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CONJUGATED EXOCYCLIC DIENES BY ADDITION OF 2-(BENZYLOXYMETHYL)-3-(BROMOZINCMETHYL)-1,3-BUTADIENE TO ALDEHYDES, KETONES AND IMINES FOLLOWED BY Pd(0)-CATALYZED CYCLIZATION

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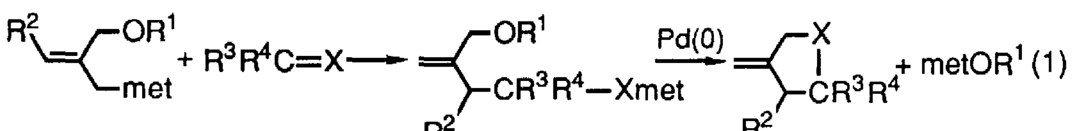
Summary: Reaction of 2-(benzyloxymethyl)-3-(bromozincmethyl)-1,3-butadiene with aldehydes, ketones and imines afforded addition products **6**, which underwent Pd(0)-catalyzed cyclization to the conjugated exocyclic dienes **7**.

2-(Metallomethyl)-2-propenyl ethers **1** (met = MgCl, ZnBr) can be used to add the trimethylenemethane unit **2** (R^2 = H, alkyl) to a variety of unsaturated systems[1] and to oxiranes,[2] *e.g.* equation 1. It was envisaged that in a similar *one-pot* procedure organozinc reagent **3** might transfer the tetramethyleneethane unit **4**, yielding conjugated exocyclic dienes **7** (equation 2). We now wish to report the synthesis of **7** (X = O, NR^5) starting from **3** (R^1 = CH_2Ph) and aldehydes, ketones and imines **5** (X = O, NR^5).



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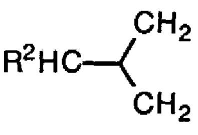

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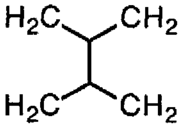
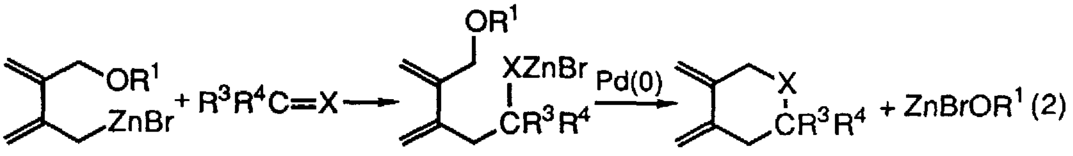
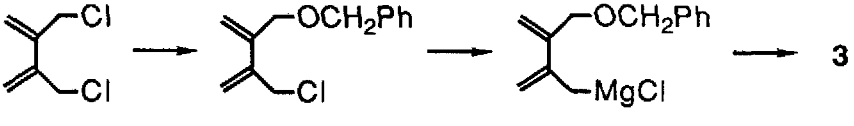




3 **5** **6** **7**

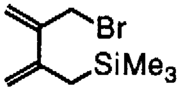
Generation of **3** started by treating dichloride **8**[3] with $NaOCH_2Ph$ (dimethoxyethane, room temperature,18h). Mono-ether **9**[4] (50%) was separated from the corresponding bis-ether (20%) and unreacted **8** (27%) by distillation.



8 **9** **10**

Chloride **9** was transformed into the Grignard reagent **10** by using anthracene-activated magnesium in THF.[5] Magnesium powder[6] (40 mmol) in THF (30 mL) was activated with 1,2-dibromoethane (1 mmol). Anthracene (3 mmol) was added and the reaction mixture was stirred overnight at room temperature. The magnesium and magnesium anthracene were allowed to settle and the supernatant was replaced by fresh THF (30 mL). Then, at -10°C, a solution of chloride **9** (10 mmol) in THF (20 mL) was added dropwise in 3h. Immediately after the addition was completed, the temperature was raised to room temperature and the unstable Grignard reagent solution was transferred to a second flask containing $ZnBr_2$ (11 mmol). After stirring for 1h the precipitated salts were allowed to settle and the supernatant, a stable solution of **3** (concentration: 0.2 M; yield: 90%, based on **9**), was used for further reaction.[7] Addition of the substrates **5** (2 mmol) to **3** (2.4 mmol) and stirring at room temperature for 1.5h gave the open chain products **6** (equation 2) in excellent yields. They were cyclized to **7** *in situ* by adding 30 mol% $(i\text{-}PrO)_3P$ and 5 mol% $Pd(OAc)_2$[8] (aldehydes, ketones) or 5 mol% $Pd(PPh_3)_4$ (imines) to the reaction mixture and heating at 65°C for 2h. Work-up (aqueous NH_4Cl, ether, brine, $MgSO_4$) afforded 7.[9] Results are given in Table 1. The instability of **6** at 65°C (complete decomposition in 2h in the absence of catalyst) may be partly responsible for the moderate yields.[10]

Conjugated exocyclic dienes like **7** are interesting building blocks in organic synthesis because, by Diels-Alder reaction, they offer an easy access to fused ring systems. Recently, **11**[11] and **12**[12] have been transformed into **7** (X = CROH, O) by sequences consisting of two or three discrete steps, respectively.[13] Due to its higher reactivity, which permits its one-pot transformation into **7**, and its potential versatility[14] **3** seems a most promising complement of these synthetically useful counterpolarized tetramethyleneethane equivalents.



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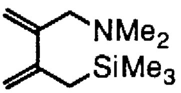

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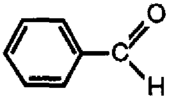
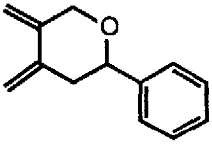
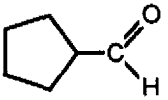
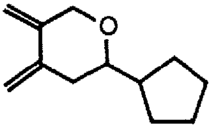
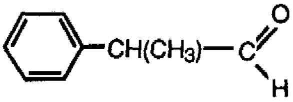
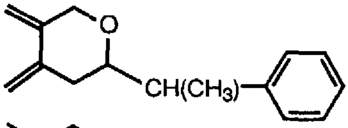
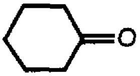
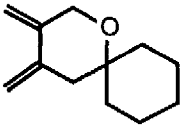
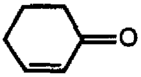
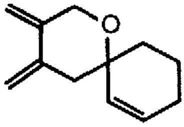
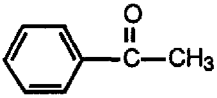
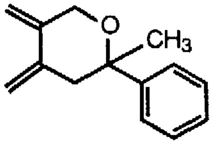
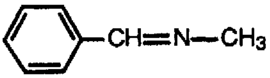
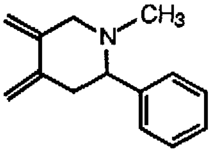
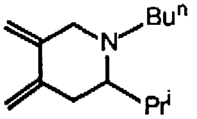
Table 1. Conjugated exocyclic dienes **7** from aldehydes, ketones and imines **5**.

System	Aldehyde, ketone **5**	Product **7**	Yields of **7** (%)[a]
a			53
b			57
c			44[b]
d			51
e			66
f			62

System	Imine **5**	Product **7**	Yields of **7** (%)[a]
g			47(55[c])
h	$PR^i—CH{=}N—Bu^n$		64

[a] GLC yields. [b] Mixture of 2 diastereomers, ratio: 2 : 1.

[c] Pd $(OAc)_2/(i\text{-}PrO)_3P$ used as catalyst for ring-closure.

References and notes.

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4 Bp. 88°C (5.10^{-3} mbar). **9** is stable in the dark at -80°C for at least 4 months but at room temperature in the light polymerization starts within 12h.

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6 Aldrich, 50 mesh, 99+ %.

7 At 0°C, decomposition of **10** was complete after 10h while **3** remained unchanged for at least 3 days.

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9 All new compounds were characterized by NMR and HRMS.

10 Under the conditions of ring closure, conjugated exocyclic dienes **7** are perfectly stable.

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14 Allylzinc compounds can carbometallate a variety of carbon-carbon multiple bonds. See ref. 1a,b,d and literature given there.

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