Reactivity of the TMM Entity in the Cyclopentene Series − Observation of a Reversed Regioselectivity in Palladium-Catalyzed [3+2] Cycloadditions

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Dedicated to Professor Jean Normant on the occasion of his 65th brithday

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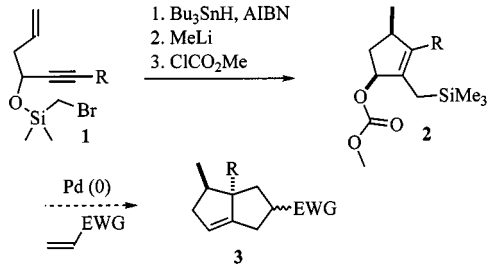
The first examples of palladium(0)-catalyzed [3+2] cycloadditions involving an electron-deficient olefin and a TMM entity incorporated into a five-membered ring are described. In the case of *gem*-dimethyl precursor **7b**, the regioselectivity is completely reversed, compared to that traditionally observed in these reactions (products **12M** and **12m**). Additional results and an interpretation of these findings are given.

Introduction

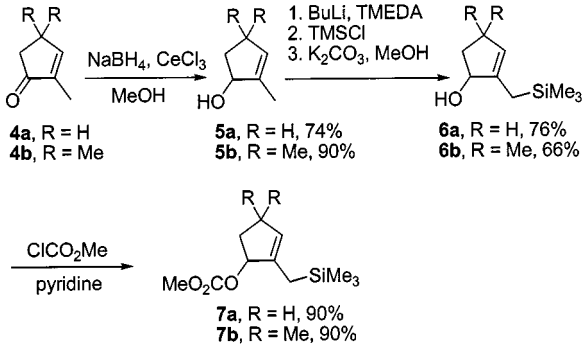
The pioneering works by Noyori[1] and Binger[2] on the trimethylenemethane (TMM) [3+2] cycloaddition have paved the way for one of the most straightforward methods for the synthesis of 5-membered rings.[3−5] Several variations of this reaction, whether metal-free,[6] or palladium-catalyzed with 2-(trimethylsilylmethyl)-2-propenyl acetates or carbonates (Trost, see refs.[7,8]), have been devised. In the latter case, in its inter- or intramolecular versions, extensive studies by Trost on the chemo-, regio- and stereoselectivities of this process have translated into numerous applications in total synthesis.[9−11] Rather surprisingly, much less is known about the palladium-catalyzed version of this reaction when the TMM reacting unit is incorporated into a ring.[12,13] To the best of our knowledge, only a few examples, in the cyclohexene series, have been reported by Trost.[14−16] With a view to exploiting cyclopentenes **2**, directly available from the radical cyclization of bromomethyldimethylsilylpropargyl ethers **1**,[17−19] as TMM precursors in [3+2] reactions, we have undertaken a study of the reactivity of the TMM entity when incorporated into a 5-membered ring (Scheme 1). This chemistry might allow the synthesis of various synthetically useful polyquinane structures such as **3**, as well as extending knowledge of the intrinsic reactivity of TMM species.



Scheme 1. General strategy

Results and Discussion

In order to test this strategy, we focused on simple precursors **7a** and **7b**, prepared in gram quantities according to the procedure in Scheme 2. Ketones **4a** and **4b**[20,21] were reduced under Luche's conditions.[22,23] The obtained alcohols **5a** and **5b** were metalated with *n*BuLi in the presence of TMEDA.[24,25] The resulting dianion was quenched with trimethylsilyl chloride. After a selective *O*-desilylation, *C*-silylated alcohols **6a** and **6b** were obtained in good overall yields. Because of their higher reactivity in these reactions,[14] carbonates **7a** and **7b** were chosen instead of the corresponding acetates, and were synthesized uneventfully.



Scheme 2. Synthesis of precursors

The [3+2] cycloadditions were conducted in the presence of an excess of olefin (2−3 equiv.) and at high concentration (0.80−1.20 M in acceptor) (Scheme 3). No reaction occurred at room temp., and the reaction mixtures had to be refluxed (THF or toluene) for a long period of time

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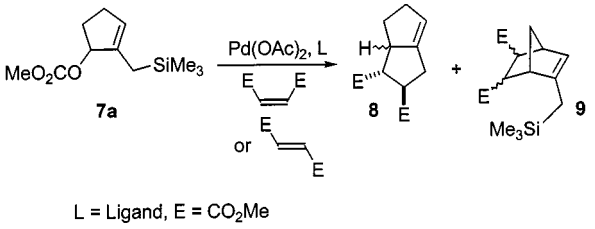
(20−72 h) to ensure a fair degree of conversion. We initially focused on acceptors which negated the issue of regioselectivity. Treatment with both dimethyl maleate and dimethyl fumarate (Table 1, Entries 1, 2) gave the same mixture of [3+2] cycloadducts **8**, in modest yield and with almost no diastereoselectivity. This reaction appeared slow, since no complete consumption of **7a** was obtained. When the reaction was performed in the presence of maleate, a significant quantity of fumarate was recovered, suggesting that isomerization of the acceptor takes place under the reaction conditions.[26] However, if this isomerization is itself not rapid enough, then the [3+2] process must be unstereospecific with the maleate: a traditional issue in these reactions.[27−29] Either way, one can safely assign a *trans* relative stereochemistry between the two methyl ester groups, the diastereomeric mixture originating from the relative stereochemistry between the methine at the ring junction and the adjacent methyl ester group. In both cases, a common side product, bicyclo[2.2.1]heptene **9**, was isolated as an equimolar ratio mixture of diastereomers. A competitive [4+2] pathway, involving a silylated diene and fumarate, takes place under these reaction conditions. Initially, we thought the formation of the reacting diene might result from a β-elimination of the π-allyl complex: a process well known and described in (π-allyl)palladium complex chemistry.[30−34]



Scheme 3. General reaction

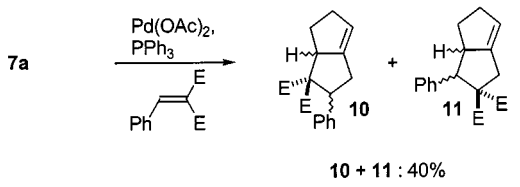
Table 1. Palladium-catalyzed cycloadditions of carbonate **7a**

Entry	Acceptor E = CO_2Me	Catalyst, mol%	Reactions Conditions	[3+2] Adducts, Yield %	[4+2] Adducts, Yield %
1	3 equiv.	$Pd(OAc)_2$, 5 $P(O\text{-}i\text{-}Pr)_3$, 20	THF, Δ, 48 h	**8**, 35 (42)[a] 2 dias. 1.5 : 1	**9**, 19 2 dias. 1.1 : 1
2	3 equiv.	"	THF, Δ, 72 h	**8**, 33 (40)[a] 2 dias. 1.3 : 1	**9**, 39 2 dias. 1.3 : 1
3	3 equiv.	"	Tol., Δ, 15 h		**9**, 63 2 dias. 1.1 : 1
4	3 equiv.	$Pd(OAc)_2$, 5	THF, Δ, 22 h		**9**, 65 2 dias. 1.2 : 1
5	3 equiv.	$Pd(OAc)_2$, 5 PPh_3, 25	THF, Δ, 20 h	**8**, 26 (31)[a] 2 dias. 1.3 : 1	-
6	2 equiv.	"	THF, Δ, 19 h	**10** + **11**, 40[b]	-

[a] Yield based on recovery of the starting carbonate **7a**. − [b] Four regioisomeric and diastereomeric adducts **10** and **11** were isolated in a 0.1:1:1:0.5 ratio; see Scheme 4 and discussion for the assignment.

However, we found that this Diels−Alder reaction could also operate in the presence of a catalytic (5 mol-%) quantity of $Pd(OAc)_2$ (65% of **9**, see Entry 4 of Table 1). Electrophilic activation of the carbonate functionality by the Pd^{II} salt would trigger the elimination of this group and the formation of the conjugated diene. Interestingly, the [4+2] cycloaddition became the major pathway in refluxing toluene (Table 1, Entry 3). Under these higher temperature conditions the catalytic system was more sensitive to oxidation. Traces of Pd^{II} salts sufficed to catalyze the Diels−Alder reaction. On adopting a more stable catalytic system, using triphenylphosphane as a ligand, no more compound **9** was observed; however, the conversion was now sluggish (Table 1, Entry 5).

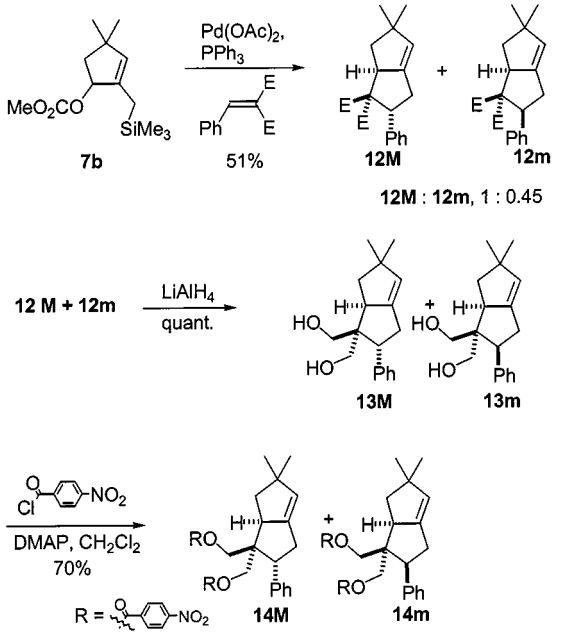
In order to shorten reaction times, we next concentrated on the use of dimethyl benzylidenemalonate as an acceptor; this has been reported to be highly reactive toward (TMM)palladium complexes.[16] Indeed, in this case (Table 1, Entry 6), no starting material was recovered, and no [4+2] adduct was isolated. However, as in most of these reactions, we noticed by TLC the formation of a nonpolar compound, the ^1H NMR spectrum of which revealed a complex mixture of silylated cyclopentadiene and cyclopentene structures: probably oligomers originating from **7a**.[35] This competitive degradation of the starting material at least partially explains why we obtained the mixture of [3+2] products (**10** + **11**) only in 40% yield (Scheme 4). Four products were actually generated in this reaction, in a ratio of 0.1:1:1:0.5, with the two major ones being distinct regioisomers. This was emphasized by examination of the ^1H NMR coupling patterns of the benzylic protons: a triplet $\delta = 4.21$ (t, $J = 7.7$ Hz) for **10** and a doublet $\delta = 3.99$ (d, $J = 7.6$ Hz) for **11**. Because of signal overlap in the ^1H NMR spectrum in $CDCl_3$ and C_6D_6, the regiochemistry of the two remaining minor products could not be determined. Nevertheless, these data indicate an intriguingly low level of regioselectivity in regard to all the literature concerning these reactions.[36,37] Indeed, experimental results,[38] supported by theoretical studies,[39] have shown that it is the most stable η^3-zwitterion, bearing the carbanion charge on the most substituted carbon atom, that is involved in the initial Michael addition of the [3+2] process.



Scheme 4. [3+2] Cycloaddition with benzylidenemalonate

This finding prompted us to examine the behavior of *gem*-dimethyl carbonate **7b**. We anticipated that the *gem*-dimethyl moiety would impose some additional steric constraints and thus force the regioselectivity in this system. Moreover, this precursor might be a valuable building block for the total synthesis of various natural sesquiterpenes, notably linear triquinanes.

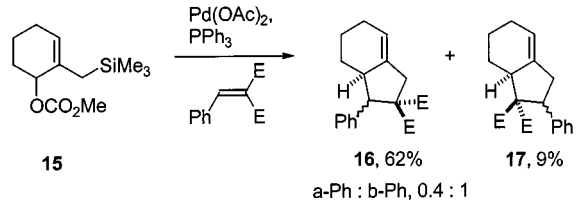
The [3+2] cycloaddition of **7b** gave two compounds **12M** and **12m** (see Scheme 5), in 51% yield and in the ratio of 1:0.45.[40] To assign the structure of these compounds fully, this mixture was reduced to diols **13M** and **13m**, which were then fully characterized as nitroaryl esters **14M** and **14m.** Suitable crystals for a X-ray diffraction analysis were obtained, enabling a structure determination to be performed for **14M**.[41] Comprehensive NMR spectroscopic data, including HMBC and HMQC, revealed that **14m** is in a diastereomeric relationship with **14M** and not a regioisomeric one. In this reaction, the regioselectivity is almost completely reversed (> 95%) relative to that generally observed.



Scheme 5. Regioselective [3+2] cycloaddition

Puzzled by this finding, we submitted 6-membered ring carbonate **15** to identical reaction conditions, and obtained the mixture of regioisomers **16** and **17** in 71% overall yield (Scheme 6). Analysis of the ^{1}H NMR spectrum showed two characteristic doublets for major regioisomer **16**: at δ = 4.06 (d, J = 7.6 Hz) and δ = 3.51 (d, J = 12.2 Hz) in a 1:0.4 ratio. In contrast, minor regioisomer **17** displayed a benzylic doublet-doublet: δ = 3.94 (dd, J = 8.6, 4.6 Hz). The relative stereochemistry of the major diastereomer of **16** was determined by NOE measurements and corresponds to a *cis* relationship between the benzylic proton and the ring junction proton. It clearly fits with that observed by Trost, and originates from an approach of the olefin with no prior coordination to the metal center, with minimization of steric interactions.[14] Thus, in terms of regioselectivity and stereoselectivity, the overall outcome of this reaction is more consistent with Trost's previous findings, in which only traces of the alternate regioisomer were tentatively assigned.

The [3+2] cycloaddition of **7a** with the benzylidenemalonate shows that two reacting TMM species (**III** and **IV**) are involved, since an almost equimolar mixture of regioisomers **10** and **11** was obtained. This would suggest that the isomerization of **III** to **IV**, a priori the most stable form[39] of the (TMM)palladium complex, is slow compared to that of **I** to **II** (Figure 1). This isomerization process, which presumably occurs via (σ-allyl)palladium intermediates, is certainly thwarted by the greater number of eclipsing interactions in the five-membered ring over that in the cyclohexene series. In the case of **7b**, the presence of the *gem*-dimethyl group results in an additional constraint. No equilibration to the traditionally involved TMM intermediate bearing the carbanion on the more substituted carbon atom seems to occur. The initially formed TMM species **V** is frozen, as demonstrated by the almost exclusive formation of products **12m** and **12M**. Moreover, after the initial Michael addition of the methylene carbanion, the subsequent 5-*endo*-*trig* cyclization of the resulting malonate anion takes place only on the sterically less hindered site, the other one being neopentylic. The diastereoselectivity can be rationalized by a more favorable approach of the benzylidenemalonate, keeping the phenyl ring away from a protruding methyl group, followed by a 5-*endo*-*trig* cyclization *anti* to the palladium complex (Scheme 7).



Scheme 6. [3+2] Cycloaddition in the cyclohexene series

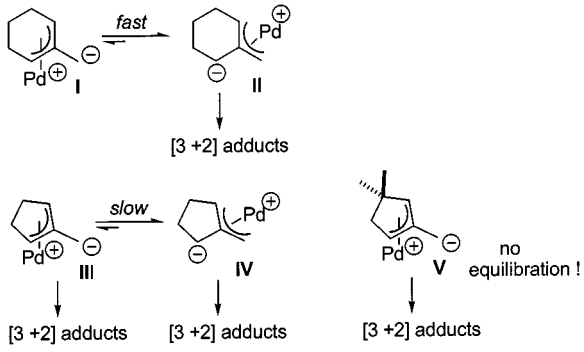
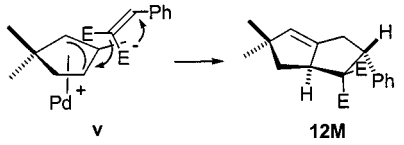


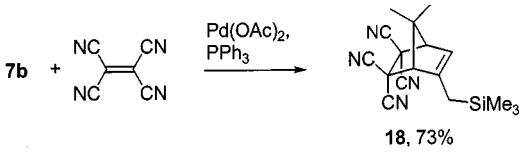
Figure 1. Equilibration of the TMM species



Scheme 7. Diastereoselective approach

In order to promote the equilibration of the TMM intermediates, we examined the [3+2] cycloaddition of **7b** with less reactive acceptors such as cyclopentenone. This reaction sequence could also give rise to interesting linear triquinane frameworks. Unfortunately, a complex mixture resulted from this reaction and no [3+2] adduct was isol-

ated. It appears that the fate of the cycloaddition depends very much on the nature of the acceptor. With tetracyanoethylene, an outstanding dienophile,[42] only the bicyclic compound **18**, resulting from a [4+2] cycloaddition, was formed (Scheme 8).



Scheme 8. [4+2] Cycloaddition with tetracyanoethylene

Conclusion

In summary, this work constitutes the first examples of palladium-catalyzed [3+2] cycloadditions involving an electron-deficient olefin and a TMM entity incorporated into a five-membered ring. Despite side reactions (oligomerizations and [4+2] cycloadditions) originating from the formation of a highly reactive diene, various versatile diquinane structures are now available on the basis of this methodology. Interestingly, we have shown that the competitive [4+2] pathway can be triggered by a catalytic amount of palladium diacetate. An intriguing feature of the [3+2] cycloaddition is its low or even reversed regioselectivity compared to that traditionally observed. A partial (or complete in the case of **7b**) freezing of the initially formed (TMM)palladium complex takes place because of an excessively large number of eclipsing interactions needing to be overcome for the isomerization process. We are now focusing on the intramolecular version of this process, which should reduce some of the side reactions by faster trapping of the TMM intermediate, and open a route to relevant angularly fused tricyclic derivatives.

Experimental Section

General: Reactions were performed in flame-dried glassware under a positive pressure of argon.

Solvents: Diethyl ether and THF were distilled from sodium/benzophenone ketyl. Toluene, dichloromethane, and pyridine were distilled from calcium hydride. Chromatography solvents: EE, PE, and EtOAc refer to diethyl ether, petroleum ether, and ethyl acetate, respectively.

Reagents: Dimethyl benzylidenemalonate,[43] cyclopentenone **4b**,[20] cyclopentenols **5a**[23] and **5b**,[44] and carbonate **15**[15] have been described previously. Unless otherwise specified, materials were used without purification.

Equipment: ^{1}H NMR and ^{13}C NMR spectra were recorded with 200 MHz Bruker AC 200, 300 MHz Bruker AM 300, and 400 MHz Bruker ARX 400 spectrometers. Chemical shifts are reported in ppm, referenced to the residual proton resonances of the solvents. − Infrared (IR) spectra were recorded with a Perkin−Elmer 1420 spectrometer. − Mass spectra (MS) were obtained with a GC-MS Hewlett-Packard HP 5971 apparatus. − Elemental analyses were performed at the Service Régional de Microanalyse de l'Université P. et M. Curie. − Thin layer chromatography (TLC) was performed on Merck F 254 silica gel 60. Merck Geduran SI (40−63 μm) silica gel was used for column flash chromatography, using Still's method.[45]

Structure Assignments: When dealing with mixtures of compounds, the major component (regio- or stereoisomer) is generally indicated by underlining the resonance.

2-(Trimethylsilylmethyl)cyclopent-2-en-1-ol (6a): To a solution of **5a** (1.47 g, 15 mmol) and TMEDA (9 mL, 60 mmol) in diethyl ether (20 mL) at 0 °C was slowly added a 2.18 M *n*BuLi solution in hexanes (20.6 mL, 45 mmol). The reaction mixture was stirred at 20 °C for 18 h, followed by addition of TMSCl (7.6 mL, 60 mmol). After stirring for 10 min at 20 °C, the reaction mixture was diluted with diethyl ether. The ethereal solution was washed with a saturated NH_4Cl solution and brine, dried with $MgSO_4$ and concentrated in vacuo. The crude residue was treated with K_2CO_3 (4.20 g, 30 mmol) in MeOH (20 mL) for 1 h at 20 °C. After this period, methanol was removed in vacuo and the residue was dissolved in diethyl ether. The ethereal solution was washed with a saturated NH_4Cl solution and brine, dried with $MgSO_4$, and concentrated in vacuo. Purification of the crude reaction mixture by flash chromatography (PE/EE, 7:3) afforded pure **6a** (1.94 g, 76%) as a colorless syrup. − IR (neat): $\tilde{\nu}$ = 3340, 3010, 2950, 1640, 1320, 1150, 1040 cm^{-1}. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.37 (s, 1 H), 4.53 (m, 1 H), 2.42 (m, 1 H), 2.30−2.23 (m, 2 H), 1.72−1.61 (m, 4 H), 0.04 (s, 9 H). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 143.6, 125.3, 80.3, 34.2, 29.7, 17.8, 1.14 (3 C). − $C_9H_{18}OSi$ (170.32): C 63.55, H 10.66; found C 63.49, H 10.69.

Methyl 2-(Trimethylsilylmethyl)cyclopent-2-enyl Carbonate (7a): To an ice-cold solution of **6a** (5.10 g, 30 mmol) and pyridine (8.5 mL) in CH_2Cl_2 (100 mL), was slowly added methyl chloroformate (4.6 mL, 60 mmol). The solution was stirred at 0 °C for 10 min, and diluted with CH_2Cl_2. The CH_2Cl_2 solution was washed with brine, dried with $MgSO_4$ and concentrated to dryness. Purification of the crude reaction mixture by flash chromatography (PE/EE, 7:3) afforded 6.15 g (90%) of **7a** as a pale yellow oil. − IR (neat): $\tilde{\nu}$ = 3020, 2950, 1740, 1650, 1250, 1020 cm^{-1}. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.45 (m, 1 H), 5.32 (s, 1 H), 3.79 (s, 3 H), 2.43 (m, 1 H), 2.37−2.29 (m, 2 H), 1.86 (m, 1 H), 1.63−1.57 (m, 2 H), 0.04 (s, 9 H). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 157.4, 151.2, 130.1, 88.2, 55.9, 32.3, 31.5, 19.3, 0.0 (3 C). − $C_{11}H_{20}O_3Si$ (228.36): C 57.93, H 8.77; found C 57.98, H 8.84.

4,4-Dimethyl-2-(trimethylsilylmethyl)cyclopent-2-en-1-ol (6b): From **5b** (2 g, 16 mmol), same procedure as for **6a**. Purification of the crude reaction mixture by flash chromatography (PE/EE, 7:3) afforded 2.09 g (66%) of **6b** as a colorless syrup. − IR (neat): $\tilde{\nu}$ = 3350, 2960, 1660, 1470, 1250, 1050 cm^{-1}. − ^{1}H NMR (C_6D_6, 400 MHz): δ = 5.17 (s, 1 H), 4.50 (dd, *J* = 7.5, 4.5 Hz, 1 H), 1.96 (dd, *J* = 12.5, 7.5 Hz, 1 H), 1.63 (m_{AB}, 2 H), 1.50 (dd, *J* = 12.5, 4.5 Hz, 1 H), 1.17 (s, 3 H), 1.05 (s, 3 H), 0.24 (s, 9 H). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 141.2, 136.5, 75.0, 46.7, 34.9, 31.8 (2 C), 18.3, 1.1 (3 C). − $C_{11}H_{22}OSi$ (198.38): C 66.60, H 11.18; found C 66.70, H 11.29.

Methyl 4,4-Dimethyl-2-(trimethylsilylmethyl)cyclopent-2-enyl Carbonate (7b): From **6b** (1.00 g, 5.0 mmol), same procedure as for **7a**. The residue was distilled under reduced pressure (150 °C, 10 Torr) to give 1.15 g (90%) of **7b** as a yellowish oil. − IR (neat): $\tilde{\nu}$ = 3060, 2860, 1750, 1650, 1270 cm^{-1}. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.43 (dd, *J* = 8.0, 4.2 Hz, 1 H), 5.29 (s, 1 H), 3.76 (s, 3 H), 2.15 (dd, *J* = 12.9, 8.0 Hz, 1 H), 1.63 (dd, *J* = 12.9, 4.2 Hz, 1 H), 1.46

(s, 2 H), 1.10 (s, 3 H), 1.04 (s, 3 H,), 0.01 (s, 9 H). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 155.9, 139.4, 136.2, 86.3, 54.5, 46.3, 43.3, 29.7, 29.5, 17.4, −1.4. − $C_{13}H_{24}O_3Si$: C 60.89, H 9.43; found C 61.09, H 9.41.

General Procedure A (GP-A) for Pd-Catalyzed Cycloadditions of 7a: The reaction was carried out under Ar in a flame-dried, 25-mL, round-bottomed flask. At 20 °C, $Pd(OAc)_2$ (11 mg, 0.05 equiv.) and either PPh_3 (66 mg, 0.25 equiv.) or $P(OiPr)_3$ (50 μL, 0.20 equiv.) were dissolved in THF (1.0 mL). After stirring this yellow solution for 10 min, a solution of silyl derivative **7a** (228 mg, 1 mmol) and of the alkene (2 or 3 equiv.) in THF (1.5 mL) was cannulated into the catalyst solution. (Caution: Dimethyl fumarate is only mildly soluble in THF. It should be loaded as a solid directly into the reaction vessel under argon.) The reaction mixture was refluxed overnight (see Table 1) and then concentrated to dryness. The crude residue was purified by flash chromatography on silica gel.

Dimethyl 1,2,3,5,6,6a-Hexahydropentalene-1,2-dicarboxylates 8M and 8m: According to GP-A in the presence of 3 equiv. of dimethyl maleate (432 mg). Chromatography (PE/EE , 95:05) afforded, in order of elution, 39 mg (17%) of **7a**, 56 mg (19%) of the mixture **9**, and 78 mg (35%) of the mixture of **8M** and **8m** in a 1.5:1 ratio. − IR (neat): $\tilde{\nu}$ = 2940, 2840, 1730, 1430, 1170 cm^{-1}. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.51 (m, 1 H), 5.43 (m, 1 H), 3.80−3.67 (m, 4 × OCH_3), 3.65 (m, 1 H), 3.48 (m, 1 H), 3.40 (m, 1 H), 3.30 (dd, *J* = 11.2, 6.6 Hz, 1 H), 3.13 (m, 1 H), 2.80−2.30 (4 H + 5 H), 2.15 (dt, *J* = 13.5, 6.6 Hz, 1 H), 2.05 (m, 1 H), 1.45 (m, 1 H), 1.25 (m, 1 H). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 174.8 (2C), 174.5, 173.9, 148.9, 148.4, 121.0, 120.6, 56.4, 52.7, 52.1(3 C), 51.7(2 C), 49.9, 48.9, 47.2, 37.5, 36.0, 30.8, 29.9, 29.3, 27.3. − CIMS (NH_3); *m*/*z* = 225 (100) $[MH]^+$, 242 (95) $[MNH_4]^+$. − $C_{12}H_{16}O_4$ (224.25): C 64.27, H 7.19; found C 64.47, H 7.51.

Dimethyl 5-Trimethylsilylmethylbicyclo[2.2.1]hept-5-ene-2,3-dicarboxylates 9M and 9m: IR (neat): $\tilde{\nu}$ = 3020, 2920, 1720, 1620, 1420, 1240, 1170, 1060 cm^{-1}. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.57 (s, 1 H), 5.38 (s, 1 H), 3.70−3.62 (s, 4 × OCH_3), 3.38 (t, *J* = 4.6 Hz, 1 H), 3.36 (t, *J* = 4.6 Hz, 1 H), 3.15 (m, 1 H), 3.00 (m, 2 H), 2.82 (dd, *J* = 4.6, 1.5 Hz, 1 H), 2.79 (m, 1 H), *2.75* (dd, *J* = 4.7, 2.3 Hz, 1 H), 1.70−1.55 (m, 3 H + 4 H), 1.33 (dd, *J* = 13.7, 1.5 Hz, 1 H). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 174.9 (2 C), 173.6, 173.2, 149.6, 146.6, 126.5, 124.4, 52.9, 51.8−51.4 (4 × OMe), 51.3, 49.7, 48.0, 47.6, 47.7, 47.3, 46.3, 46.2, 20.8, 20.0, −0.1 (2 × 3 C). − $C_{15}H_{24}O_4Si$ (296.43): C 60.77, H 8.16; found C 60.71, H 8.13.

1,1-Dimethyl 2-Phenyl-1,2,3,5,6,6a-hexahydropentalene-1,1-dicarboxylates 10 and 2,2-Dimethyl 3-Phenyl-1,2,3,3a,4,5-hexahydropentalene-2,2-dicarboxylates 11: According to GP-A in the presence of 440 mg (2 equiv.) of dimethyl benzylidenemalonate. Chromatography (PE/EE, 90:10) afforded 120 mg (40%) of a mixture of **10** and **11** as a colorless syrup. − IR (neat): $\tilde{\nu}$ = 3020, 2860, 1730, 1605, 1500, 1455, 1430 cm^{-1}. − ^{1}H NMR ($CDCl_3$, 400 MHz, 2 major dias.): δ = 7.40−7.00 (m, 5 H), 5.50 (s, 1 H), 5.43 (s, 1 H), 4.21 (t, *J* = 7.7 Hz, 1 H), 4.07 (m, 1 H), 3.99 (d, *J* = 7.6 Hz, 1 H), 3.75 (m, 1 H), 3.78 (s, 3 H), 3.74 (s, 3 H), 3.43 (m, 1 H), 3.22 (s, 3 H), 3.21 (s, 3 H), 2.85−2.75 (m, 1 H + 1 H), 2.70−2.50 (m, 2 H, 1 H), 2.50−2.40 (m, 1 H + 1 H), 2.17 (quint, *J* = 6.1 Hz, 1 H), 1.72 (dt, *J* = 12.2, 7.6 Hz, 1 H), 1.35 (m, 1 H), 1.10 (dq, *J* = 12.2, 9.6 Hz, 1 H). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 172.9, 171.4, 170.9, 169.9, 149.1, 148.7, 141.1, 138.6, 132.7, 129.7, 128.5, 128.1, 128.0, 127.9, 120.7, 120.0, 70.7, 66.7, 56.6, 54.6, 53.1, 52.7, 53.0, 52.1 (2 C), 52.0, 51.8, 37.8, 35.9, 31.8 (2C), 30.5, 25.9. − $C_{18}H_{20}O_4$ (300.35): C 71.98, H 6.71; found C 71.83, H 6.90.

General Procedure B (GP-B) for Pd-Catalyzed Cycloadditions of 7b and 15: The reaction was carried out under Ar in a flame-dried, 25-mL, round-bottomed flask. At 20 °C, $Pd(OAc)_2$ (0.09 equiv.) and PPh_3 (0.62 equiv.) were dissolved in THF (1.5 mL). After stirring this yellow solution for 10 min, a solution of silyl derivative (1 equiv.) and acceptor (4 equiv.) in THF (2 mL) was cannulated into the catalyst solution. The mixture was refluxed overnight and then concentrated to dryness. The crude residue was purified by flash chromatography.

Dimethyl 5,5-Dimethyl-2-phenyl-1,2,3,5,6,6a-hexahydropentalene-1,1-dicarboxylates 12M and 12m: According to GP-B from **7b** (410 mg, 1.6 mmol) in the presence of 1.40 g of dimethyl benzylidenemalonate. Chromatography (PE/EE, 9:1) afforded 268 mg of pure **12** (51%) as a mixture of diastereomers (**12M:12m**, 2:1). − IR (neat): $\tilde{\nu}$ = 3040, 2940, 1730, 1455, 1270, 1205, 1160 cm^{-1}. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.43−7.15 (m, 5 H), 5.51 (br. s, 1 H), 5.30 (br. s, 1 H), 4.19 (m, 1 H), 4.17 (t, *J* = 7.8 Hz, 1 H), 3.98 (dd, *J* = 10.7, 7.1 Hz, 1 H), 3.73 (m, 1 H), 3.72 (s, 3H + 3 H), 3.26 (s, 3 H), 3.19 (s, 3 H), 2.76−2.63 (m, 2 H + 2 H), 2.60 (m, 1 H), 2.08 (dd, *J* = 14.2, 3.5 Hz, 1 H), 1.92 (dd, *J* = 12.0, 7.2 Hz, 1 H), 1.27 (s, 3 H), 1.25 (m, 1 H), 1.17 (s, 3 H), 1.11 (s, 3 H), 0.89 (s, 3 H). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 172.1, 172.0, 171.3, 171.0, 147.7, 146.0, 141.3, 141.1, 131.7, 129.0 (2 C), 128.9 (2 C), 128.4 (2 C), 128.3 (2 C), 127.5, 127.4, 119.0, 67.2, 64.4, 54.9, 54.5, 53.7, 53.4, 52.4 (1 C + 1 C), 52.3, 52.1 (1 C + 1 C), 49.8, 48.5, 45.6, 32.2, 31.9, 30.2, 28.0, 27.2, 22.6; − $C_{20}H_{24}O_4$ (328.40): C 73.15, H 7.37; found C 73.28, H 7.24.

5,5-Dimethyl-1,2,3,5,6,6a-hexahydropentalene-1,1-bis(ylmethyl) Bis(4-nitrobenzoates) 14M and 14m: LAH (102 mg, 2.70 mmol) was added in small portions to a stirred solution of **12M** and **12m** (220 mg, 0.74 mmol) in THF (10 mL). After 1 h at 20 °C, AcOEt and 1 M H_2SO_4 were added to decompose excess hydride. Diethyl ether was then added and the organic layer was washed with saturated, aqueous NaCl, and dried with $MgSO_4$. After concentration in vacuo, the crude product was purified by rapid filtration through silica gel (flash chromatography) to afford 199 mg (99%) of diols **13M** and **13m**. This mixture of diols was then diluted in 10 mL of CH_2Cl_2 and *p*-nitrobenzoyl chloride (406 mg, 3 equiv.) was added. This was followed by the addition of a solution of DMAP (267 mg, 3 equiv.) in dichloromethane (4 mL) at 0 °C. The reaction mixture was stirred 0 °C for 1.5 h, and at 20 °C for 1.5 h. After this period, the mixture was diluted with dichloromethane (15 mL), washed with 1 M HCl and water, dried with $MgSO_4$, and concentrated to dryness. The residue was purified by flash chromatography (PE/EE, 75:25) to give 290 mg (70%) of **14M** and **14m**. Compound **14M** crystallized from a hexane/EtOAc mixture. The mother liquor was used to isolate **14m** after recrystallization.

Compound 14M: White needles; m.p. 168−171 °C. − IR (KBr): $\tilde{\nu}$ = 3000, 2860, 1725, 1610, 1530, 1270. − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.34 (d, *J* = 9.1 Hz, 2 H), 8.26 (d, *J* = 9.1 Hz, 2 H), 8.21 (d, *J* = 9.1 Hz, 2 H), 7.97 (d, *J* = 9.1 Hz, 2 H), 7.35−7.20 (m, 5 H), 5.37 (d, *J* = 1.5 Hz, 1 H), 4.58 (d, *J* = 11.2 Hz, 1 H), 4.49 (d, *J* = 11.2 Hz, 1 H), 4.25 (d, *J* = 11.2 Hz, 1 H), 3.96 (d, *J* = 11.2 Hz, 1 H), 3.59 (dd, *J* = 8.0, 5.8 Hz, 1 H), 3.50 (dd, *J* = 10.7, 7.1 Hz, 1 H), 2.83 (ddd, *J* = 17.1, 8.0, 1.5 Hz, 1 H), 2.68 (dd, *J* = 17.1, 5.8 Hz, 1 H), 1.81 (dd, *J* = 12.2, 7.1 Hz, 1 H), 1.67 (dd, *J* = 12.2, 10.7 Hz, 1 H), 1.19 (s, 6 H, 2 × CH_3). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 164.7, 164.2, 150.8, 150.6, 146.1, 141.4, 135.3 (2 C), 131.4, 130.8 (2 C), 130.6 (2 C), 128.7 (2 C), 128.4 (2 C), 127.2, 123.8 (2 C), 123.6 (2 C), 68.0, 66.2, 55.5, 53.7, 50.8, 47.6, 42.1, 31.4, 29.8, 27.0. − $C_{32}H_{30}N_2O_8$ (570.59): C 67.36, H 5.30; found C 67.39, H 5.35.

Compound 14m: White crystals; m.p. 164−166 °C. − IR (KBr): $\tilde{\nu}$ = 3010, 2880, 1725, 1610, 1560, 1350, 1270 cm^{-1}. − ^{1}H NMR

($CDCl_3$, 500 MHz): δ = 8.24 (2d, *J* = 9.1 Hz, 2 × 2 H), 7.97 (2d, *J* = 9.1 Hz, 2 × 2 H), 7.30−7.23 (m, 5 H, Ph), 5.55 (s, 1 H), 4.97 (d, *J* = 11.2 Hz, 1 H), 4.65 (d, *J* = 11.2 Hz, 1 H), 4.41 (d, *J* = 11.2 Hz, 1 H), 4.18 (d, *J* = 11.2 Hz, 1 H), 3.55 (t, *J* = 7.6 Hz, 1 H), 3.06 (m, 1 H), 2.83−2.70 (m, 2 H), 2.65 (m, 1 H), 2.23 (dd, *J* = 15.3, 2.0 Hz, 1 H), 1.27 (s, 3 H), 1.23 (s, 3 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 164.7 (2C), 150.9, 147.6, 140.7, 135.3, 130.9, 130.8, 128.8, 127.4, 123.8, 119.5, 66.3, 66.9, 65.9, 55.5, 54.4, 50.0, 47.3, 31.3, 29.9, 25.8. − $C_{32}H_{30}N_2O_8$ (570.59): C 67.36, H 5.30; found C 67.26, H 5.25.

Dimethyl 3-Phenyl-2,3,3a,4,5,6-hexahydroindene-2,2-dicarboxylates 16M and 16m and Dimethyl 2-Phenyl-2,3,5,6,7,7a-hexahydroindene-1,1-dicarboxylates 17: According to GP-B from **15** (387 mg, 1.60 mmol), in the presence of 1.40 g of dimethyl benzylidenemalonate. Chromatography (PE/EA, 90:10) afforded 357 mg (71%) of a mixture of **16M**, **16m**, and **17** in a 7:1 ratio and as a clear oil. − IR (neat): $\tilde{\nu}$ = 3030, 2970, 1730, 1610, 1430, 1250 cm^{-1}. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.40−7.15 (m, 4 H), 7.12 (m, 1 H), 5.66 (m, 1 H), 5.53 (m, 1 H), 4.06 (d, *J* = 7.6 Hz, 1 H), 3.78 (s, 3 H), 3.74 (s, 3 H), 3.61 (dt, *J* = 18.4, 2.3, 1 H), 3.51 (d, *J* = 12.2 Hz, 1 H), 3.45 (m, 1 H), 3.25 (s, 3 H), 3.24 (s, 3 H), 2.93 (m, 1 H), 2.86 (d, *J* = 18.4 Hz, 1 H), 2.78 (m, 1 H), 2.58 (dt, *J* = 16.5, 1.5 Hz, 1 H), 1.95 (m, 2 H), 1.81 (m, 2 H), 1.70−1.30 (m, 3 H + 2 H), 0.98−0.65 (m, 1 H + 2 H). − **17:** (characteristic signals): δ = 5.61 (m, 1 H), 3.94 (dd, *J* = 8.6, 4.6 Hz, 1 H), 3.75 (s, 3 H), 3.45 (m, 1 H), 3.31 (s, 3 H), 2.93 (m, 1 H), 2.61 (m, 1 H). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 172.7, 172.5, 171.4, 171.1, 170.0, 169.7, 140.1, 139.8, 138.9, 138.5, 138.4, 129.2, 128.5, 128.4, 127.8, 128.4, 127.8, 127.7, 126.9, 126.8, 126.6, 119.8, 119.4, 119.1, 64.1, 63.5, 56.9, 54.7, 52.8, 52.4, 51.9, 51.8, 51.5, 49.0, 44.9, 44.8, 42.8, 39.7, 37.6, 37.3, 29.6, 27.3, 25.7, 25.0, 24.8, 24.7, 22.6, 23.3, 21.7. − $C_{19}H_{22}O_4$ (314.37): C 72.59, H 7.05; found C 72.54, H 6.75.

7,7-Dimethyl-5-trimethylsilylmethylbicyclo[2.2.1]hept-5-ene-2,2,3,3-tetracarbonitrile (18): According to GP-B from **7b** (128 mg, 0.5 mmol), in the presence of 272 mg of tetracyanoethylene. Chromatography (PE/EE, 7:3) afforded 112 mg (73%) of white solid **18**. − M.p. 124−125 °C. − IR (KBr): $\tilde{\nu}$ = 3040, 2960, 2225, 1610, 1470, 1300, 1260 cm^{-1}. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.98 (q, *J* = 1.5 Hz, 1 H), 3.48 (dd, *J* = 3.0, 2.2 Hz, 1 H), 3.27 (s, 1 H), 2.08 (dd, *J* = 14.2, 1.5 Hz, 1 H), 1.84 (dd, *J* = 14.2, 1.5 Hz), 1.60 (s, 3 H), 1.23 (s, 3 H), 0.18 (s, 9 H). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 151.8, 127.5, 112.0 (2 C), 111.9 (2 C), 67.5, 63.1, 59.6, 46.6, 45.7, 24.0, 23.6, 23.5, −0.9. − $C_{17}H_{20}N_4Si$ (308.45): C 66.20, H 6.54, N 18.16; found C 66.08, H 6.65, N 18.01.

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