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3-METHYLENETETRAHYDROFURANS AND 3-METHYLENEPYRROLIDINES BY ADDITION OF 2-BROMOZINCMETHYL-2-PROPENYL ETHERS TO ALDEHYDES, KETONES AND IMINES FOLLOWED BY Pd(0)-CATALYZED CYCLIZATION

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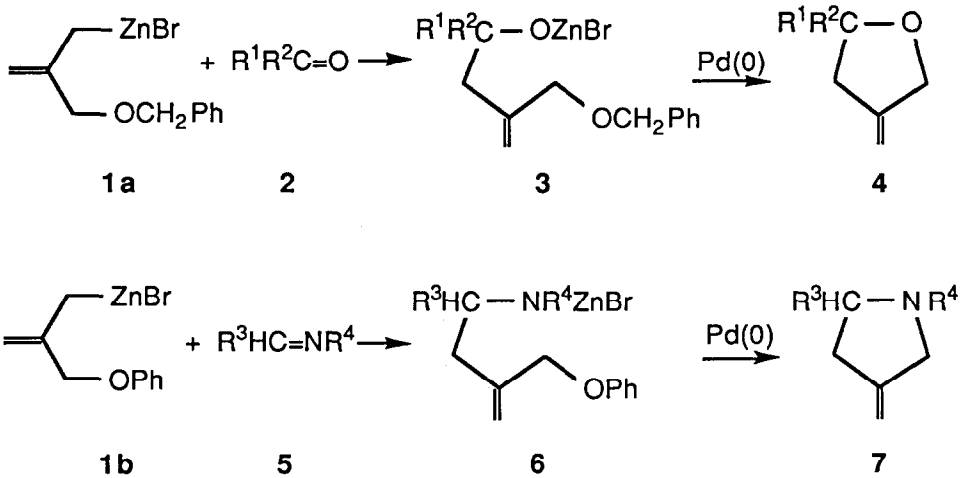
Summary : Reaction of 2-(benzyloxymethyl)- and 2-(phenoxymethyl)allylzinc bromides **1a** and **1b** with aldehydes, ketones and imines afforded the addition products **3** and **6**, which underwent Pd(0)-catalyzed cyclization to the tetrahydrofurans **4** and pyrrolidines **7**.

Our recent one-pot synthesis of 4-methylenecyclopentenes[1] starts with the regiospecific allylzincation of 1-silylalkynes by 2-bromozincmethyl-2-propenyl ethers **1a,b**. Subsequent addition of 10 mol% of $Pd(PPh_3)_4$ to the reaction mixture and heating causes the products to cyclize by elimination of BrZnOR (R = CH_2Ph, Ph). In an analogous way, certain ω-(3-methylenecyclopentyl)alkanols could be prepared.[2] The current interest in the synthesis of 3-methylenetetrahydrofurans and 3-methylenepyrrolidines by [3+2] cycloaddition[3] and radical cyclization[4] prompted us to explore the feasibility of our tandem addition-cyclization method for the construction of these versatile heterocycles from **1a,b** and aldehydes, ketones (**2**), and imines (**5**), respectively (see Scheme).



Scheme

Adding 2 mmol of the substrate **2** or **5** dropwise to 2.4 mmol of **1a,b** (0.25 M solution in THF, 0°C) and stirring overnight at room temperature resulted in the formation of the addition products **3** or **6**[5,6] in excellent yields. Addition of 5-10 mol% $Pd(PPh_3)_4$, heating the reaction mixture for 16 - 24 h (aldehydes, ketones) or 3 - 6 h (imines) at 65°C and subsequent aqueous work-up afforded the desired heterocyclic compounds **4** or **7**.[6]

Table. Reactions of **1a,b** with aldehydes, ketones **2** (R^1, R^2) and imines **5** (R^3, R^4) followed by Pd(0)-catalyzed cyclization (see Scheme).

Entry	R^1	R^2	Yield of **3** (%)[a]	Yield of **4** (%)[a,b]
1	Ph	H	95	82
2	cyclopentyl	H	92	80
3	Ph	CH_3	100	83
4	cyclohexanone		100	96
5	2-cyclohexenone		98 [c]	53
6	$C(CH_3)$=CHPh	CH_3	- [c,d,e]	76
	R^3	R^4	Yield of **6** (%)[a]	Yield of **7** (%)[a,b]
7	Ph	CH_3	90	78
8	$CH(CH_3)_2$	$(CH_2)_3CH_3$	91	58

[a] GLC yields. [b] Overall yields. [c] 1,2-addition only. [d] The addition reaction was completed by refluxing the reaction mixture for 3.5 h. [e] The addition product decomposed upon GLC.

As shown by the results collected in the Table, our procedure seems well-suited for the synthesis of heterocycles **4** and **7**, whose exocyclic methylene group makes them useful compounds for further structural elaboration.[7] It supplements the existing trimethylenemethane methodologies of Trost and Binger [8] and, moreover, is applicable to a wide range of substrates.

References and Notes

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