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Regioselectivity of Intermolecular Pauson−Khand Reaction of Aliphatic Alkynes: Experimental and Theoretical Study of the Effect of Alkyne Polarization

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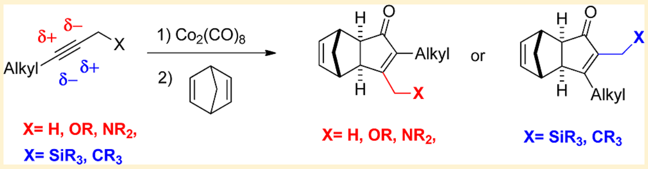
Supporting Information



ABSTRACT: Generally judged poor electronic regioselectivity of alkyne insertion in intermolecular Pauson−Khand reaction (PKR) has severely restricted its synthetic applications. In our previous rational study concerning diarylalkynes (Fager-Jokela, E.; Muuronen, M.; Patzschke, M.; Helaja, J. *J. Org. Chem.* **2012**, *77*, 9134−9147), both experimental and theoretical results indicated that purely electronic factors, i.e., alkyne polarization via resonance effect, induced the observed modest regioselectivity. In the present work, we substantiate that the alkyne polarization via inductive effect can result notable, synthetically valuable regioselectivity. Computational study at DFT level was performed to disclose the electronic origin of the selectivity. Overall, the NBO charges of alkynes correlated qualitatively with regioisomer outcome. In a detailed computational PKR case study, the obtained Boltzmann distributions of the transition state (TS) populations correlate closely with experimental regioselectivity. Analysis of the TS-structures revealed that weak interactions, e.g., hydrogen bonding and steric repulsion, affect the regioselectivity and can easily override the electronic guidance.

■ INTRODUCTION

The Pauson−Khand reaction, the carbonylative cycloaddition between an alkyne and an alkene promoted by cobalt carbonyl complexes, is one of the most reliable methodologies for the construction of cyclopentenone rings.[1] The intramolecular version of the reaction has been used widely in the synthesis of complex polycyclic compounds.[2] Although less common, the intermolecular version can efficiently provide key intermediates that have been used in several total syntheses of biologically active compounds.[3] The main advantages of the intermolecular version are the rapid construction of the cyclopentenone ring from simple fragments and the existence of reliable asymmetric versions.[4] However, its use is hampered by the small range of reactive olefins and, in the case of internal alkynes, by the difficult prediction of the regioselectivity.

It has been established that the regiochemistry of the alkyne fragment is controlled by both steric and electronic factors: large and electron donating groups (EDG) tend to favor cyclopentenone α-position, while small and electron withdrawing groups (EWG) have a preference for the β-position.[5] The pioneering work of Gimbert and co-workers showed several examples in which the initial C−C bond is formed with the more electron rich alkyne carbon according to the NBO charges.[6] In the case of functionalized diarylalkynes, we have shown that in certain cases the electronic effects had been overestimated although they can induce a clear regioselectivity that can be predicted quantitatively from α-alkyne NBO charges.[7] In the case of aliphatic internal alkynes, the regioselectivity is in some cases surprisingly high: Ethyl butynoate,[8] trifluoromethyl[3a] and silyloxymethylacetylenes[3f] have proved to react with norbornene, norbornadiene or ethylene in a completely regiolective manner (Figure 1).

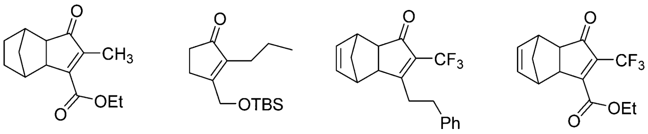


Figure 1. Literature examples of PK adducts of completely regioselective intermolecular PK reactions of internal alkynes.

Encouraged by these results, we decided to undertake a systematic study of the regioselectivity of internal aliphatic alkynes on intermolecular PKR to find out the rules that could allow us to predict such regiochemistry. We report herein that several internal alkynes gained substantial regioguidance in intermolecular PKR due to electronic factors. We also show

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that computational NBO charge values have a certain degree of prediction value, and demonstrate computationally, with three case studies, that small attractive/repulsive interactions may play critical role on the regioguidance in addition to steric and electronic factors.

RESULTS AND DISCUSSION

In general, the polarization of an alkyne can take place via two mechanisms, namely through resonance and inductive effects (Figure 2). In the case of diarylalkynes, we showed the intermolecular PKR to yield a regiochemical outcome with an excellent correlation with the NBO charges of the sp^2-hybridized carbons next to the triple bond.[7] It was concluded that with sp^2-hybridized propargylic carbon, the polarization originated from EDG/EWG substituents was mainly due to the resonance effect. As a consequence, the regioselectivity was inversed when the aryl ring substituents changed from *para* to *meta* position, or by protonating dimethyl amine group as a substituent. However, the regioselectivity did not change in the case of the CF_3−group where the large inductive effect overrides the resonance effect.[7]

Here, our focus was to test aliphatic alkyne substrates where the carbon−carbon triple bond is polarized via inductive effect and that would result electronic regioguidance in PKR (Figure 2). Additionally, we were interested to find out whether experimental regioselectivity could be predicted computationally from alkyne polarization and to confirm theoretically the factors affecting the regioselectivity at DFT level. In order to investigate the specific alkyne polarization by the inductive effect, we needed to select a set of substrates in which the resonance effect was restrained or ruled out. For this purpose, aliphatic alkynes bearing two sp^3-hybridized carbons linked to the triple bond and connected to an alkyl chain in one side and to a EDG/EWG functional group at the other (Figure 2). As in our previous PKR study[7] the computations were performed in gas phase with TPSS-D3 meta-GGA functional together with high quality triple ζ basis set def2-TZVPP (see Experimental Section for full details and references of all computations). The alkyl tail was treated as propyl in all computations.

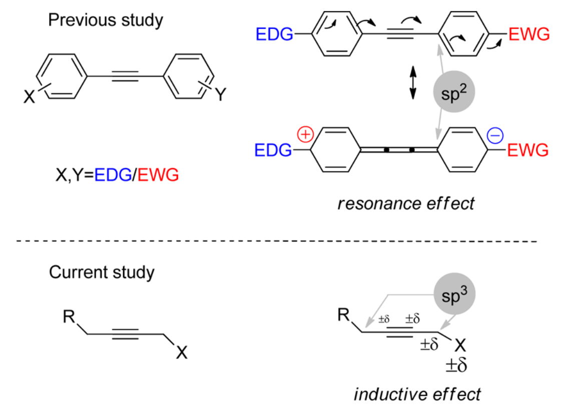


Figure 2. Description of the system used to study the inductive effect in PKR.

Preparation of the Substrates and the PKR. To this end, we chose a series of 1-substituted-2-hexynes (Figure 3). The oxygenated derivatives **1b−d** were prepared from 2-hexyn-1-ol (**1a**) by described or standard procedures. Alkynes with a nitrogenated function at the propargylic position **2a−d** were also prepared from **1a** by mesylation followed by substitution either with dimethyl amine (**2a**,**b**) or with sodium azide followed by reduction and functionalization of the primary amine by standard procedures. Alkyne **3** with a second carbon atom bearing an electron-withdrawing methyl ester was prepared from hept-3-yn-1-ol by oxidation. Finally, an alkyne with a trimethylsilyl group was pursued to have a more electropositive atom at the propargylic position. To avoid purification problems due to its volatility, tetradec-2-yn-1-yltrimethylsilane **4** was prepared by alkylation of tridec-1-yne with (chloromethyl)trimethylsilane. To check the steric effect of the trimethylsilylmethyl group, 2,2-dimethylhexadec-4-yne **5** was prepared as a carbon analog of this compound for the sake of comparison. Disubstituted alkyne **6** was prepared from but-2-yne-1,4-diol as a test to measure the directing effect of two similar substituents.

The cobalt complexes of the selected alkynes were prepared either by treatment in hexane with octacarbonyldicobalt or in situ in toluene prior to PKR. Then, the PK reactions with norbornadiene (NBD) were performed in thermal conditions at 70 °C. The crudes were chromatographed, and the ratio of the four possible PK adducts was measured by NMR (Scheme 1).

Effect of the Reaction Conditions. We first examined the possible role of the reaction conditions on the regioselectivity. The reactions were performed with the methoxy-substituted alkyne (**1b**) in several reaction conditions by changing one variable at a time. The results are shown in Figure 4. In general, it seems that the reaction conditions do not have a prominent effect on the isomer ratio, even though the yields of **PK1b** are

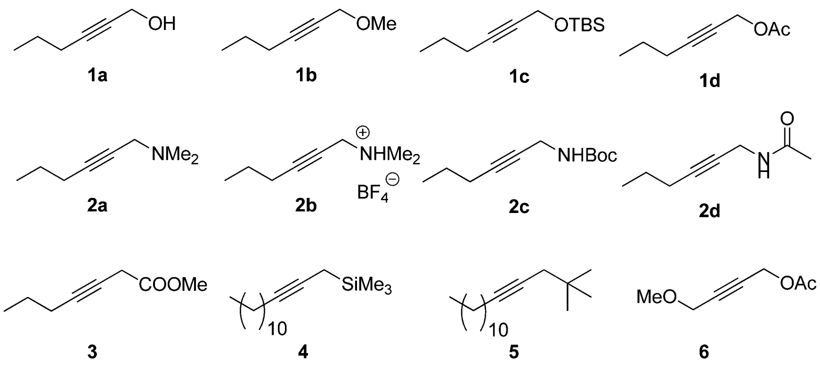
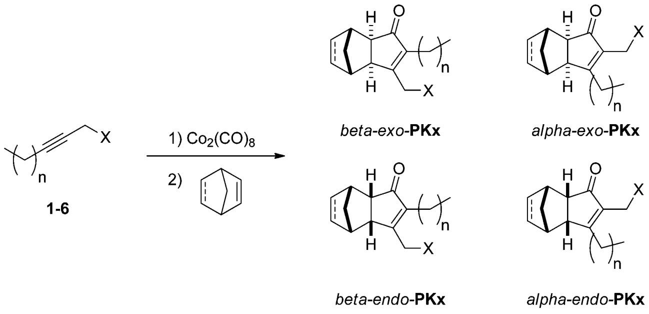


Figure 3. Alkynes selected for this study. In the following PKR results, the regioselectivity (α/β) is reported related to the priority side (CIP rules; right side on the figure) of the compounds.

Scheme 1. PKR's of Selected Alkynes with Norbornadiene[a]

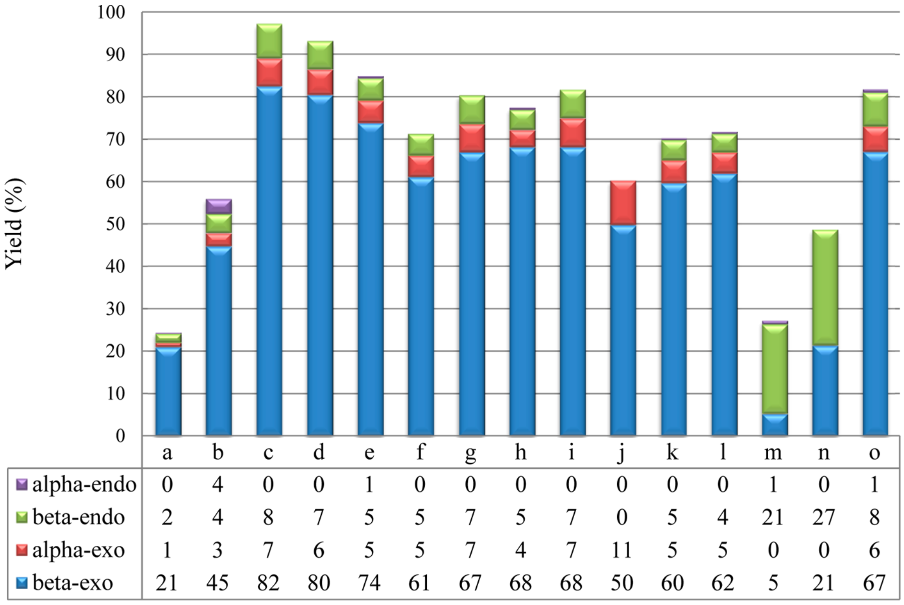


[a]See conditions and ratios on Figures 4 and 5.

somewhat affected. The amount of alkene (Figure 4a−d), the dilution (Figure 4e,f), the reaction temperature (Figure 4g,h) and the use of microwaves do not have remarkable effect on the isomer ratio. The use of norbornene (NBN) instead of norbornadiene (NBD) lowers the amount of the *endo* isomers,[9] *α-exo* and *β-exo* being the only isomers detected. In this case, the regioselectivity was slightly lower than that of NBD. This less regioselective behavior of NBN has been previously described with other substrates as well.[10] The solvent is the only parameter that has dramatic effect on stereo- and regioselectivity. DCE and THF (Figure 4k,l) did not make any notable difference, but when the reaction was performed in acetonitrile *endo*-isomer became clearly dominating one over usual *exo* isomer (Figure 4m). In fact, we were unable to find any *α-exo*-isomers. Weakness of this method is that yields were dramatically lower (27%) compared to those in toluene. We tried to optimize the conditions by performing the reaction in toluene/acetonitrile mixtures as solvent. When the reaction was performed in 1:1 mixture the yield increased into 49%, while the *endo* isomer was still dominating to some extent *exo*:*endo* ratio being 21:27 (Figure 4n). A change of solvent to toluene/acetonitrile 9:1 mixture produced high yield (82%) but the unusual stereoselectivity was not any more visible (Figure 4o).

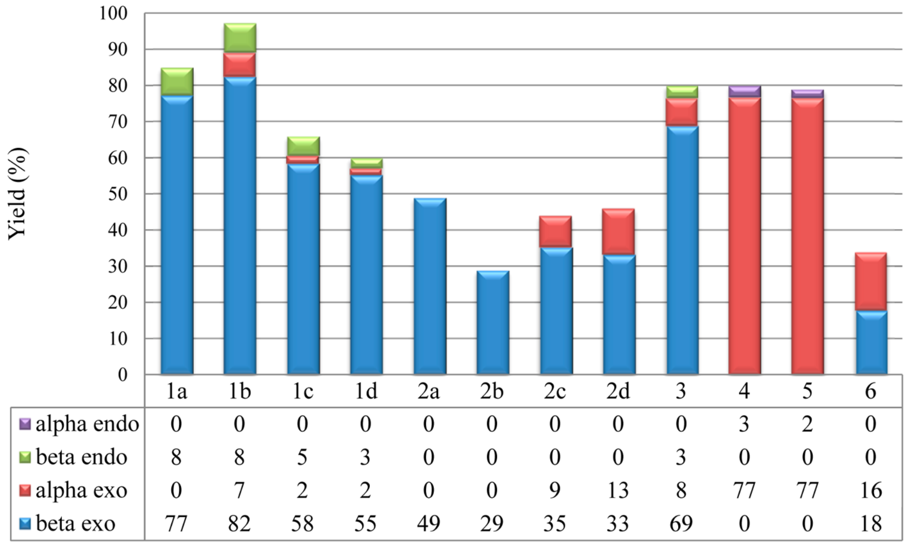
Electronic Effect on the Regioselectivity. The regioselectivity was next studied for different alkynes. The PKR under thermal conditions in toluene at 70 °C afforded the cyclopentenones as a mixture of regio- and stereoisomers, but with remarkably high selectivities. In most cases, only the major *β-exo* isomer could be isolated and characterized. The yields of the minor isomers were determined by ratios of ^{1}H NMR integrals of corresponding protons. The ratios of different isomers in the mixtures are presented in Figure 5. The sum of the yields of different isomers is the isolated yield of the product mixture, although not all of them could be isolated in pure form. Against the widely existing presumption, the observed regioexcesses proofs that intermolecular PKR can yield truly regioselective and synthetically useful outcomes even with sterically similar alkynes.

The alkynes with oxygen in the propargylic position (**1a**−**1d**) gave PK adducts with excellent selectivity toward the *β-exo* isomer. The highest yield of *β-exo* isomer was obtained with 1-methoxyhex-2-yne (82%, **1b**). The *β-exo* yield from hex-2-yn-1-ol (77%, **1a**) is very similar, yet, with slightly higher selectivity, although sometimes aldehydes were obtained as side products due to oxidation of the alcohol. The acetylated derivative **1d** and the OTBS derivative **1c** both gave almost complete regioselectivity. Somewhat surprisingly, the steric hindrance of the OTBS group does not seem to affect the regioselectivity when comparing that to other oxygen derivatives (**1a**−**1d**). The computed NBO charge differences of the alkynyl carbons (C^2−C^3) and the *α*-carbons (C^1−C^4) (see Figure 6) both correlate well with the experiment suggesting that the C−C bond is formed with the more electron rich alkynyl carbon that in turn has more electron poor *α*-carbon (Figure 2). Noticeably, the C^1−C^4 prediction is slightly more quantitative, predicting



	a	b	c	d	e	f	g	h	i	j	k	l	m	n	o
🟪 alpha-endo	0	4	0	0	1	0	0	0	0	0	0	0	1	0	1
🟩 beta-endo	2	4	8	7	5	5	7	5	7	0	5	4	21	27	8
🟥 alpha-exo	1	3	7	6	5	5	7	4	7	11	5	5	0	0	6
🟦 beta-exo	21	45	82	80	74	61	67	68	68	50	60	62	5	21	67

Figure 4. PKR of 1-methoxy-2-hexyne **1b** in different reaction conditions. Standard conditions: 3 mmol of isolated alkyne-cobalt complex, 5 equiv of NBD, 3 mL of toluene, 70 °C thermal heating. To these conditions the following variables were introduced: (1) amount of alkene (a−d) a = 1 equiv, b = 3 equiv, c = 5 equiv, d = 10 equiv; (2) solvent amount (e,f) e = 6 mL of toluene, f = 1.5 mL of toluene; (3) reaction temperature (g,h) g = 90 °C, h = 50 °C; (4) heat source (i) MW (70 °C); (5) alkene (j) NBN; (6) type of solvent (k−p) k = DCE, l = THF, m = MeCN, n = 1:1 toluene/MeCN, o = 9:1 toluene/MeCN.



	1a	1b	1c	1d	2a	2b	2c	2d	3	4	5	6
🟪 alpha endo	0	0	0	0	0	0	0	0	0	3	2	0
🟩 beta endo	8	8	5	3	0	0	0	0	3	0	0	0
🟥 alpha exo	0	7	2	2	0	0	9	13	8	77	77	16
🟦 beta exo	77	82	58	55	49	29	35	33	69	0	0	18

Figure 5. Yields of regio- and stereoisomers of cyclopentenones **PK1-PK6** obtained by PKRs of alkynes **1−6** and norbornadiene.

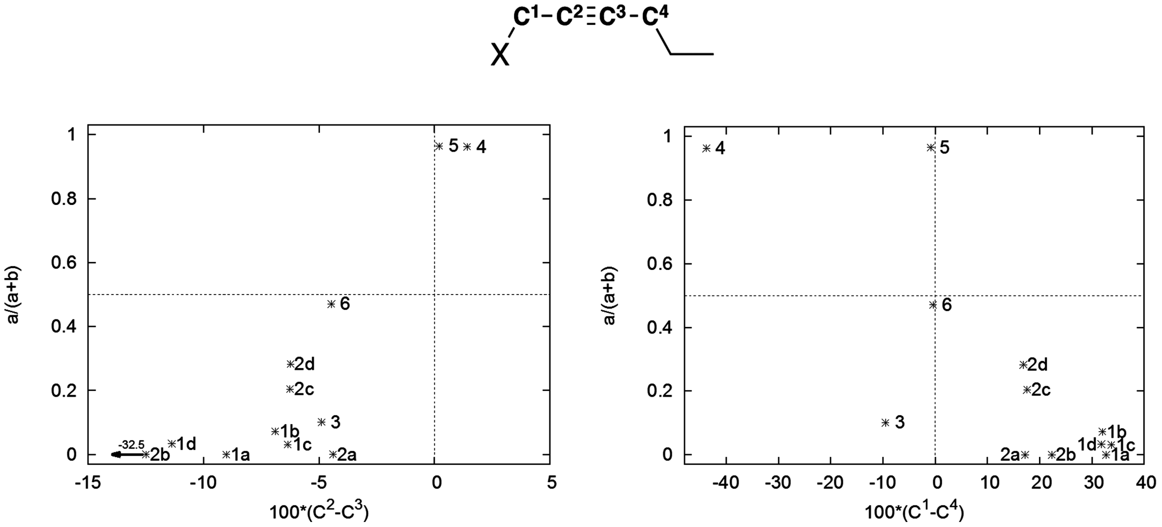


Figure 6. Plot of the NBO charge differences ($C^2−C^3$/$C^1−C^4$) of alkynyl carbons (TPSS-D3/def2-TZVPP) versus the regiochemical outcome of the PKR ($\alpha/\alpha{+}\beta$). Both *endo* and *exo* contribution are taken into account for α/β ratio.

similar selectivities for all, whereas $C^2−C^3$ values predict **1a** and **1d** to gain slightly higher β-selectivity.

Nitrogenated alkynes **2a−d** gave also good selectivity toward the β-*exo* isomer, but the yields were generally lower than with oxygen alkynes. Particularly, *N*,*N*-dimethylhex-2-yn-1-amine **2a** and its tetrafluoroborate salt **2b** afforded exclusively the β-*exo* isomer. Related to oxygen, nitrogen is slightly less electronegative. This also visible in the NBO charges which indicate a weaker alkyne polarization is induced for **2a** than for **1a−1d**. Interestingly, the protonation of the dimethyl amine group (**2a** → **2b**) does not inverse the alkyne polarization but intensifies it. This is a characteristic property of the σ-bond mediated inductive effect that contrasts the π-bond mediated resonance effect that was prevailing in related arylalkyne amines.[7] The acid coordination on *N*-group might also increase the β-selectivity of **2a** in solution where Lewis-acidic species, for instance from decomposed cobalt complexes, are present. The *N*-Boc and *N*-acetyl derivates **2c** and **2d** both gave β-*exo* isomer as the major product accompanied by noticeable amounts of α-*exo* adducts. They are similarly polarized on the $C^2−C^3$ as the oxygen derivates **1b**, **1c** but less on the α-positions. This fits to the experimental outcome well, where the selectivity is lower than in **1a−1d** and **2a**-**2b**.

The selectivity of the alkyne **3**, equipped with methyl ester, is similar to the oxygenated alkynes. The major isomer, β-*exo*, was obtained with 65% yield, whereas the amount of α-*exo* was only 9%. The alkyne polarization ($C^2−C^3$) on **3** predicts the selectivity to be smaller compared to oxygenated alkynes. Notably, the α-position is inversely polarized now, while the heteroatom is located one carbon further from the alkyne, at γ-position; therefore the short-range inductive effect is not any more visible in the charge difference of the α-position.

As could be anticipated, the alkyne with the more electropositive trimethylsilyl substituent **4** gave the α-*exo* isomer as the only product. Since sterics might also play a role in this regioselectivity, the carbon analog **5** was also tested. The PKR was again highly regioselective affording only the adduct with the neopentyl group in α position (α-*exo*-**PK5**). The NBO charges show the C−C bond to be forming in these both cases on the more electron rich carbon, but on the other

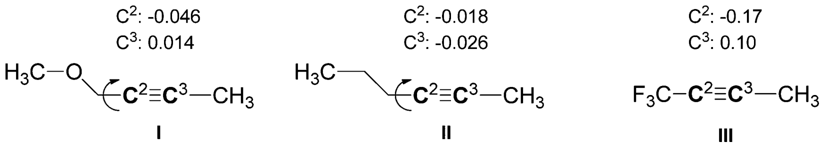


Figure 7. Studied model compounds **I**−**III** and their NBO charges based on TPSS-D3/def2-TZVPP.

hand, the polarization effect is small compared to other studied alkynes. This fact reveals that small steric factors (the *tert*-butyl group is placed at β position to the alkyne) are decisive for the regioselectivity of the intermolecular PKR.

Last we performed PKR with disubstituted alkyne **6**. Despite the higher regioselectivity of the acetylated derivative **1d** compared to the methoxy derivative **1b**, the disubstituted alkyne **6** was almost unselective giving 1:1.1 regioisomeric ratio. Surprisingly, the methoxy substituent that was less selective in previous experiments slightly dominated in the β position. Yet, the outcome was qualitatively in agreement with alkynyl NBO charges even though the selectivity was clearly overestimated.

Overall, the observed regioselectivity in the intermolecular PKR of alkynes **1**−**6** with NBD clearly indicates that, in the absence of strong steric effects, the electronegativity of the atom bonded to the propargylic sp^3-hybridized carbon plays a fundamental role. We can therefore assume that the propargylic substituents can polarize the carbon−carbon triple bond via inductive effects providing highly regioselective reactions. From NBO charges, it is clear that the initial C−C bond formation, that dictates the regiochemistry, takes place with the more electron rich carbon, even though quantitatively the data obtained does not allow curve fitting (Figure 6). In similar fashion, inspection of the carbons at the propargylic position (C^1−C^4) predicts the regiochemistry surprisingly well, although the prediction fails to give correct outcome for substrates **3** and **6**.

The Role of Weak Interactions. The current moderate quantitative correlation on alkyne moiety NBO charge vs regioselectivity contrasts our recent quantitative correlation obtained for corresponding diarylalkynes.[7] A probable reason is that in the case of the arylalkynes, we did not need to consider neither steric factors nor the field effects since in the conjugated system the polarization of the alkyne was affected from a distance by EWG/EDG groups. With the present set of alkyne PKR substrates (Figure 3) we cannot exclude the possibility that weak intramolecular interactions or steric factors could contribute critically on the α/β-regioguidance in addition to electronic factors. For instance, according to alkyne polarization, the α-selectivity of TMS and *tert*-butyl groups was expected, but based on the NBO charges with lesser extent (**4** and **5**, Figures 5 and 6). Obviously, in this case, the steric effects act in concert with the electronic effect.

To take steric factors along with other weak attractive and repulsive interactions into account, we performed a more detailed computational study for selected model substrates: **I**−**III** (Figure 7). To reduce the amount of the possible conformers caused by the flexible aliphatic chain, the alkyl group was reduced to methyl. The methoxymethyl group in model **I** would account for a group with an electronegative atom and small steric effects. Thus, the propyl in model **II** would serve as comparison. For reasoning the rival of steric and electronic effect in the one and same group, we chose trifluoromethyl group in model **III** to demonstrate this effect. Our intent was not to fully reproduce the experimental data, but to discover the effect of the each alkyne substituent separately compared to methyl as internal standard.

The calculated NBO charges in Figure 7 suggest that the electronic effects should drive methoxy ether to the β-selectivity (this occurs experimentally for substrate **1b**), whereas *n*-propyl tail should favor the α-position. Even though, in the both cases, the steric factors should drive selectivities toward α-regioisomer. Nonetheless, when the *n*-propyl tail is compared to methoxy-ether, the electronic factors alone point only toward rather small regioselectivity in **II**. On the other hand, the NBO values would predict the CF_3 to be in β position contrasting the experimental observation.[3a] Therefore, in order to take complete electronic interactions into account in our computational model, we leaned on the well-established mechanism for the reaction (Figure 8). We studied the transition states (TS) for these model substrate complexes that lead to the regiochemistry determining C−C bond formation. Only TS structures leading to *exo*-selectivity were taken under consideration, which is in accordance with the experimental results where only minor amounts of *endo*-isomers were isolated. The computational level was as earlier described with the exception that slightly smaller triple ζ basis set def2-TZVP was employed.

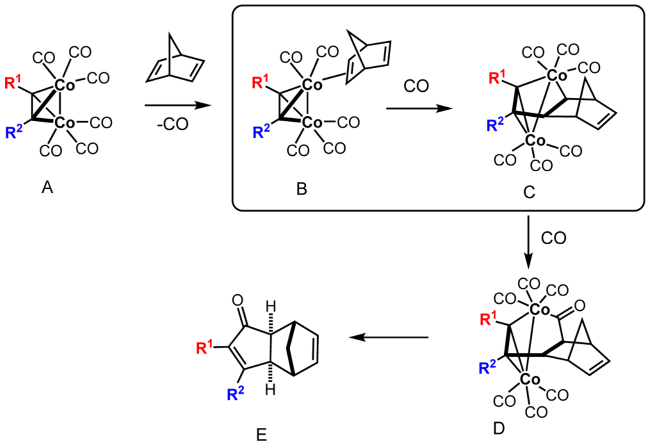


Figure 8. Mechanism of the PKR showing the step that determines the regiochemistry.

We studied first the possible TSs for C−C bond formation from intermediate **B** (Figure 8) (For more comprehensive discussion, see Supporting Information). Because of low activation energy barrier for pseudorotation of pentacarbonyl dicobalt complex (**B**), we located four TS's to be taken into consideration. The pseudorotation has been discussed previously by Gimbert and Milet and our results are in accordance with the earlier ones.[11,12] Because of the flexibility of the aliphatic side chain, we needed to discover the conformational space in the transition states leading to the α/β-regioisomers for models **I** and **II**. Hence, we took all three torsional conformations of the bridge sp^3-carbon under consideration (marked in Figure 7 with a curved arrow).

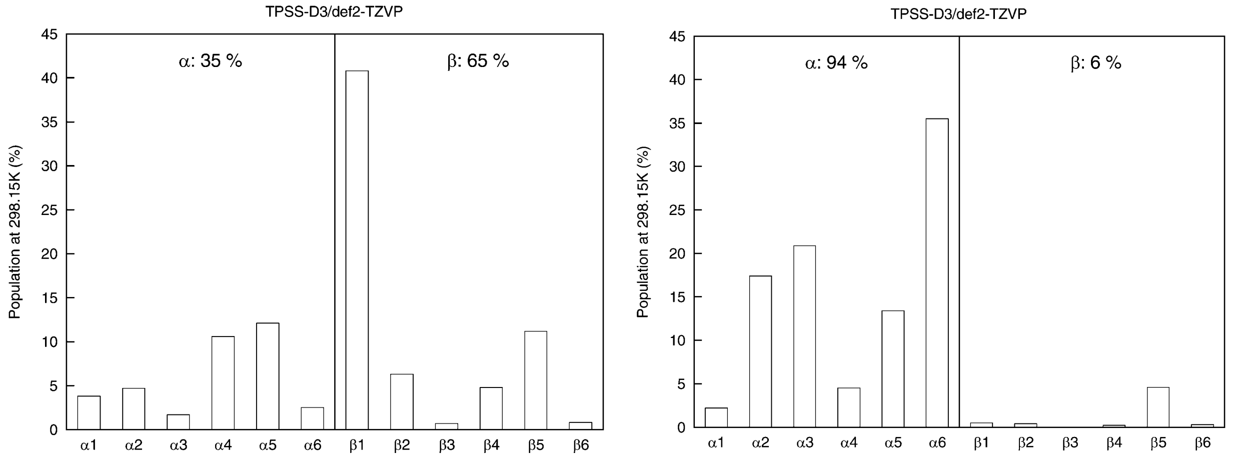


Figure 9. Populations of the transition states leading to α and β regioselectivities for substrates **I** (left) and **II** (right).

Altogether, 12 transition states were studied for the both substrates, whereas for **III**, only four were needed to take in to account. Especially for model **I**, the conformation of aliphatic tail had critical impact on the regioselectivity (Figure 9). The effect of the heteroatom can be illustrated by inspecting the same conformations for the model **II** with propyl tail where similar effect is not visible. The analysis of the energetics suggests α/β ratios of 35/65 and 94/6 for substrates **I** and **II**, respectively (Figure 9). Noteworthy, there are clearly some dominating TS populations; for instance the population of substrate I leading to β-isomer is cumulated on TS's β1 and β5. The origin of this occurrence are discussed vide infra. Populations of each state were calculated according to Boltzmann equation at 298.15 K according to ΔG(298.15 K). The computational results were confirmed to be solid with higher basis set (def2-TZVPP) and performing single point energy calculations with wider variety of functionals (see Supporting Information). To our delight, these values correlate well with the experimental results on regioselectivity where *n*-propyl favors α and methoxy-ether β-selectivity in substrate **1b** (α/β-*exo* = 7:82). To verify also the model **II** experimentally, PKR was performed for **II** with slightly longer alkyl tail (n = 7, substrate 7, Figure 10) and obtaining complete α-selectivity (the methyl in β position). Thus, based on the population analysis of models **I** and **II** the electronic factors predicts regioselective outcomes but with a lesser extent than was observed experimentally.

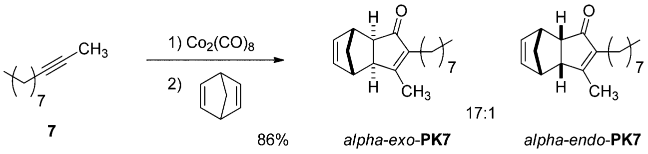


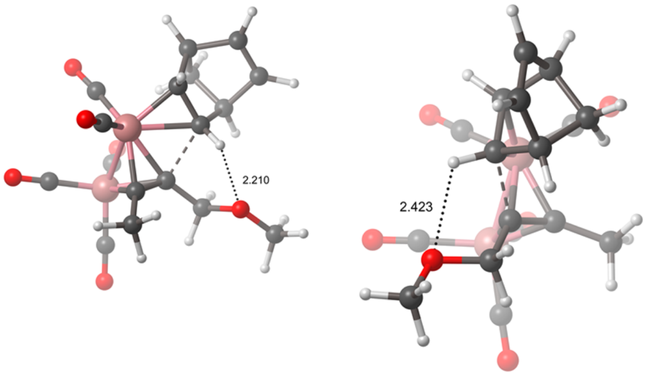
Figure 10. PKR of undec-2-yne (7) as a model of 2-alkynyl hydrocarbons.

Turning to model compound **III** experimental PKRs results have shown that the CF_3 group accommodates α-position overriding thus the electronic effect. When NBD has been used as alkene, alkyl chain and CF_3 group substituted alkynes have provided complete α-selectivity for CF_3 group.[3a] Meanwhile, the change of alkene to NBN has slightly lowered the α-selectivity but it has been still notable.[10] These results indicate that, even though the CF_3 group induces clear α regioselectivity, we can still expect that the computational ΔG differences between the transition states should be decently small as the regioselectivity can be dramatically affected by the small changes in the geometry and electronic structure of the substrate or alkene. Our computational results predicted α/β isomer ratio 97:3, which is in excellent correlation with the experimental data. It should be noted that albeit the difference in the alkyne NBO charges is much greater for the trifluoromethyl substrate **III** than for **II** or **I**, the selectivity is driven opposite to the electronic effect.

To accomplish the discussion on the selectivity of the model compounds, it should be noted that all the ΔG(298.15 K) values of studied transition states are inside 3 kcal/mol. This implies that even weak attractive or repulsive forces, either intra- or intermolecular, can have critical impact on the regioselectivity. Accordingly, one should consider the system as a whole while performing computational predictions for the PKR in quantitative manner. This is also supported by the experimental data, which indicate that regioselectivities were affected by small changes in the alkene (NBD/NBN, j in Figure 4) or the *exo*/*endo*-ratio with the coordinative properties of the solvent (MeCN, m and n in Figure 4).

To examine the origin and role of the weak interactions in the regioguidance, we returned to models **I** and **II** in order to illustrate these effects in more detail. A closer inspection of the transition state populations shows large differences in the ones leading to β-regioselectivity for alkyne with methoxy ether (model **I**, Figure 9). These differences can be originated to arise from hydrogen bonding between a NBD proton and the ether oxygen (Figure 11). Depending on the functional, the most populated transition states were either ***β*1** or ***β*5**. In common, both of these structures show a weak hydrogen bond interaction between the oxygen and the NBD-hydrogen involved to the C−C bond forming transition state. The hydrogen bond can be considered to be rather weak but still evident according to the bond length (2.2−2.4 Å). Meanwhile, with *n*-propyl tail (**II**) the orientation of the corresponding carbon atom does not seem to have notable effect on the populations of the states that are leading to β-regioselectivity. Notably, for the model compound **I** the hydrogen bonded states bring almost the all of β-population, underlining the critical effect of this weak interaction on the regioselectivity.

To visualize these weak interactions, the noncovalent interaction (NCI) plots are presented in Figure 12. In the NCI plot, the noncovalent weak attractive interactions are



β1 **β5**

Figure 11. Two lowest energy transition states for the insertion step of the model system **I**.

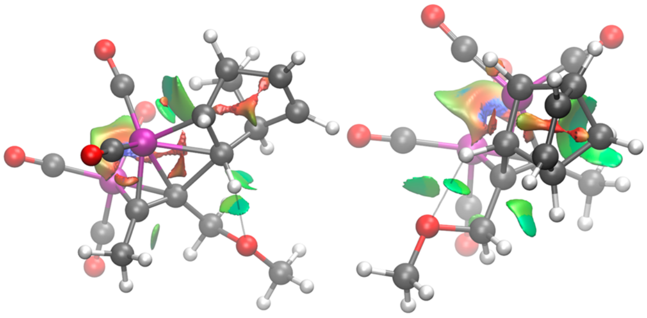


Figure 12. Noncovalent interaction plots on transition states ***β*1** and ***β*5** for substrate **I**.

presented as green, stronger attractive interactions as blue, while repulsive surfaces are depicted as red. In both transition states the NCI plot reveals hydrogen bond interaction between the oxygen and NBD hydrogen. This can be seen to be slightly stronger for TS ***β*1** as denoted by the 0.2 Å shorter hydrogen bond distance for ***β*1** than for ***β*5**. Notably, the NCI plots display also other relevant attractive interactions in the system, including interactions between several hydrogen atoms. Therefore, we examined the role of O−H hydrogen bonding more specifically on terms of NBO charges and NMR shifts.

Consequently, to trace how these weak attractive interactions stabilize the TS of the insertion step of the model system **I**, we inspected the NBO charges of the NBD protons H^1−H^4 in these structures (Figure 13). In the most TS structures the H^4 is only slightly more acidic than the other three marked hydrogens. Interestingly, the effect is pronounced in the presence of the weak hydrogen bond. In substrate **I** transition states ***β*1**/***β*5** the NBO charge of H^4 is increased to 0.25 compared to 0.21 for H^1/H^2. Meanwhile, without the attractive interaction, the NBO charge is increased only slightly being 0.22−0.23. Actually, these findings suggest that the role of the heteroatom as a hydrogen bond acceptor is not to stabilize the acidic H^4 but to allow the cobalt coordinating proton H^4 bond to become more electron deficient. In this manner, this specific polarization stabilizes the TS structure and facilitates this reaction pathway. It has been reported that both experimental and computed chemical shifts are expedient parameters to assess H-bonding interactions.[13] To uncover the H-bonding polarization effect, we compared the computed NMR shifts for protons H^3 and H^4 for substrate **I** in transition states ***β*1**, ***β*3** and ***α*6** at TPSSh-D3/def2-TZVPP level. The isotropic shielding effect for H^3 is similar in all cases (inside 0.3 ppm) but in the case of H_4 the shielding in the weakly interacting complex ***β*1** provokes a downfield of 1.5 ppm compared to ***β*3** and ***α*6**. This is in agreement with the NBO analysis that the formed weak hydrogen bond affects the acidity of the H^4.

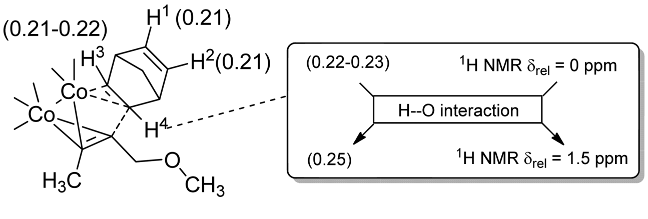


Figure 13. Parameters calculated for the insertion step TS of model system **I** (pentacarbonyl complex, COs have been omitted for clarity) with and without H-bond donor; (a) in the parentheses: the NBO charges for the selected protons H^1−H^4 and (b) in the box: the relative $\Delta\delta_H$ for the hydrogen bonding proton H^4.

■ CONCLUSIONS

The regioselectivity of the intermolecular Pauson−Khand reaction has been studied using a full set of aliphatic alkynes bearing sterically similar but electronically unequivalent substituents. We have shown that electronic polarization alone can result significant regioselectivity in PKR. Electronegative substituents with $-I$ effect placed in propargylic position yielded cyclopentenones with a remarkably high selectivities being *β-exo* isomer the major stereoisomer. The computational NBO charges indicate the polarization of alkyne, which is inductively mediated from the heteroatom. As a limiting factor, the alkyne polarization alone does give only qualitative prediction of regioisomer outcome, since other attractive and repulsive substituent interactions compete with it. Remarkably, even seemingly small steric factors can easily override the electronics or weak interactions, such as hydrogen bonding, can contribute significantly to the regioselectivity. Nevertheless, the remarkable regioselectivity in intermolecular PKR of aliphatic alkynes has been explained by theoretical calculations.

■ EXPERIMENTAL SECTION

All structure optimizations and single point energy calculations were performed using the Turbomole 6.4 program package.[14] Computations were done in gas-phase as experimental results indicated low impact of the solvent toward the regioselectivity. The TPSS-D3[15,16] functional was employed with triple ζ quality basis set, def2-TZVP or def2-TZVPP,[17] as described in the text. The MARI-J approximation was used in all computations with suitable auxiliary basis set.[18,19] Default settings of the Turbomole program were used throughout expect finer grid option *m4* (cobalt complexes) or *m5* (alkynes) was chosen. Analytical frequency calculations were performed to all optimized structures to confirm the nature of the potential energy surface (minima/maxima) and to obtain the chemical potential (chem. pot.) for Gibbs free energies. The Gibbs free energies were then calculated as $G = E(0) + \text{chem.pot.}$ To inspect transition state energy differences more closely, single-point energy calculations were also performed with PW6B95-D3,[17,20] TPSSh-D3[16,17,21] and PBE0-D3[17,22,23] functionals, to ensure the nature of the result. NCI-plots were generated using NCIplot-program[24,25] using TPSS-D3/def2-TZVP wave function from Turbomole. Pictures were generated using Cylview[26] and VMD.[27] The ^1H NMR shieldings were calculated with Orca 3.0 program package (IGLO/TPSSh-D3/def2-TZVPP).[28] Additional settings “TightSCF” and “Grid4” were used.

All commercial reagents were used without further purification. The used solvents were reagent or HPLC grade. Anhydrous *N*,*N*-dimethylformide and toluene were purchased and used directly unless otherwise stated. Tetrahydrofuran, ether and dichloromethane were obtained using a Solvent Purification System (SPS) or Et_2O was dried over 4 Å molecular sieves. All reactions were carried out under a nitrogen or argon atmosphere in oven-dried glassware. Analytical TLC was performed on silica gel 60 F254 plates and visualized by UV, if possible, and phosphomolybdic acid, potassium permanganate or *p*-anisaldehyde stainings. ^1H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ at ambient temperature unless otherwise stated. ^1H spectra were referenced to tetramethylsilane (TMS, 0 ppm) or residual solvent and ^{13}C spectra were referenced to solvent carbon (77.0 ppm for $CDCl_3$) unless otherwise noted. Proton and carbon assignments were made based on COSY, HSQC, HMQC, HMBC and NOESY spectra. The isomer ratio was determined by NMR by integration of ^1H spectrum. IR spectra were obtained by depositing a film of the product on a NaCl window. Absorptions are given in wavenumbers (cm^{-1}). ^1H and ^{13}C spectra of all new compounds are available in the Supporting Information.

Preparation of Alkynes 1−9. Hex-2-yn-1-ol (**1a**) and 3-heptyn-1-ol were commercial and used as such. **1b**,[29] 1-(*tert*-butyldimethylsilyloxy)hex-2-yne (**1c**)[30] and hex-2-yn-1-yl acetate (**1d**)[31] were prepared according to literature procedures. 3-Heptynoic acid methyl ester (**3**)[32] was prepared from heptynoic acid[33] by treatment with (trimethylsilyl)diazomethane.

Hex-2-yn-1-yl methanesulfonate. Title compound was prepared by mesylation of hex-2-yn-1-ol **1a**. **1a** (4.40 mL, 40 mmol, 1 equiv) was dissolved in DCM (50 mL) and triethylamine (6.14 mL, 44 mmol, 1.1 equiv) was added at 0 °C followed by mesyl chloride (3.40 mL, 44 mmol, 1.1 equiv). After stirring for 15 min at 0 °C and for 3 h at rt, the reaction was quenched with water. The organic phase was washed with NH_4Cl (aq.) and $NaHCO_3$ (aq.) and dried with brine and over Na_2SO_4. Removing solvents gave the crude product (6.677 g, 37.89 mmol, 95%) as a pale yellow liquid which was used as such. ^1H NMR (300 MHz, $CDCl_3$) δ 4.85 (t, J = 2.2 Hz, 2H), 3.11 (s, 3H), 2.24 (tt, J = 7.0, 2.2 Hz, 2H), 1.56 (m, 2H), 0.99 (t, J = 7.4 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 90.9, 72.3, 58.5, 38.9, 21.6, 20.6, 13.4.

*N,N-Dimethylhex-2-yn-1-amine **2a**.* Title compound was prepared from hex-2-yn-1-yl methanesulfonate.[34] Hex-2-yn-1-yl methanesulfonate (2.643 g, 15 mmol, 1 equiv) was added on a 33% solution of dimethylamine in EtOH. The reaction mixture was stirred at rt overnight, extracted with DCM and dried with brine and over Na_2SO_4. The crude product was purified by distillation giving 813 mg (6.49 mmol, 43%) of the *N*,*N*-dimethylhex-2-yn-1-amine **2a** with bp. 57.5 °C (19 mmHg). HRMS (ESI-TOF) *m*/*z* calcd for $[C_8H_{16}N]^+$ 126.1277, found 126.1275 (Δ = 1.67 ppm).^1H NMR (300 MHz, $CDCl_3$) δ 3.20 (t, J = 2.2 Hz, 2H), 2.28 (s, 6H), 2.18 (tt, J = 7.0, 2.2 Hz, 2H), 1.54 (m, 2H), 0.99 (t, J = 7.3 Hz, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ 85.1, 75.1, 48.2, 44.1, 22.3, 20.7, 13.5.

*N,N-Dimethylhex-2-yn-1-aminium tetrafluoroborate **2b**.* Title compound was prepared by dissolving *N*,*N*-dimethylhex-2-yn-1-amine **2a** (1 equiv) in dry Et_2O and adding $HBF_4{\cdot}Et_2O$ (1.05 equiv) at 0 °C. After stirring at rt for 5 min solvents were removed in high vacuum overnight. The resulting salt **2b** turned out to be liquid, which did not crystallize even in freezer. We were unable to measure either HRMS, due to ionic nature, or elemental analysis, due to the liquid state of the compound **2b**. However, no solvents or other impurities can be seen in the ^1H NMR spectrum. Quantitative yield. ^1H NMR (500 MHz, $CDCl_3$) δ 4.03 (s, 2H), 3.00 (s, 6H), 2.25 (t, J = 6.9 Hz, 2H), 1.57 (m, 2H), 1.00 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 93.1, 66.8, 48.3, 42.6, 21.5, 20.6, 13.4.

Hex-2-yn-1-amine. Title compound was prepared from hex-2-yn-1-yl methanesulfonate via hex-2-yn-1-yl azide in a one-pot reaction. Sodium azide (4926 mg, 75.77 mmol, 2 equiv) was dissolved in DMSO (170 mL) and hex-2-yn-1-yl methanesulfonate (6677 mg, 37.89 mmol, 1equiv) was added with DMSO (20 mL). The reaction mixture was stirred at rt for an hour. (It should be noted that propargyl azides tend to rearrange to allenyl azides and further on. For this reason, hex-2-yn-1-yl azide was not isolated and reaction times should not be prolonged.[35]) Triphenylphosphine (19.954 g, 76.08 mmol, 2.008 equiv) was added, the reaction mixture was stirred at rt for 4 h, 20 mL of water was added and then stirred at rt overnight. The solid byproducts were filtered off, water was added, and the solution was extracted with ether. The organic phase was made acidic with 2 M HCl and extracted with water followed by basification of the aqueous phase with 2 M NaOH and extraction with ether. The organic phase was then washed with water and brine, and solvents were removed. The crude product was carefully distilled to give hex-2-yn-1-amine (bp. 50.5 °C (15 mmHg)) in 55% yield (2.032 g, 20.92 mmol). The measured boiling point corresponded well to the previously reported ones.[36] HRMS (ESI-TOF) *m*/*z* calcd for $[C_6H_{12}N]^+$ 98.0964, found 98.0985 (Δ = 6.27 ppm). ^1H NMR (300 MHz, $CDCl_3$) δ 3.40 (t, J = 2.2 Hz, 2H), 2.15 (tt, J = 7.0, 2.2 Hz, 2H), 1.52 (m, 2H), 1.33 (s (br), 2H), 0.97 (t, J = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 82.5, 81.0, 31.7, 22.2, 20.7, 13.5.

*tert-Butyl hex-2-yn-1-yl carbamate **2c**.* Title compound was prepared from hex-2-yn-1-amine. Hex-2-yn-1-amine (486 mg, 5 mmol, 1 equiv) was dissolved in DCM (50 mL) and Boc-anhydride (1200 mg, 5.5 mmol, 1.1 equiv) was added at 0 °C. The reaction mixture was stirred at rt overnight and quenched with general workup: washed with NH_4Cl (aq.) and $NaHCO_3$ (aq.) and dried with brine and over Na_2SO_4. Removing solvents gave *tert*-butyl hex-2-yn-1-yl carbamate **2c** (92%, 906 mg, 4.6 mmol) as a clear colorless liquid which was used as such. HRMS (ESI-TOF) *m*/*z* calcd for $[C_{11}H_{19}NO_2Na]^+$ 220.1308, found 220.1305 (Δ = 1.29 ppm). ^1H NMR (500 MHz, $CDCl_3$) δ 4.74 (br. s, 1H), 3.89 (br. s, 2H), 2.14 (tt, J = 7.0, 2.2 Hz, 3H), 1.55−1.40 (m, 11H), 0.97 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.3, 83.4, 79.7, 76.1, 30.8, 28.3, 22.0, 20.6, 13.4.

*N-(Hex-2-yn-1-yl)acetamide **2d**.* Title compound was prepared from hex-2-yn-1-amine. Hex-2-yn-1-amine (486 mg, 5 mmol, 1 equiv) was dissolved in DCM (50 mL) and triethylamine (697 μL, 5 mmol, 1 equiv) was added at 0 °C followed by acetic anhydride (519 μL, 5.5 mmol, 1.1 equiv). The reaction mixture was stirred at rt overnight. Some hex-2-yn-1-amine was left in the reaction mixture and therefore 350 μL (2.5 mmol, 0.5 equiv) of triethylamine and 0.1 mL (1.06 mmol, 0.21 equiv) of acetic anhydride were added. The reaction was stirred overnight at rt again and then quenched with general workup: washed with NH_4Cl (aq.) and $NaHCO_3$ (aq.) and dried with brine and over Na_2SO_4. Removing solvents gave *N*-(hex-2-yn-1-yl)acetamide **2d** (88%, 612 mg, 4.40 mmol) as a clear pale yellow liquid which was used as such. HRMS (ESI-TOF) *m*/*z* calcd for $[C_8H_{13}NONa]^+$ 162.0889, found 162.0888 (Δ = 0.75 ppm). ^1H NMR (500 MHz, $CDCl_3$) δ 5.58 (s (br), 1H), 4.02 (dt, J = 4.7, 2.2 Hz, 2H), 2.15 (tt, J = 7.1, 2.2 Hz, 2H), 1.99 (s, 3H), 1.52 (m, 2H), 0.97 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.8, 83.8, 75.4, 29.8, 22.9, 22.0, 20.6, 13.4.

*1-Trimethylsilyltetradec-2-yne **4**.* *n*-Butyl lithium (2.5M, 1.3 mL, 2.66 mmol, 2.4 equiv) was added dropwise to anhydrous diisopropylamine (0.2 mL, 2.8 mmol, 2.5 equiv) in freshly distilled Et_2O (3 mL) at −78 °C. The resulting mixture was stirred for 30 min at 0 °C and cooled down again to −78 °C. A solution of undecyne (0.2 mL, 1.1 mmol, 1 equiv) in freshly distilled Et_2O (2 mL) was added to the reaction mixture. After 30 min of stirring (chloromethyl)-trimethylsilane (0.77 mL, 5.5 mmol, 5 equiv) and hexamethylphosphoramide (1.1 mL, 5.8 mmol, 5.3 equiv) were added. The reaction mixture was stirred at −78 °C for 4 h, allowed to warm, and stirred overnight at rt. NH_4Cl (aq.) was added to the mixture at 0 °C and the aqueous layer was extracted with Et_2O. Organic phases were dried over $MgSO_4$ and concentrated at reduced pressure. Purification over SiO_2 with pentane afforded the 1-trimethylsilyltetradec-2-yne 4 (86%, 258 mg, 0.97 mmol) as an oil. HRMS (APCI- LTQ Orbitrap) *m*/*z* calcd for $[C_{17}H_{33}Si]^+$ 265.2346 found 265.2343 (Δ = 1.13 ppm). ^1H NMR (400 MHz, $CDCl_3$) δ 2.11−2−15 (m, 2H), 1.45−1.50 (m, 2H), 1.42 (t, J = 2.7 Hz, 2H), 1.33−1.39 (m, 2H), 1.24−1.30 (m, 14H), 0.88 (t, J = 6.9 Hz, 3H), 0.09(s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 79.1, 77.4, 32.1, 29.79, 29.76, 29.6, 29.5, 29.4, 29.0, 22.9, 19.1, 14.2, 7.1, −2.0. IR (film, ν) 2937, 2853, 2155, 1707, 1464, 1251, 848.4 cm^{-1}.

*1,1-Dimethyl-hexadec-4-yne **5**.* *n*-Butyl lithium, 2.5 M (0.8 mL, 2.0 mmol, 1.1 equiv) was added dropwise on tridecyne (0.4 mL, 1.75

mmol, 1 equiv) in dry THF (8 mL) at −66 °C, followed by hexamethylphosphoramide (50 vol %, 4.5 mL, 15 equiv). The resulting mixture was stirred for 30 min and a solution of 1-iodo-2,2-dimethylpropane (0.25 mL, 1.93 mmol, 1.1 equiv) in dry THF (1 mL) was added. Reaction was warmed up to rt and heated at 78 °C for 2 days. The reaction was quenched with NH_4Cl (aq.), extracted with hexane, dried over $MgSO_4$ and concentrated at reduced pressure. Purification over SiO_2 with pentane afforded 1,1-dimethyl-hexadec-4-yne 5 (70%, 306 mg, 1.22 mmol) as an oil. HRMS (APCI- LTQ Orbitrap) *m*/*z* calcd for $[C_{18}H_{33}]^+$ 249.2577 found 249.2574 (Δ = 1.20 ppm). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.14−2−18 (m, 2H), 2.02 (t, *J* = 2.4 Hz, 2H), 1.45−1.51 (m, 2H), 1.35−1.42 (m, 2H), 1.26−1.30 (m, 14H), 0.97 (s, 9H), 0.88 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 81.8, 78.5, 34.0, 32.1, 31.2, 29.9, 29.8, 29.5, 29.4, 29.3, 29.1, 29.0, 22.9, 18.9, 14.27. IR (film, ν) 2930, 1469, 1296, 1200, 982 cm^{-1}.

4-Methoxybut-2-yn-1-ol. Title compound was prepared from 2-butyne-1,4-diol. 2-butyne-1,4-diol (4.305 g, 50 mmol, 1 equiv) was dissolved in DMSO (50 mL) and KOH (2.805 g, 50 mmol, 1 equiv) was added. The reaction mixture was stirred at rt for 30 min and MeI (3.11 mL, 50 mmol, 1 equiv) was slowly added to the reaction mixture. After 4h at rt the reaction was quenched by addition of water followed by extractions with Et_2O and drying with brine and over Na_2SO_4. Solvents were removed. Purification was performed by filtration trough silica. Filtration was started with 5:1 Hexane/EtOAc to remove the double alkylated side product and after that the 4-methoxybut-2-yn-1-ol was collected with 1:1 Hexane/EtOAc in 25% yield (1.25 g, 12.49 mmol). NMR data matched well with the reported ones.[37,38] ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.31 (t, *J* = 1.8 Hz, 2H), 4.15 (t, *J* = 1.8 Hz, 2H), 3.39 (s, 3H), 2.85 (br. s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 84.9, 81.0, 59.8, 57.5, 50.7.

4-Methoxybut-2-yn-1-yl acetate (6). Title compound was prepared from 4-methoxybut-2-yn-1-ol. 4-methoxybut-2-yn-1-ol (500.579 mg, 5 mmol, 1 equiv) was dissolved in DCM (50 mL) and the reaction mixture was taken to 0 °C. Triethylamine (708 μL, 7.5 mmol, 1.5 equiv) was added followed by acetic anhydride (1046 μL, 7.5 mmol, 1.5 equiv). The reaction mixture was stirred at 0 °C for 30 min and at rt over weekend. Reaction was quenched with general workup: washed with NH_4Cl (aq.) and $NaHCO_3$ (aq.) and dried with brine and over Na_2SO_4. After solvents were removed, the pure **6** was obtained in 89% yield (636 mg, 4.47 mmol) as a liquid. HRMS (ESI-TOF) *m*/*z* calcd for $[C_7H_{10}O_3Na]^+$ 165.0522, found 165.0523 (Δ = 0.43 ppm). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.73 (t, *J* = 1.7 Hz, 2H), 4.14 (t, *J* = 1.7 Hz, 2H), 3.38 (s, 3H), 2.10 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.1, 82.5, 80.4, 59.7, 57.6, 52.1, 20.6.

PK Reactions of Alkynes 1−6. *General Procedure for Alkyne Dicobalthexacarbonyl Complex Formation.* To a solution of alkyne 0.5 M in hexane, dicobaltoctacarbonyl (1.1 equiv) was added. The mixture was stirred at room temperature for 2−3 h under nitrogen depending on alkyne used. The solvent was evaporated at reduced pressure and purified over SiO_2 (hexane/EtOAc gradient if necessary) to afford the complex.

General Procedure for PKRs with Preformed Complex. To a solution of the cobalt complex of alkyne 0.1 M in anhydrous toluene under nitrogen, was added norbornadiene (5 equiv). The mixture was heated at 70 °C overnight. Purification by flash chromatography on SiO_2 (hexane/EtOAc gradient) afforded the Pauson−Khand adducts.

General Procedure for PKRs with Complex Prepared in Situ. Alkyne 0.1 M is dissolved in toluene and $Co_2(CO)_8$ (1 equiv) is added. The reaction mixture is stirred under argon over 60 min at rt. Thereafter, norbornadiene (5 equiv) is added and the reaction mixture is heated at 70 °C. After the reaction is completed, the reaction mixture is adsorbed onto a small amount of silica and purified by silica column chromatography (hexane/EtOAc).

PK1a. PKR of hex-2-yn-1-ol **1a** was performed according to the general procedure in 0.3 mmol scale with overnight heating affording **PK1a** in 85% combined yield (56 mg, 0.26 mmol) as white amorphous solid. Isomers ***β-exo*-PK1a** and ***β-endo*-PK1a** were formed in 10/1 ratio. 3-(hydroxymethyl)-2-propyl-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ***β-exo*-PK1a**. HRMS (ESI-TOF) *m*/*z* calcd for $[C_{14}H_{19}O_2]^+$ 219.1380, found 219.1381 (Δ = 0.58 ppm). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.30 (dd, *J* = 5.5, 3.1 Hz, 1H), 6.21 (dd, *J* = 5.5, 2.9 Hz, 1H), 4.66 (dd, *J* = 14.7, 2.3 Hz, 1H), 4.51 (dd, *J* = 14.7, 4.6 Hz, 1H), 2.91 (m, 3H), 2.29 (d, *J* = 5.1 Hz, 1H), 2.24−2.08 (m, 3H), 1.47−1.34 (m, 3H), 1.18 (d, *J* = 9.3 Hz, 1H), 0.88 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 209.8, 171.2, 144.7, 138.3, 137.2, 59.6, 52.1, 48.1, 43.6, 42.4, 41.2, 25.1, 21.9, 14.1.

PK1b. Complexation of **1b** was performed according to the general method in 20 mmol scale and 4 h stirring affording **C1b** in 95% yield (7.56 g) as an oil. **PK1b** was prepared from previously formed complex according to the general procedure in 0.3 mmol scale with overnight heating affording **PK1b** in 97% combined yield (71 mg, 0.31 mmol) as an oil. Isomers ***α-exo*-PK1b**, ***β-exo*-PK1b** and ***β-endo*-PK1b** were formed in 1/12.5/1.3 ratio. 3-(Methoxymethyl)-2-propyl-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ***β-exo*-PK1b**. HRMS (ESI-TOF) *m*/*z* calcd for $[C_{15}H_{21}O_2]^+$ 233.1536, found 233.1532 (Δ = 1.65 ppm). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.29 (dd, *J* = 5.5, 3.1 Hz, 1H), 6.20 (dd, *J* = 5.5, 2.9 Hz, 1H), 4.34−4.25 (m, 2H), 3.41 (s, 3H), 2.91 (br s, 1H), 2.85 (s, 1H), 2.82 (d, *J* = 5.1 Hz, 1H), 2.28 (d, *J* = 5.2 Hz, 1H), 2.25−2.08 (m, 2H), 1.47−1.35 (m, 3H), 1.17 (d, *J* = 9.3 Hz, 1H), 0.89 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 209.4, 168.9, 145.6, 138.4, 137.1, 69.1, 58.9, 52.1, 48.4, 43.6, 42.4, 41.2, 25.2, 21.8, 14.0. 2-(Methoxymethyl)-3-propyl-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ***α-exo*-PK1b**. HRMS (ESI-TOF) *m*/*z* calcd for $[C_{15}H_{20}NaO_2]^+$ 255.1356, found 255.1352 (Δ = 1.31 ppm).^{1}H NMR (500 MHz, $CDCl_3$) δ 6.27 (dd, *J* = 5.4, 3.1 Hz, 1H), 6.23 (dd, *J* = 5.5, 2.9 Hz, 1H), 4.05 (br s, 2H), 3.33 (s, 3H), 2.95 (br s, 1H), 2.79 (br s, 1H), 2.76 (d, *J* = 5.2 Hz, 1H), 2.70−2.62 (m, 1H), 2.41−2.34 (m, 1H), 2.32 (d, *J* = 5.2 Hz, 1H), 1.77−1.66 (m, 1H), 1.61−1.50 (m, 1H), 1.38 (d, *J* = 9.3 Hz, 1H), 1.22 (d, *J* = 9.3 Hz, 1H), 1.00 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 208.5, 180.3, 141.0, 138.0, 137.7, 62.9, 58.5, 52.4, 50.1, 43.5, 42.4, 41.5, 31.9, 21.2, 14.3. 3-(Methoxymethyl)-2-propyl-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ***β-endo*-PK1b**. HRMS (ESI-TOF) *m*/*z* calcd for $[C_{15}H_{21}O_2]^+$ 233.1536, found 233.1546 (Δ = 4.07 ppm).^{1}H NMR (500 MHz, $CDCl_3$) δ 5.90 (dd, *J* = 5.5, 2.9 Hz, 1H), 5.74 (dd, *J* = 5.5, 2.9 Hz, 1H), 4.22 (d, *J* = 13.8 Hz, 1H), 4.06 (d, *J* = 13.8 Hz, 1H), 3.41 (s, 3H), 3.36 (t, *J* = 4.8 Hz, 1H), 3.19 (s, 1H), 3.05 (s, 1H), 2.80 (t, *J* = 5.2 Hz, 1H), 2.14−2.06 (m, 1H), 2.02−1.93 (m, 1H), 1.73 (d, *J* = 8.3 Hz, 1H), 1.60 (d, *J* = 8.4 Hz, 1H), 1.35−1.25 (m, 2H), 0.82 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 209.5, 168.0, 143.9, 132.9, 132.3, 69.7, 59.1, 52.4, 50.0, 46.0, 44.4, 44.0, 24.9, 21.9, 13.9.

PK1c. Complexation of **1c** was performed according to the general method in 3.25 mmol scale and 2 h stirring affording **C1c** in quantitative manner (1 g) as a red oil. **PK1c** was prepared from previously formed complex according to the general procedure in 1.01 mmol scale with overnight heating affording **PK1c** in 66% combined yield (220 mg, 0.66 mmol) as an oil. Isomers ***α-exo*-PK1c**, ***β-exo*-PK1c** and ***β-endo*-PK1c** were formed in 1/27/2.5 ratio. 3-((*tert*-Butyldimethylsiloxy)methyl)-2-propyl-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ***β-exo*-PK1c**. HRMS (ESI-TOF) *m*/*z* Calcd for $[C_{20}H_{33}O_2Si]^+$ 333.22443, found 333.22463 (Δ = 0.59 ppm). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.26 (dd, *J* = 3.2 Hz, *J* = 3.2, Hz, 1H), 6.18 (dd, J = 2.8 Hz, *J* = 2.8 Hz, 1H), 4.58 (d, *J* = 14.8 Hz, 1H), 4.48 (d, *J* = 15.2 Hz, 1H), 2.9 (s, 1H), 2.85 (s, 2H), 2.25 (d, *J* = 5.2 Hz, 1H), 2.18 (m, 1H), 2.08 (m, 2H), 1.39 (m, 1H), 1.34 (d, *J* = 5.6 Hz, 1H), 1.17 (d, *J* = 9.2 Hz, 1H), 0.93 (s, 9H), 0.88 (t, *J* = 7.6 Hz, 3H), 0.12 (s, 3H), 0.11 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.5, 172, 143.6, 138.3, 137.1, 60.8, 52.6, 48.8, 44.2, 43.2, 41.8, 26.4, 25.8, 22.4, 18.8, 14.7, −4.8, −4.9. IR (film, ν) 2949, 1726, 1424, 1200, 1167, 1104 cm^{-1}.

PK1d. Complexation of **1d** was performed according to the general method in 2.47 mmol scale and 3 h stirring affording **C 1d** in quantitative manner (820 mg) as a red oil. **PK 1d** was prepared from previously formed complex according to the general procedure in 2.29 mmol scale with overnight heating affording **PK 1d** in 60% combined yield (357 mg, 1.37 mmol) as an oil. Isomers ***α-exo*-PK 1d**, ***β-exo*-PK 1d** and ***β-endo*-PK 1d** were formed in 1/30/1.5 ratio. 4-Propyl-5-acetoxymethyl-tricylo[5,2,1,0^{2,6}]deca-4,8-dien-3-one ***β-exo*-PK 1d**. HRMS (ESI-TOF) *m*/*z* calcd for $[C_{16}H_{21}O_3]^+$ 261.14852, found

261.14845 (Δ = −0.27 ppm). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.25 (dd, J = 3.1, J = 3.1 Hz, Hz, 1H), 6.19 (dd, J = 2.9 Hz, J = 2.9 Hz, 1H), 4.98 (d, J = 14.3 Hz, 1H), 4.90 (d, J = 14.3 Hz, 1H), 2.91 (s, 1H), 2.78 (s, 1H), 2.72 (d, J = 5.10 Hz, 1H), 2.28 (d, J = 5.10 Hz, 1H), 2.12 (s, 3H), 2.18 (m, 2H), 1.41 (m, 2H), 1.35 (d, J = 9.1 Hz, 1H), 1.14 (d, J = 9.2 Hz, 1H), 0.87 (t, J = 7.6 Hz, 3H) . ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.6, 170.8, 165.8, 147.1, 137.6, 60.9, 52.5, 48.9, 44.0, 42.7, 41.0, 25.5, 22.2, 20.9, 14.4. IR (film, ν) 2961, 1746, 1699, 1373, 1223, 1040, 835 cm^{-1}.

PK2a. PKR of *N*,*N*-dimethylhex-2-yn-1-amine **2a** was performed according to the general procedure in 0.3 mmol scale with overnight heating affording ***β*-*exo*-PK2a** in 49% yield (36 mg, 0.147 mmol) as white amorphous solid. Only one isomer was seen. 3-((Dimethylamino)methyl)-2-propyl-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ***β*-*exo*-PK2a**. HRMS (ESI-TOF) *m*/*z* calcd for $[C_{16}H_{24}NO]^+$ 246.1852, found 246.1853 (Δ = 0.30 ppm). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.30 (dd, J = 5.5, 3.1 Hz, 1H), 6.20 (dd, J = 5.5, 2.9 Hz, 1H), 3.27 (d, J = 13.9 Hz, 1H), 3.14 (d, J = 13.8 Hz, 1H), 2.90 (s, 1H), 2.86−2.81 (m, 2H), 2.27 (d, J = 5.2 Hz, 1H), 2.24 (s, 6H), 2.25−2.08 (m, 2H), 1.47−1.36 (m, 2H), 1.36 (d, J = 8.9 Hz, 1H), 1.14 (d, J = 9.2 Hz, 1H), 0.89 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 209.8, 171.0, 146.6, 138.4, 137.2, 57.7, 52.1, 48.9, 46.1, 43.6, 42.4, 41.3, 25.1, 22.0, 14.1.

PKR of *N*,*N*-dimethylhex-2-yn-1-aminium tetrafluoroborate **2b** was performed according to the general procedure in 0.3 mmol scale with heating for a week. Workup: NaOH+EtOAc, brine, adsorbed on silica and purified by column chromatography. The reaction product was isolated as an amine **PK2a** in 29% yield (21 mg, 0.085 mmol) and only *β* exo isomer was found. ***β*-*exo*-PK2a** HRMS (ESI-TOF) *m*/*z* calcd for $[C_{16}H_{24}NO]^+$ 246.1852, found 246.1858 (Δ = 2.41 ppm). All NMR data matched well with the data presented for ***β*-*exo*-PK2a**.

PK2c. PKR of *tert*-butyl hex-2-yn-1-yl carbamate **2c** was performed according to the general procedure in 0.3 mmol scale with overnight heating affording **PK2c** in 44% combined yield (42 mg, 0.132 mmol) as white amorphous solid. Isomers ***α*-*exo*-PK2c** and ***β*-*exo*-PK2c** were formed in 1/4 ratio. *tert*-Butyl ((1-oxo-2-propyl-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-3-yl)methyl)carbamate ***β*-*exo*-PK2c**. HRMS (ESI-TOF) *m*/*z* calcd for $[C_{19}H_{27}NO_3Na]^+$ 340.1883, found 340.1871 (Δ = 3.63 ppm). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.26 (m, 1H), 6.21 (s, 1H), 4.81 (s (br.), 1H), 4.15 (d, J = 5.6 Hz, 2H), 2.91 (s, 1H), 2.85 (s, 1H), 2.73 (d, J = 3.7 Hz, 1H), 2.27 (d, J = 4.9 Hz, 1H), 2.25−2.08 (m, 2H), 1.47 (s, 9H), 1.44−1.36 (m, 3H), 1.16 (d, J = 9.3 Hz, 1H), 0.89 (t, J = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 209.2, 169.3, 155.8, 145.7, 138.2, 137.3, 79.9, 52.2, 48.5, 43.5, 42.3, 41.2, 38.9, 28.3, 25.1, 21.9, 14.1.

PK2d. PKR of *N*-(hex-2-yn-1-yl)acetamide **2d** was performed according to the general procedure in 0.3 mmol scale with overnight heating affording **PK2d** in 46% combined yield (36 mg, 0.139 mmol) as white amorphous solid. Isomers ***α*-*exo*-PK2d** and ***β*-*exo*-PK2d** were formed in 1/2.6 ratio. *N*-((1-Oxo-2-propyl-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-3-yl)methyl)acetamide ***β*-*exo*-PK2d**. HRMS (ESI-TOF) *m*/*z* calcd for $[C_{16}H_{21}NO_2Na]^+$ 282.1465, found 282.1474 (Δ = 3.19 ppm). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.26 (dd, J = 5.4, 3.2 Hz, 1H), 6.21 (dd, J = 5.5, 2.9 Hz, 1H), 5.61 (s (br.), 1H), 4.36 (dd, J = 15.8, 7.2 Hz, 1H), 4.20 (dd, J = 15.8, 4.6 Hz, 1H), 2.91 (s, 1H), 2.82 (s, 1H), 2.69 (d, J = 5.1 Hz, 1H), 2.27 (d, J = 5.2 Hz, 1H), 2.18 (m, 2H), 2.06 (s, 3H), 1.50−1.36 (m, 3H), 1.15 (d, J = 9.3 Hz, 1H), 0.90 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 209.1, 170.0, 168.3, 146.3, 138.2, 137.3, 52.2, 48.6, 43.6, 42.3, 41.2, 37.6, 25.2, 23.1, 22.0, 14.1.

PK3. Complexation of **3** was performed according to the general method in 1.79 mmol scale and 2 h stirring affording **C3** in 96% yield (736 mg) as an oil. **PK3** was prepared from previously formed complex according to the general procedure in 0.76 mmol scale with overnight heating affording **PK3** in 80% combined yield (159 mg, 0.65 mmol) as an oil. Isomers ***α*-*exo*-PK3, *β*-*exo*-PK3** and ***β*-*endo*-PK3** were formed in 1/9/0.5 ratio. Methyl 2-(1-oxo-2-propyl-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-3-yl)acetate ***β*-*exo*-PK3a**. HRMS (ESI-TOF) *m*/*z* calcd for $[C_{16}H_{21}O_3]^+$ 261.1484, found 261.1485 (Δ = −0.43 ppm). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.20 (dd, J = 8.5, 3.0 Hz), 6.25 (dd, J = 5.4, 3.1 Hz, 2H), 3.50 (d, J = 14.8 Hz, 1H), 3.36 (d, J = 15.3 Hz, 1H), 2.92 (s, 1H), 2.77 (d, J = 5.2 Hz, 1H), 2.74 (s, 1H), 2.30 (d, J = 5.2 Hz, 1H), 2.18−2.10 (m, 2H), 1.49−1.37 (m, 2H), 1.37 (d, J = 11.1 Hz, 1H), 1.17 (d, J = 9.3 Hz, 1H), 0.89 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 209, 170.3, 165.1, 148.3, 138.6, 138.2, 53.1, 53.0, 51.1, 44.1, 42.7, 42.0, 35.9, 26.2, 22.2, 14.8. IR (film, ν) 2960, 1696, 1639, 1162, 1014, 709 cm^{-1}.

PK4. Complexation of **4** was performed according to the general method in 0.57 mmol scale, 3 h stirring and quick purification over SiO_2 (pentane), affording **C4** in in quantitative yield (297 mg) as a red oil. To a solution of norbornadiene (5.9 mmol, 0.6 mL) in anhydrous toluene (2 mL) at 100 °C was added dropwise a solution of dicobalt complex **C4** in anhydrous toluene (3 mL) at a rate of 1.5 mL/hour. The reaction mixture was stirred for 2 h, evaporated and purified over SiO_2 (Hexane/EtOAc) to afford a yellow oil affording **PK4** in 80% combined yield (182 mg, 0.47 mmol). Isomers ***α*-*exo*-PK4 and *α*-*endo*-PK4** were formed in 24/1 ratio. 2-((Trimethylsilyl)methyl)-3-undecyl-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ***α*-*exo*-PK4**. HRMS (ESI-TOF) *m*/*z* calcd for $C_{25}H_{43}OSi(M+H^+)$ 387.3078, found 387.3108 (Δ = 7.72 ppm). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.25 (dd, J = 5.3, 3.0 Hz, 1H), 6.20 (dd, J = 5.5, 2.9 Hz, 1H), 2.87 (s, 1H), 2.71 (s, 1H), 2.67 (d, J = 5.2 Hz 1H), 2.46−2.39 (m, 1H), 2.25−2.18 (m, 1H), 2.21 (d, J = 5.0 Hz, 1H), 1.67 (d, J = 13.4 Hz, 1H), 1.57−1.64 (m, 1H), 1.54 (d, J = 13.4 Hz, 1H), 1.50−1.39 (m, 2H), 1.35 (d, J = 9.3 Hz, 1H), 1.17−1.14 (m, 14H), 1.11 (d, J = 9.1 Hz, 1H), 0.88 (t, J = 6.8 Hz, 3H), 42.77, 42.02, 32.56, 30.60, −0.01 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.6, 171.4, 143.4, 138.6, 138.2, 52.5, 49.8, 43.9, 30.6, 30.28, 30.26, 30.19, 30.12, 29.99, 28.0, 23.3, 14.8, 14.2, −0.2. IR (film, ν) 2917, 1693, 1578, 842 cm^{-1}.

PK5. Complexation of **5** was performed according to the general method in 0.69 mmol scale, 2 h stirring and quick purification over SiO_2 (pentane), affording **C5** in quantitative yield (305 mg) as a red oil. **PK5** was prepared from previously formed complex according to the general procedure in 1.31 mmol scale with overnight heating at 100 °C affording **PK5** in 79% combined yield (388 mg, 1.05 mmol) as a yellow oil. Isomers ***α*-*exo*-PK5** and ***α*-*endo*-PK5** and were formed in 32/1 ratio. 2-Neopentyl-3-undecyl-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ***α*-*exo*-PK5**. HRMS (ESI-TOF) *m*/*z* calcd for $[C_{26}H_{43}O]^+$ 371.3314, found 371.3310 (Δ = 1.08 ppm). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.26 (dd, J = 5.6, 3.0 Hz, 1H), 6.21 (dd, J = 5.6, 2.9 Hz, 1H), 2.89 (s, 1H), 2.74 (s, 1H), 2.71 (d, J = 5.3 Hz, 1H), 2.60−2.53 (m, 1H), 2.29−2.22 (m, 1H), 2.26 (d, J = 5.3 Hz, 1H), 2.16 (d, J = 13.1 Hz, 1H), 2.02 (d, J = 13.1 Hz, 1H), 1.45 (m, 1H), 1.45 (m, 1H), 1.33 (d, J = 9.2 Hz, 1H), 1.24 (m, 16H), 1.23 (d, J = 9.2 Hz, 1H), 0.87 (m, 12H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 209.9, 177.0, 143.2, 138.0, 137.8, 52.0, 49.1, 43.6, 42.4, 41.6, 36.4, 32.0, 30.5, 30.1, 30.0, 29.76, 29.75, 29.67, 29.58, 29.49, 29.47, 27.5, 22.8, 14.3. IR (film, ν) 2952, 1732, 1701, 1437, 1152 cm^{-1}.

PK6. PKR of 4-methoxybut-2-yn-1-yl acetate **6** was performed according to the general procedure with 3 h heating, affording **PK6** in 34% combined yield (27 mg, 0.103 mmol). Isomers ***α*-*exo*-PK6** and ***β*-*exo*-PK6** were formed in 1.1/1 ratio (*α* and *β* referring to acetate substituent position). (3-(Methoxymethyl)-1-oxo-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-2-yl)methyl acetate ***α*-*exo*-PK6 OAc *α*, OMe *β*** (major). HRMS (ESI-TOF) *m*/*z* calcd for $[C_{15}H_{19}O_4]^+$ 263.1278, found 263.1285 (Δ = 2.85 ppm). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.31 (dd, J = 5.5, 3.0 Hz, 1H), 6.23 (dd, J = 5.5, 2.9 Hz, 1H), 4.79−4.71 (m, 2H), 4.46 (d, J = 15.0 Hz, 1H), 4.36 (d, J = 15.0 Hz, 1H), 3.42 (s, 3H), 2.96 (br. s,, 1H), 2.89 (m, 2H), 2.35 (m, 1H), 2.04 (s, 3H), 1.41 (d, J = 9.4 Hz, 1H), 1.19 (d, J = 9.4 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.4, 175.0, 170.7, 139.0, 138.4, 137.4, 69.4, 59.28, 55.1, 52.3, 49.1, 43.8, 42.8, 41.4, 20.8. (2-(Methoxymethyl)-1-oxo-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-3-yl)methyl acetate ***β*-*exo*-PK6 OMe *α*, OAc *β*** (minor). HRMS (ESI-TOF) *m*/*z* calcd for $[C_{15}H_{18}O_4Na]^+$ 285.1097, found 285.1086 (Δ = 3.92 ppm). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.29 (dd, J = 5.5, 3.2 Hz, 1H), 6.23 (dd, J = 5.5, 2.9 Hz, 1H), 5.20 (d, J = 15.4 Hz, 1H), 5.02 (d, J = 15.4 Hz, 1H), 4.12 (s, 2H), 3.33 (s, 3H), 2.96 (br. s, 1H), 2.86 (br. s, 1H), 2.82 (m, 1H), 2.36 (m, 1H), 2.15 (s, 3H), 1.43 (d, J = 9.5 Hz, 1H), 1.24 (d, J = 9.5 Hz, 1H). ^{13}C NMR (75

MHz, CDCl$_3$) δ 207.5, 170.8, 170.5, 141.9, 138.2, 137.5, 63.6, 60.8, 58.8, 52.5, 48.9, 43.7, 42.6, 41.4, 20.7.

2-Undecyne 7. *n*-Butyl lithium, 1.74 M (1.2 mL, 2.1 mmol, 1.2 equiv) was added dropwise at 0 °C on diisopropylamine (0.151 mL, 2.08 mmol, 1.25 equiv) in dry THF (4.5 mL) and the reaction was stirred for 40 min. 1-decyne (0.3 mL, 1.66 mmol, 1 equiv) in dry THF (3 mL) was slowly added, and the mixture was stirred for 2 h at 0 °C. Iodomethane (0.156 mL, 2.5 mmol, 2.5 equiv) was added and the reaction was allowed to warm to rt and stirred for 4 h. The reaction was quenched with water, extracted with hexane, washed with brine, dried with MgSO$_4$ and concentrated under reduced pressure. Purification over SiO$_2$ with hexane afforded undecy-2-yne (**7**) as a colorless oil (64%, 160 mg, 1.05 mmol). NMR data matched well with the reported one.[39] ^{1}H NMR (400 MHz, CDCl$_3$) δ 2.14−2.08 (m, 2H), 1.78 (t, J = 3.0 Hz, 3H), 1.51−1.43 (m, 2H), 1.39−1.27 (m, 10H), 0.88 (t, J = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 79.43, 75.28, 31.85, 29.21, 29.15, 29.1, 28.9, 22.7, 18.7, 14.1, 3.5. IR (film, ν) 2952, 1732, 1701, 1437, 1152 cm^{-1}.

PK7. Complexation of **7** was performed according to the general method in 1.05 mmol scale, 1equiv of dicobaltoctacarbonyl and 2 h stirring affording **C7** in quantitative yield (476 mg) as a red oil. **PK7** was prepared from previously formed complex according to the general procedure in 1.03 mmol scale with overnight heating at 70 °C affording **PK7** in 86% combined yield (240 mg, 0.88 mmol) as a yellow oil. Isomers ***α-exo*-PK7** and ***α-endo*-PK7** and were formed in 17/1 ratio. 3-Methyl-2-octyl-3a,4,7,7a-tetrahydro-1*H*-4,7-methanoinden-1-one ***α-exo*-PK7**. HRMS (ESI-TOF) *m*/*z* calcd for [C$_{19}$H$_{29}$O]$^+$ 273.2213, found 273.2215 (Δ = 0.76 ppm). ^{1}H NMR (400 MHz, CDCl$_3$) δ 6.25 (dd, J = 3.0 Hz, 1H), 6.21 (dd, J = 2.9 Hz, 1H), 2.90 (s, 1H), 2.74 (s, 1H), 2.56 (d, J = 5.2 Hz, 1H), 2.25 (d, J = 5.2 Hz, 1H), 2.22−2.07 (m, 2H), 2.02 (s, 3H), 1.33 (d, J = 8.91 Hz, 1H), 1.37−1.22 (m, 12H), 1.15 (d, J = 9.2 Hz, 1H), 0.86 (t, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 209.3, 170.8, 145.2, 138.0, 137.6, 52.3, 52.0, 43.3, 42.1, 41.3, 31.9, 29.7, 29.4, 29.3, 28.5, 23.2, 22.7, 15.7, 14.1. IR (film, ν) 2926, 2847, 1706, 1627, 1446, 1355, 700 cm^{-1}.

Figure 4, Entry j. PKR of 1-methoxyhex-2-yne **1b** with norbornene (1.5 mmol, 141 mg, 5 equiv) was performed according to the general procedure with 3h heating affording the cyclopentenone in 61% combined yield (42 mg, 0.181 mmol) as an oil. Isomers *α-exo* and *β-exo* were formed in 1/4.7 ratio. 3-(Methoxymethyl)-2-propyl-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methanoinden-1-one *β-exo* (major) HRMS (ESI-TOF) *m*/*z* calcd for [C$_{15}$H$_{22}$O$_2$Na]$^+$ 257.1512, found 257.1509 (Δ = 1.04 ppm). ^{1}H NMR (500 MHz, CDCl$_3$) δ 4.31 (d, J = 13.8 Hz, 1H), 4.25 (d, J = 13.8 Hz, 1H), 3.39 (s, 3H), 2.68 (d, J = 5.2 Hz, 1H), 2.39 (m, 1H), 2.32 (m, 1H), 2.25−2.09 (m, 3H), 1.71−1.63 (m, 1H), 1.61−1.53 (m, 1H), 1.46−1.24 (m, 4H), 0.94 (s, 2H), 0.88 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 210.7, 168.8, 144.6, 69.1, 58.9, 53.4, 48.9, 39.1, 37.4, 31.2, 29.2, 28.6, 25.1, 21.9, 14.0. 2-(Methoxymethyl)-3-propyl-3a,4,5,6,7,7a-hexahydro-1*H*-4,7-methanoinden-1-one *α-exo* (minor) HRMS (ESI-TOF) *m*/*z* calcd for [C$_{15}$H$_{22}$O$_2$Na]$^+$ 257.1512, found 257.1507 (Δ = 2.14 ppm). ^{1}H NMR (500 MHz, CDCl$_3$) δ 4.06 (m, 2H), 3.32 (s, 3H), 2.70−2.60 (m, 2H), 2.43 (m, 1H), 2.40−2.32 (m, 1H), 2.28 (m, 1H), 2.20 (d, J = 5.3 Hz, 1H), 1.75−1.63 (m, 2H), 1.63−1.49 (m, 2H), 1.36−1.27 (m, 2H), 1.03−0.92 (m, 5H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 209.7, 180.4, 139.8, 62.9, 58.5, 53.7, 50.7, 38.8, 37.4, 31.8, 31.4, 29.2, 28.6, 21.2, 14.3.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C spectra of all new compounds, HMBC spectra of PK products, and full computational details (coordinates and energies). This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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