A Tandem Iridium-Catalyzed “Chain-Walking”/Cope Rearrangement Sequence

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Supporting Information

ABSTRACT: An iridium-catalyzed tandem olefin migration/Cope rearrangement of alkenyl ω-ene cyclopropanes is reported. By this means, a variety of complex annulenes are obtained as single diastereomers starting from cyclopropyl ester derived from simple 1,ω-dienes and alkenyldiazo compounds. Long-range olefin migration over up to 10 positions could be realized and coupled with an efficient Cope rearrangement to yield valuable scaffolds. Various functional groups are well-tolerated, giving rise to densely functionalized products. Furthermore, the present methodology could be successfully extended to yield bicyclic cycloheptenones starting from readily available alkenyl cyclopropanols via a Kulinkovich reaction.

KEYWORDS: chain-walking, remote functionalization, iridium catalysis, Cope rearrangement, alkenyl cyclopropane
access to stereodefined dialkenylcyclopropanes en route to diversely functionalized cycloheptadiene structures (Scheme 3e).

With the goal of developing an experimentally user-friendly protocol, we decided to prepare the catalyst in situ by simply mixing commercially available \([\text{Ir} (\text{COD}) \text{Cl}]_2, \text{PCy}_3\) and \(\text{NaBArF}_4\) without recurring to the semihydrogenation reaction of the supporting COD-ligand prior to the catalytic reaction.59 Under these conditions, the obtained \([\text{Ir} (\text{PCy}_3)_3\]BArF4 complex exerted excellent activity even at room temperature. At the outset, we turned our attention toward styrenyl ω-ene cyclopropanes, easily accessible through the rhodium-catalyzed decomposition of the respective alkenyl diazoester with various \(1,\omega\)-dienes.60,61 To our delight, olefin isomerizations over up to four positions with subsequent Cope rearrangement occurred rapidly upon heating to 85 °C with only 1.0 mol % of Ir-dimer complex (Table 1, entries 1−3). Extending the chain-length required slightly increased catalyst loading (2.5 mol % of Ir-dimer complex) but still furnished the products in moderate to good yields with isomerizations over up to 10 positions (Table 1, entries 4,5).62 It should be noted that separation of the product from small amounts of remaining internal olefin isomers proved to be challenging and was only achieved after reduction of the ester functionality (Table 1, entry 5). The relative stereochemistry of 2a was determined by comparison with reported data.61

It should be highlighted that the present methodology allowed for the synthesis of enantioenriched cycloheptadiene 2a in only two catalytic steps utilizing only minute amounts of catalyst (Scheme 4).

Having established a protocol for the long-range olefin isomerization/Cope rearrangement for styrenylcyclopropanes, we examined the scope of various olefinic counterparts with \(1,6\)-hexadiene- and \(1,7\)-octadiene-derived alkenylcyclopropanes (Table 2). To this end, a variety of alkenyldiazo derivatives were synthesized following established procedures and subsequently transformed in the rhodium-catalyzed cyclopropanation reaction (see Supporting Information). Various annulenes were obtained in moderate to good yields with excellent diasterocontrol. Simple cyclopentyl- and cyclohexyl-annelated compounds (Table 2, entries 1−4) could be accessed in good yield with as low as 1.0 mol % of catalyst loading. However, incorporating Lewis-basic groups (i.e., ketones or ethers) necessitated the utilization of slightly increased catalyst loading (2.5 mol % of Ir-dimer complex, Table 2, entries 5−11). Nevertheless, the corresponding annulenes were obtained in good yields including benzofuranes (Table 2, entries 7, 8) or cyclic ketones (Table 2, entries 5, 6, and 9). As reported by Davies, upon Cope rearrangement of benzofuran 2l and 2m, the deearomatized products were obtained.63,64 Even quaternary carbon stereocenters could be efficiently installed, giving rise to densely functionalized...
scaffolds (Table 2, entries 5, 6). Interestingly, without the quaternary carbon center, isomerization of the newly formed olefin into conjugation with the ketone was observed (Table 2, entry 9). It should be noted that in this case only the syn-isomer underwent the crucial Cope rearrangement. The corresponding anti-isomer merely furnished a mixture of internal olefins, advocating the existence of an iridium-catalyzed olefin equilibration. Finally, challenging sulfonyl-piperidine derived annulenes were obtained in good yield (Table 2, entries 10, 11) after prolonged heating (48 h).

In order to expand the utility of the present methodology, we then turned our attention toward the synthesis of bicyclic cyclopentones. As the required starting materials are not accessible by the above-presented sequence, a complementary approach was envisioned. The utilization of a Kulinkovich reaction would provide a straightforward access to simple alkenyl cyclopropanols which can subsequently be transformed into valuable ketoannulenes. Utilizing a modified Kulinkovich procedure, the thus-obtained cyclopropanols were exposed to the
Facile cyclic enol ether formation was observed in the presence of only 1.0 mol % of Ir-dimer complex and subsequent mild desilylation delivered the products in good yield (Table 3, entries 1−4). Annulated cycloheptenones comprising cyclohexane and cyclopentane cores with different tether lengths were again well-tolerated. All bicyclic cycloheptenones (2q−2t) were again formed as a single diastereomer, advocating the perfect control over the double-bond geometry. Interestingly, during the deprotection step, we could observe in two cases (Table 3, entries 1 and 3) partial isomerization of the olefin into the corresponding α,β-unsaturated ketones. The sensitive α′-position at the ring-junction remained unchanged under these conditions.

Herein we report a facile protocol for the synthesis of valuable annulenes starting from simple olefinic precursors obtained in one or two catalytic steps. In the presence of a highly reactive,
Table 3. Iridium-Catalyzed Olefin Migration/Cope Rearrangement of Alkenyl Cyclopropan Ethers\(^{a}\)

| No | Alkenyl-CP | Product | Yield\(^{a}\)  |
|----|-----------------|---------|-------------------------------|
| 1  | 1q \(n=1\) | 2q \(n=1\) | 61\% (20:1) |
| 2  | 1r \(n=2\) | 2r \(n=2\) | 63\% (20:1) |
| 3  | 1s \(n=3\) | 2s \(n=3\) | 41\% (20:1) |
| 4  | 1t \(n=3\) | 2t \(n=3\) | 77\% (20:1) |

\(^{a}\)Reaction conditions: \(\omega\)-Ene alkenylcyclopropan derivative (0.5 mmol), [Ir(COD)Cl] \(_2\) (1.0 mol %), PCy\(_3\) (6.0 mol %), NaBArF\(_4\) (2.5 mol %), 1,2-DCE (1.0 mL), 85 °C. \(^{b}\)Yield of isolated product after purification by flash chromatography. \(^{c}\)Inseparable mixture of olefin isomers.

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