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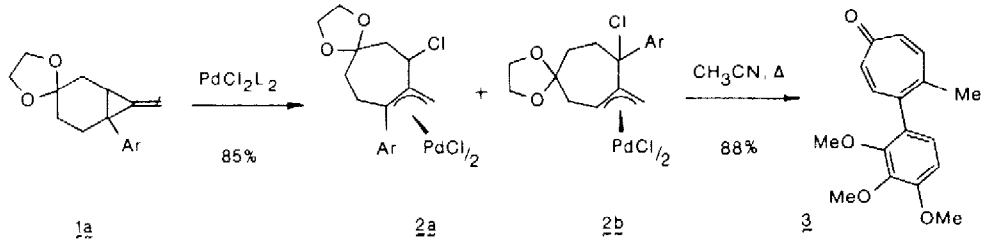
REACTIVITY OF (3-CHLORO-2-METHYLENECYCLOALKYL)PALLADIUM CHLORIDE DIMERS: PALLADIUM CATALYSED TROPONE FORMATION[1]

William A. Donaldson* and Daniel J. Stepuszek
Department of Chemistry, Marquette University, Milwaukee, WI 53233 USA

SUMMARY: The formation of 4-(2',3',4'-trimethoxyphenyl)-5-methyltropone from the palladium catalysed ring opening--oxidation of 7-methylenebicyclo[4.1.0]heptane is described.

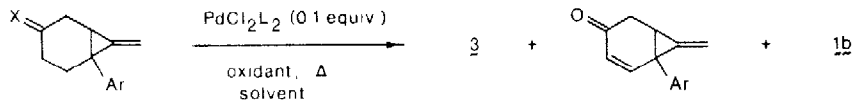
We have recently shown that the chloropalladation of **1a** affords a mixture of cycloheptyl π-allyl complexes **2a** and **2b**.[2a] Furthermore, this mixture can be utilized, in a stoichiometric fashion, for the preparation of tropones related to the antimitotic agent colchicine.[2] This letter reports on a novel palladium catalysed preparation of 4-(2',3',4'-trimethoxyphenyl)-5-methyltropone (**3**).

We have previously shown that the chloropalladation of 1-aryl-7-methylenebicyclo[4.1.0]heptanes (CH_2Cl_2, 23°C), which yields the isomeric (1-aryl)- and (3-aryl-3-chloro-2-methylenecycloheptyl)palladium chloride dimers, is a kinetically controlled reaction.[3] However, an equilibrium favoring the more thermodynamically stable isomer may be achieved in refluxing acetonitrile. Surprisingly, heating a mixture of **2a** and **2b** in acetonitrile at reflux resulted in the formation of a palladium mirror and the isolation of tropone **3**.[4] The formation of **3**, from either **2a** or **2b**, must involve (*i*) deketalization, (*ii*) dehydrochlorination, (*iii*) β-hydride elimination and (*iv*) isomerization of the exocyclic olefin to form the tropone ring. The exact order of these events is unknown.



1a 2a 2b 3

It should be noted that, in comparison to our previous synthesis of tropones from **2a/b**,[1a] the formation of **3** does not involve the use of any carbon nucleophile. Therefore the transformation of 7-methylenecyclo[4.1.0]heptane **1** into tropone **3** in the presence of a catalytic amount of palladium and a reoxidant should not be impeded by oxidative coupling of the nucleophile. The results of a study concerning the catalytic tropone formation appear in Table 1.



1a X = OCH_2CH_2O
1b, X = O

TABLE 1. CATALYTIC TROPONE FORMATION

Entry	subst.	oxidant	cat.	conditions	isolated yield 3	4	1b
1	**1a**	$CuCl_2$ (2 eq)	$PdCl_2L_2$ (0.1 eq)	CH_3CN/2-butanone (9:1), Δ, 24h	35	40	
2	"	"	"	C_3H_7CN/3-hexanone (9:1), 115°C, 24h	38	43	
3	**1b**	"	"	CH_3CN, Δ, 24h	56	39	
4	"	"	"	dioxane, Δ, 24h CH_3CN (10 eq)	65	19	
5	"	"	"	dioxane, Δ, 24h	72	24	
6	**4**	"	"	CH_3CN, Δ, 24h		92	
7	**1a**	"	none	CH_3CN/2-butanone (9:1), Δ, 24h		57	35
8	**1b**	"	none	CH_3CN, Δ, 24h		39	56
9	"	none	none	CH_3CN, Δ, 24h			96

A by-product is the α,β-unsaturated ketone **4**,[5] which can easily be separated from tropone **3**. It appears that **4** is formed in a competitive side reaction involving copper mediated oxidation of the ketal **1a** or the ketone **1b** (entries 7 and 8), and that it is not an intermediate in the formation of **3** (entry 6).[6] The best conditions for the preparation of **3** involve the use of **1b**[1a] and dioxane as solvent (entries 4 and 5).

ACKNOWLEDGMENTS: We thank the Donors of The Petroleum Research Fund, administered by the American Chemical Society, for financial support of this research. Acknowledgement is due to Johnson Matthey, Inc. for generous donations of palladium chloride and to the National Science Foundation (CHE-8905465) for partial funding of the purchase of the 300 MHz NMR spectrometer used in this research. High resolution mass spectral determinations were performed at the Midwest Center for Mass Spectrometry, an NSF Regional Instrumentation Center. W.A.D. thanks the Alexander von Humboldt Foundation for a Research Fellowship (1990-91) during which time this manuscript was prepared.

REFERENCES AND NOTES

1. For previous papers in this series see: (a) Donaldson, W.A.; Stepuszek, D.J. *Synthesis, J. Org. Chem.*, submitted for publication: (b) Donaldson, W.A.; Wang, J. *J. Organometal. Chem.* **1990**, *395*, 113; (c) Donaldson, W.A.; Stepuszek, D.J.; Gruetzmacher, J.A. *Tetrahedron* **1990**, *46*, 2273; (d) Donaldson, W.A.; Wang, J.; Cepa, V.G.; Suson, J.D. *J. Org. Chem.* **1989**, *54*, 6056; (e) Donaldson, W.A.; Grief, V.J. *Tetrahedron Lett.* **1986**, 2345; (f) Donaldson, W.A.; Taylor, B.S. *Tetrahedron Lett.* **1985**, 4163.
2. 2-Methoxy-5-(trimethoxyphenyl)tropone has shown potent antimitotic activity; Fitzgerald, T.J. *Biochem. Pharmacol.* **1976**, *25*, 1383.
3. (a) Donaldson, W.A.; North, J.T.; Gruetzmacher, J.A.; Finley, M.; Stepuszek, D.J. *Tetrahedron* **1990**, *46*, 2263.
4. **3**: 300 MHz ^1H NMR ($CDCl_3$) δ 7.17 (d, J=12.6, 1H), 7.08 (d, J=12.3, 1H), 6.98 (dd, J=12.3, 3.0, 1H), 6.88 (dd, J=12.6, 3.0, 1H), 6.78 (d, J=8.4, 1H), 6.72 (d, J=8.4, 1H), 3.90, 3.89, 3.72, 2.12 (4s, 12H); 75 MHz ^{13}C NMR ($CDCl_3$) δ 187.6, 154.4, 151.1, 144.3, 143.5, 143.1, 142.2, 142.1, 140.4, 138.4, 130.1, 124.3, 108.1, 61.8, 61.7, 56.7, 25.9; IR ($CHCl_3$) 1628, 1598; Anal. Calcd. for $C_{17}H_{18}O_4$: C, 71.31; H,6.34; Found C, 71.08; H, 6.49.
5. **4**: 300 MHz ^1H NMR ($CDCl_3$) δ 6.98 (d, J=10.3, 1H), 6.87 (d, J=8.2, 1H), 6.60 (d, J=8.2, 1H), 5.92 (d, J=10.3, 1H), 5.42 (s, 1H), 4.98 (s, 1H), 3.87, 3.81, 3.76 (3s, 9H), 2.31 (ddd, J=9.6, 4.6, 1.4, 1H), 1.99 (dd, J=9.6, 4.6, 1H), 1.49 (t, J=4.6, 1H); ^{13}C NMR ($CDCl_3$) δ 197.6, 154.3, 153.7, 145.6, 144.1, 138.1, 128.3, 125.4, 125.3, 122.3, 108.5, 61.4, 61.3, 56.3, 34.8, 32.3, 21.0; IR ($CHCl_3$) 1675, 1598; HRMS m/z 286.1207 [Calc. for $C_{17}H_{18}O_4$ m/z 286.1200].
6. A somewhat similar 7-methylenebicyclo[4.1.0]hept-4-en-3-one was found to isomerize to a 4-substituted tropone under highly basic conditions; Banwell, M.G.; Gravatt, L.G.; Rickard, C.E.F. *J. Chem. Soc., Chem. Comm.* **1985**, 514.

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