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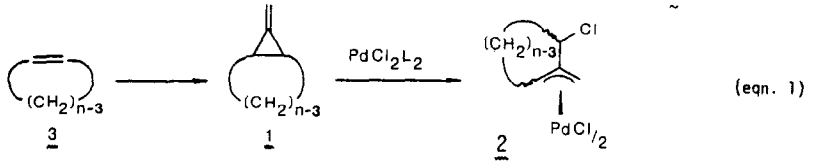
REACTIVITY OF (3-CHLORO-2-METHYLENECYCLOALKYL)PALLADIUM CHLORIDE DIMERS: PD-ALLYL CLEAVAGE, SYNTHESIS OF (±)-13-METHYLTRIDECANOLIDE.

William A. Donaldson* and Barbara S. Taylor

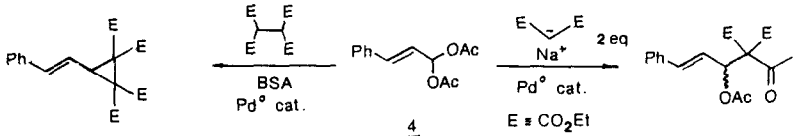
Department of Chemistry, Marquette University, Milwaukee, Wisconsin 53233

SUMMARY: The reactions of the title compounds under cleavage conditions affords the corresponding cycloalkenes as the major product. This methodology was used in the synthesis of 13-methyltridecanolide from cyclododecene.

The chloropalladation of Ω-methylenebicyclo[n.1.0]alkanes (1) quantitatively affords crystalline, air-stable (3-chloro-2-methylenecycloalkyl)palladium chloride dimers (2, eqn. 1).[1,2] Compounds 1 may be prepared from the corresponding cyclic olefins 3 in good yield, based on consumed starting material.[1,3] Because of the great potential for the elaboration of the π-allyl moiety, we have investigated the reactivity of compounds 2, as the final step in a methodology for overall ring homologation--functionalization of olefins 3. Recent conflicting accounts of the reactivity of 1,1-allylic diacetates (4) as potentially "1,1-doubly activated" π-allyls,[4,5] have prompted us to report our initial results on the cleavage of compounds 2.



3 1 2 (eqn. 1)

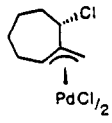
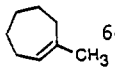
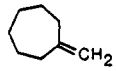
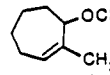
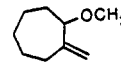
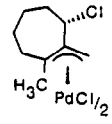
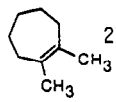
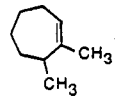
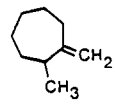
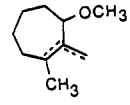
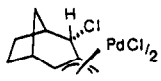
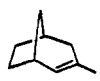
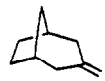
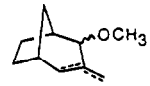
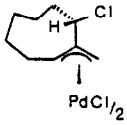
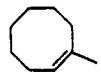
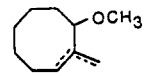
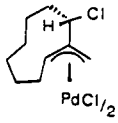
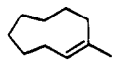
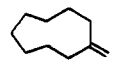
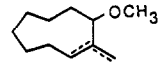


(Ref. 4) 4 (Ref. 5)

Perhaps the simplest reaction of π-allyl complexes which liberates the organic ligand is cleavage in methanolic potassium hydroxide,[6] however the mechanism for Pd-allyl cleavage remains a matter of some controversy.[7] We herein report on the π-allyl cleavage of a series of compounds (2).

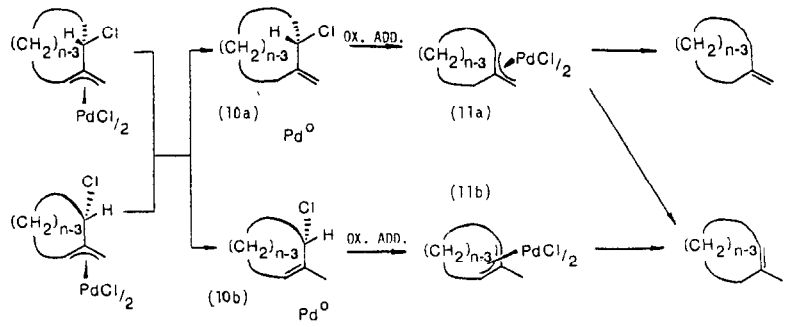
The preparation of compounds 5 - 9 is reported elsewhere.[1,2] These compounds were treated with 1M methanolic KOH (1h at 23°C, Xh at 50°C) with the following work up: filtration of the Pd(0) biproduct (which should be recovered), dilution with H_2O, extraction of the cloudy aqueous solution (CH_2Cl_2 or $CHCl_3$) and removal of the solvent under reduced pressure. The results are recorded in Table I. Yields are generally good, however the anticipated α-methoxy olefin was obtained only as a minor product. The major product was the corresponding methylcycloalkene and its exocyclic isomer indicating not only cleavage of the Pd-allyl bond but reduction of the C3-Cl bond, as well.

TABLE I. Cleavage of (3-Chloro-2-methylenecycloalkyl)Palladium Chloride Dimers.

π-Allyl Complex	Reaction Conditions[a]	Products[b] [Reg. #] olefins	α-methoxy olefins	Combined Yield
5 	4h	 64%[c] [1453-25-4]  8%[c] [2505-03-5]	 24%[d]  4%	93%
6 	4h	 27%[e] [20053-89-8]  33%[e] [81505-07-9]  10%[f] [76802-29-4]	 30%	45%[g]
7 	4h	 66%[h] [4877-38-7]  33%[i] [4877-39-8]	 1%	91%
8 	4h	 98%[j] [15840-64-9]	 2%	43%[g]
9 	4h	 71%[k] [13151-62-7]  28%[l] [56133-38-1]	 1%	78%

[a] 1M KOH/MeOH, 1h @ RT, Xh @ 50°C. [b] As % of total yield based on ^{1}H NMR integration (± 4%). Olefins identified by comparison to literature spectral data. [c] Ref. 18. [d] Identified by comparison with sample prepared by independent synthesis. Ref. 19. [e] Ref. 20. [f] Identified by comparison with sample prepared by independent synthesis. Ref. 21. [g] Low yield may be due to volatility of products. [h] Ref. 22. [i] Ref. 23. [j] Ref. 24. [k] Ref. 25. [l] Ref. 26.

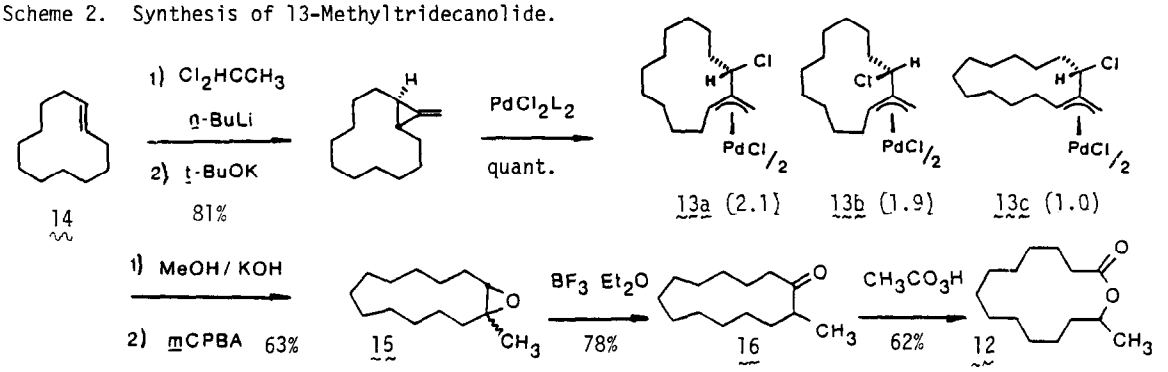
Scheme 1.



We propose that the major product is formed via cleavage of complex 2 to afford the allylic chlorides 10a and 10b and Pd(0)(Scheme 1).[8] Oxidative addition of the finely divided Pd(0) into the allylic chloride bond affords the new π-allyl complexes 11a and 11b. Subsequent cleavage of

the new complexes 11 under the reaction conditions would afford the major product.[9] The preparation of π-allyl complexes from the reaction of Pd(0) with allylic halides is well precedented.[10] *These results demonstrate that the (3-chloro-2-methylenecycloalkyl)palladium complexes (2) may react as "1,3 doubly activated" π-allyls under cleavage conditions.*

Scheme 2. Synthesis of 13-Methyltridecanolide.



The presence of the α-methoxy olefin as a minor product might arise from solvolysis of the allylic halides 10.[11] Alternatively, solvolysis of the C3 chloride in the precursor 2,[12] followed by cleavage of the resultant methoxy substituted π-allyl complex would also afford the α-methoxy olefin products. Experiments are in progress to examine the exact mechanistic details for the formation of all products.

Although the cleavage of compounds 2 would not constitute a good general route to the homologation of cycloalkenes 3, we have been able to apply this sequence to the synthesis of (±)-13-methyl-tridecanolide (12) (Scheme 2), the major macrolide constituent of *Galbanum* resin (0.03%).[13] The mixture of π-allyls 13a, 13b, and 13c(2.1 : 1.9 : 1.0) may be prepared from trans-cyclododecene (14) (81% yield, based on consumed 14).[1b] Cleavage of the mixture (1M KOH/MeOH, 50°C, 24h) followed by oxidation (mCPBA, CH_2Cl_2, 23°C, 24h) gave a mixture of diastereomeric epoxides (15) (63% yield).[14] Pinacol rearrangement of the mixture ($BF_3 \cdot Et_2O$, 23°C, 15 min)[15] afforded the known[13,16] 2-methylcyclotridecanone (16) (78% yield).[17] Bayer-Villager oxidation of 16 according to the literature procedure of Kaiser and Lamparsky (CH_3CO_3H, $BF_3 \cdot Et_2O$, $CHCH_3$, 23°C, 62% yield)[13] completed the total synthesis of (±)-13-methyltridecanolide.

We are currently investigating the reactivity of the unique "1,3 doubly activated" π-allyls (2) with one and two equivalents of carbon nucleophiles in the presence of phosphine ligands.

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8. The cleavage of alkyl substituted π-allyls is known to afford the corresponding olefins (Ref. 6)
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14. (15): bp 102°C, 0.30 mm Hg(Kugelrohr); IR (cm^{-1}, film) 2975 s, 2850 s, 1470 m, 1270 w, 920 m; 60 MHz ^1H NMR ($CDCl_3$) δ 2.8(m), 2.0(m), 1.3(br s), 1.28(s).
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17. (16): bp 104-110°C, 0.30mm Hg(Kugelrohr); IR(cm^{-1}, film)1710; 200 MHz ^1H NMR ($CDCl_3$)δ2.42 (ddd, J=4.0, 9.2, 16.4 Hz, 1H), 2.42(dq, J=3.2, 7.2 Hz, 1H, $CHCH_3$), 2.34(ddd, J=4.0, 7.2, 16.4 Hz, 1H), 1.8-1.1(m,20H), 1.04(d, J=7.2 Hz, 3H, CH_3); 15 MHz $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 215.52, 46.26, 40.21, 32.91, 26.62, 26.34, 26.13, 25.65, 25.58, 25.00, 24.39 22.68, 17.00, 14.04.
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