1H), 7.69 (s, 2H), 7.35−7.31 (m, 3H), 7.14−7.10 (m, 2H), 3.24 (d, *J* = 5.4 Hz, 1H), 2.66 (s (br), 1H), 2.58 (d, *J* = 5.4 Hz, 1H), 2.10 (m, 1H), 1.77−1.65 (m, 2H), 1.50−1.41 (m, 2H), 1.24 (d, *J* = 10.7 Hz, 1H), 1.10 (d, *J* = 10.7 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 207.8, 165.1, 145.4, 137.3, 131.9 (q, *J* = 33.6 Hz, 2C), 130.7, 129.0 (2C), 128.8 (2C), 128.7, 128.5 (m, 2C), 122.9 (q, *J* = 273 Hz, 2C), 122.82 (m, 1C), 54.2, 50.4, 39.6, 38.1, 31.7, 29.0, 28.7.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C spectra of all new compounds and NOESY spectra of the PK products, as well as computationally optimized Cartesian coordinates, NBO charges, and energies for the presented systems. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

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