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PALLADIUM DICHLORIDE CATALYZED COPE REARRANGEMENTS OF FUNCTIONALIZED ACYCLIC 1,5-DIENES[1]

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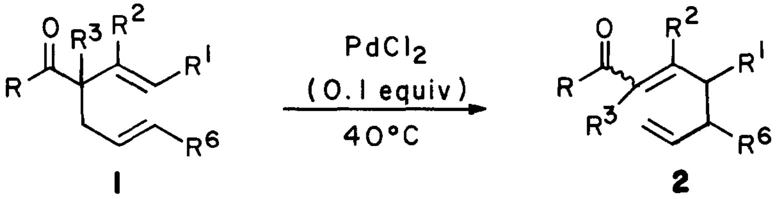
Summary: The Cope rearrangement of acyclic 1,5-dienes having an electron-withdrawing group at carbon-3 and an alkyl substituent at carbon-2 is effectively catalyzed by palladium dichloride. This reaction can be employed to achieve clean γ-allylation of vinyl esters and acids.

Palladium dichloride catalyzed Cope rearrangements of acyclic 1,5-dienes were first reported from these laboratories in 1980.[2] We have subsequently demonstrated[3] that the rearrangement of an enantiomerically pure substrate occurs via a chair topology with virtually complete transfer of chirality. The use of this method to catalyze oxy-Cope rearrangements has also been reported recently by other investigators.[4] One of the aims of our current studies in this area is to determine the functional group compatibility of this catalytic method. In this Letter, we report that acyclic 1,5-dienes containing an electron-withdrawing group at carbon-3, and an alkyl substituent at carbon-2, undergo palladium dichloride catalyzed Cope rearrangements in good yields at 40°C.[5] Importantly, these transformations (eq 1) are not complicated by competing carbon-carbon double migrations, which can plague related thermal Cope rearrangements.[6,7]

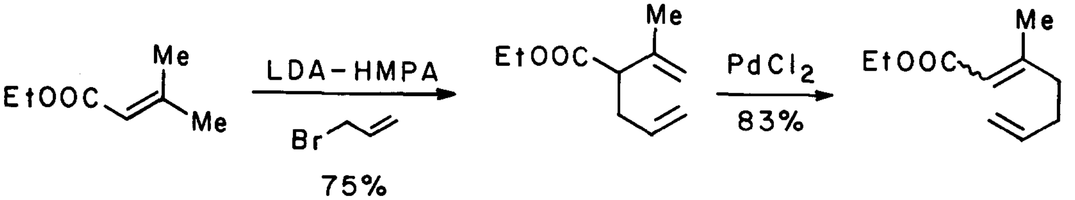


The results of our preliminary study are summarized in the Table. Catalytic rearrangements were conducted at 0.1 M in CH_2Cl_2 using 0.1 equiv of bis-

(acetonitrile)palladium dichloride. After the reaction was judged complete by GC analysis, silica gel (1 g/25 mg of catalyst) was added, the concentrated residue was layered on top of a silica gel chromatography column, and products[8] were eluted with mixtures of hexane and ethyl acetate. The rearrangement of 3 (R=COOEt) could be successfully conducted in THF or toluene, although the rate was somewhat slower[2] than in CH_2Cl_2. Diene products were typically characterized[8] by their diagnostic[9] high field ^1H NMR spectra, and in the case of 9 by preparation[10] from 4-methyl-6-hexen-3-one. The reported E/Z ratios do not reflect kinetic stereoselectivities, since pure samples of Z-4(R=COOEt) and E-4(R=COOEt) underwent significant[11] equilibration when treated at 40°C for 3 h with 0.1 equiv of $PdCl_2(MeCN)_2$.

This catalyzed reorganization proceeds with ester, ketone, carboxylic acid, and nitrile substituents, although the rearrangement of the nitrile substrate was less clean. The failure of the rearrangement with a tertiary amide substituent may in part reflect binding of the catalyst by the amide group, since the rearrangement of 3(R=COOEt) was <u>ca.</u> 10 times slower in the presence of 1.0 equiv of N,N-dimethylformamide. The advantages of the palladium dichloride catalyzed method are nicely illustrated by the high yielding rearrangements of 5 and 7. Conia has reported[6] thermal Cope rearrangements of these dienes at 220-240°C, and ene cyclizations (Conia reaction) of the product diene mixtures at 300°C. A major complication[6] of the thermal Cope rearrangements of 5 and 7 is the formation of major[12] amounts of the β,γ-unsaturated isomers of 6 and 8.[13]

Many of the dienes employed in this study were prepared by α-alkylation[14] of the corresponding α,β-unsaturated starting material. Thus, α-allylation followed by palladium dichloride catalyzed Cope rearrangement provides a two-step procedure for clean γ-allylation[15] of vinyl esters and acids. This sequence is illustrated for an ester substrate in eq. 1.



(1)

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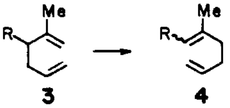
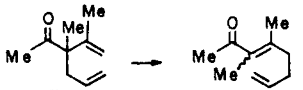
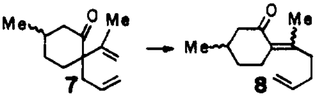
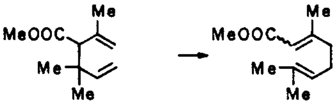
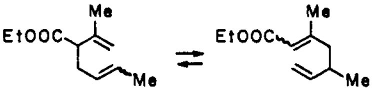
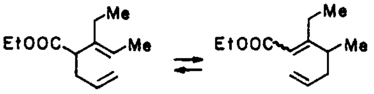
TABLE: PALLADIUM DICHLORIDE CATALYZED COPE REARRANGEMENTS

Reaction		Conditions Time	Yield[a]	Product Ratios		
				I	E-2	Z-2
 3 → 4	R = COOEt	5h	83	–	65	35
	R = COMe	5.5h	94	1	68	31
	R = CN	36h[b]	(77%)[c]	–	75	25
	R = COOH	24h	64	–	65	35
	R = CON	36h	no reaction			
 5 → 6		2.5h	77	–	50	50
 7 → 8		4h	81	–	50	50
		5h	90	–	24	76
		4h	80[d]	25	54	21
 9		12h	76[d]	19	66[e]	15[e]

[a] Isolated yield of the mixture of stereoisomers 2 (and 1 if the rearrangement was reversible). Other compounds were present to the extent of <5% (capillary GC analysis), unless otherwise noted. [b] 0.3 Equiv of $PdCl_2(MeCN)_2$ was employed. [c] A 91% weight recovery of Cope product, which was contaminated with 15% of uncharacterized byproducts. [d] The ratio of starting material to Cope products was unchanged upon resubmission of the product mixture. [e] Tentative stereoisomer assignments.

References and Notes

1. Catalyzed Sigmatropic Rearrangements. 8. For part 7, see: Overman, L.E.; Renaldo, A.F. Tetrahedron Lett. 1983, in press.

2. Overman, L.E.; Knoll, F.M. J. Am. Chem. Soc. 1980, 102, 865-867.

3. Overman, L.E.; Jacobsen, E.J. J. Am. Chem. Soc. 1982, 104, 7225-7231.

4. Bluthe, N.; Malacria, M.; Gore, J. Tetrahedron Lett. 1983, 24, 1157-1160.

5. Acyclic 1,5-dienes containing electron-withdrawing groups at carbon-3 and alkyl substituents at carbon-5 do not undergo catalyzed Cope rearrangements under these conditions, see reference 1.

6. Rhoades, S.J.; Rawling, S. Org. Reactions, 1975, 22, 1-107.

7. Cf. Conia, J.-M.; LePerchec, P. Bull. Soc. Chim. Fr. 1966, 273-277; 278-281

8. New compounds showed IR, 250 MHz ^{1}H NMR and mass spectra consistent with their assigned structures. Stereoisomeric products were typically separated by preparative GC and their stereostructures followed from diagnostic[9] chemical shift differences of the β-substituents.

9. Cf. Jackman, L.M.; Sternhell, S. "Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry"; Pergamon: Oxford, 1969, pp 222-225.

10. Shimoji, K.; Taguchi, H.; Oshima, K.; Yamamoto, H.; Nozaki, H. J. Am. Chem. Soc. 1974, 96, 1620-1621.

11. Approximately 35% equilibration, assuming that the equilibrium ratio is 1:1.

12. The deconjugated isomer of 6 comprises 28% and 65% of the Cope product mixture at 220°C and 240°C, respectively, while the deconjugated isomer of 8 is the major Cope product at 220°C.[7]

13. Deconjugated isomers were present to the extent of <1% in the catalyzed rearrangements of 5 and 7.

14. Herrmann, J.L.; Kieczykowski, G.R.; Schlessinger, R.H. Tetrahedron Lett. 1973, 2433-2436.

15. For recent examples and leading references, see, inter alia, Majewski, M.; Mpango, G.B.; Thomas, M.T.; Wu, A.; Snieckus, V. J. Org. Chem. 1981, 46, 2029-2045. Savu, P.M.; Katzenellenbogen, J.A. J. Org. Chem. 1981, 46, 239-250. Fleming, I.; Goldhill, J.; Paterson, I. Tetrahedron Lett. 1979, 3207-3210. Kende, A.S.; Constantinides, D.; Lee, S.J.; Liebskind, L. Ibid. 1975, 405-408.

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