Tetrahedron Letters 51 (2010) 5886–5888

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

An efficient one-pot method for the synthesis of mono- and biscyclopentenones via zirconium-catalyzed cycloalumination of cyclic alkynes and diynes

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ARTICLE INFO

Article history:
Received 13 July 2010
Revised 2 August 2010
Accepted 31 August 2010
Available online 8 September 2010

Keywords:
Homogeneous catalysis
Organoaluminium compounds
Cycloalkynes
Cycloalumination
Dzhemilev reaction
Cyclic diynes
Cyclopentenones
Zirconocene dichloride

ABSTRACT

Mono- and bisaluminacyclopentenes obtained via zirconium-catalyzed cycloalumination with Et_3Al and cyclic alkynes or diynes can be converted into the corresponding mono- and biscyclopentenones by treatment with CO_2, ClCOOEt, or $CO(OEt)_2$ in yields of 34–73%.

Cyclopentenones have attracted the attention of organic chemists due to their wide use as building blocks in organic synthesis. In addition, they are often encountered in drugs and flavoring compounds.[1]

Efficient and widely used procedures for preparing cyclopentenones include the Nazarov cyclization, the Pauson-Khand reaction, and methods based on intramolecular cyclization of dienes, enynes, and diynes catalyzed by Ru, Ir, Rh, Au, Pd, or Ni complexes.[2]

Another method for the synthesis of cyclopentenones includes intramolecular carbocyclization of aluminacyclopentenes[3] generated in situ in Zr-catalyzed cycloalumination reactions of alkynes and Et_3Al (*Dzhemilev reaction*),[4] and their subsequent treatment with CO_2, ClCOOEt, or $CO(OEt)_2$.

We have investigated, for the first time, the activity of cyclic mono- and diynes in catalytic cycloaluminations with Et_3Al and also their ability to give the corresponding aluminacyclopentenes in the presence of Cp_2ZrCl_2 as the catalyst. This confirms the high activity and selectivity in cycloaluminations of unsaturated compounds.[5]

Cycloalkynes [cyclododecyne (**1**), cyclotridecyne (**2**)][6a] and cyclic diynes [cyclododeca-1,7-diyne (**7**), cyclotetradeca-1,8-diyne (**8**), cyclooctadeca-1,10-diyne (**9**), cyclodocosa-1,12-diyne (**10**)][6b] were selected for investigation.

We established that the reaction of cycloalkynes **1** and **2** with Et_3Al (excess) under the developed conditions (cycloalkyne:Et_3Al = 10:30, 5 mol % Cp_2ZrCl_2, 4 h, hexane) gave organoaluminium compounds (OAC) **3** and **4**, which after deuterolysis gave 2-deutero-1-deuteroethylcyclododecene or 2-deutero-1-deuteroethylcyclotridecene (>95% D in both positions) in 91–94% yields (Scheme 1).

Treatment of OACs **3** or **4** with 3 equiv of CO_2, ClCOOEt, or $CO(OEt)_2$ produced the desired bicyclo[10.3.0]pentadec-1(12)-en-13-one (**5**)[7] and bicyclo[11.3.0]hexadec-1(13)-en-14-one (**6**)[8] in the yields indicated in Table 1.

Taking into account the experimental data obtained from the catalytic cycloalumination of cyclic acetylenes on the example of cyclotetradeca-1,8-diyne (**8**), we elaborated the reaction conditions (cycloalkadiyne:Et_3Al:[Zr] = 1:6:0.1, hexane, 20–22 °C, 6 h). The cycloalkadiyne underwent cycloalumination with Et_3Al in the presence of 10 mol % Cp_2ZrCl_2 involving both triple bonds to form the regioisomeric tricyclic bisaluminacyclopentenes **12a** and **12b** in 87% yield (Scheme 2).

Carbocyclization of OACs **12a**,**b** using 6 equiv of CO_2 or ClCOOEt gave rise to 8,20-dioxotricyclo[15.3.$0^{1,17}$.$0^{7,11}$]icosa-1(17),7(11)-diene **16a** and 8,18-dioxotricyclo[15.3.01,17.$0^{7,11}$]icosa-1(17),7(11)-diene **16b**, respectively, a 1:1 ratio (as determined by NMR spectroscopic experiments) in 59–68% overall yields (Table 1).

Other cyclic diynes (Table 1) participated in this reaction to afford the corresponding doublytethered biscyclopentenones **15**–**18**[2j,2k] in high yields (50:50 mixture of regioisomers in all cases).

It is interesting to note that cyclopentenone **5** has been successfully used in the synthesis of exaltone, muscone, and bicyclo[10.3.0]pentad-

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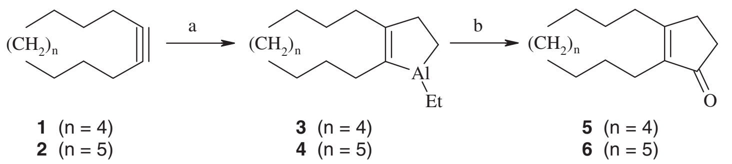
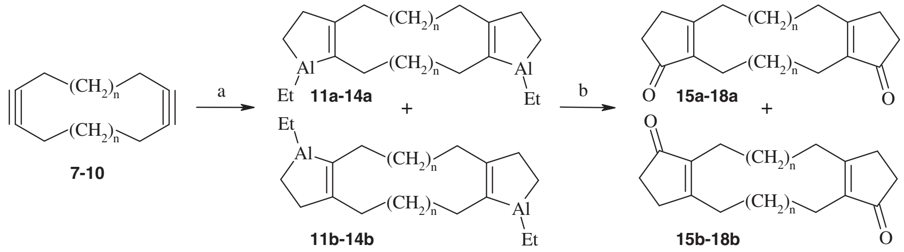
doi:10.1016/j.tetlet.2010.08.120



n = 4, 5. (a): Et_3Al, [Zr], (b): CO_2, ClCOOEt or $CO(OEt)_2$

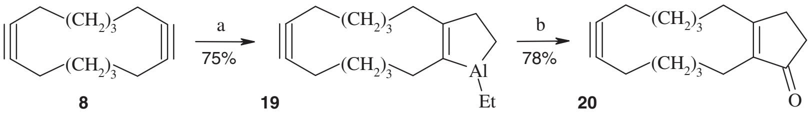
Scheme 1.



n = 2, 3, 5, 7. (a): Et_3Al, [Zr], (b): CO_2, ClCOOEt or $CO(OEt)_2$

[Zr] = Cp_2ZrCl_2; (n = 2) **7**, **11**, **15**; (n = 3) **8**, **12**, **16**; (n = 5) **9**, **13**, **17**; (n = 7) **10**, **14**, **18**

Scheme 2.



[Zr] = Cp_2ZrCl_2; (a): Et_3Al, [Zr], (b): CO_2

Scheme 3.

Table 1

Synthesis of mono- (5,**6**) and biscyclopentenones (**15**–**18**) via cycloalumination of cyclic mono- and diynes

Entry	Cyclic alkyne or diyne	Cyclopentenone	Isolated yield (%)
1	Cyclododecyne (**1**)	**5**	71[a], 62[b], 34[c]
2	Cyclotridecyne (**2**)	**6**	73[a], 63[b]
3	Cyclododeca-1,7-diyne (**7**)	**15**	59[a], 48[b]
4	Cyclotetradeca-1,8-diyne (**8**)	**16**	68[a], 59[b]
5	Cyclooctadeca-1,10-diyne (**9**)	**17**	70[a], 63[b]
6	Cyclodocosa-1,12-diyne (**10**)	**18**	72[a], 62[b]

[a] Reaction of OAC with CO_2.

[b] Reaction of OAC with ClCOOEt.

[c] Reaction of OAC with $CO(OEt)_2$.

ecan-13-one—substances having a musk-like odor,[7] and biscyclopentenones **15**–**18** have been employed as starting materials for *ansa*-metallocene synthesis.[9]

We envisaged that the cycloalumination of cyclic diynes could be used to synthesize cycloalkynes substituted with functional groups in one preparative step. Zr-catalyzed cycloalumination of one triple bond of the cycloalkadiyne is followed by subsequent transformation of the resulting OAC into carbo-[10] or heterocycles[11] annulated to various cycloalkynes.

For example, we found that cyclotetradeca-1,8-diyne (**8**) reacted with Et_3Al (cycloalkadiyne:Et_3Al = 1:3, hexane, 20–22 °C, 3 h) in the presence of Cp_2ZrCl_2 (5 mol %) to give cycloalkyne **19** with an annulated aluminacyclopentene fragment. Subsequent reaction between OAC **19** and CO_2 produced bicyclo[12.3.0^{1,14}]heptadec-1(14)-en-7(8)-yn-15-one (**20**)[12] in 59% overall yield (Scheme 3).

In conclusion, this catalytic cyclometallation reaction represents an efficient methodology, which allows the preparation of mono- and bis(cyclopentenones) from the cyclic acetylenes via the in situ generation of aluminacyclopentene intermediates in yields greater than 80% and their carbocyclization with the aid of CO_2, ClCOOEt or $CO(OEt)_2$.

Acknowledgment

This work was supported financially by the Russian Foundation for Basic Research (Grant No. 10-03-00046) and by the Russian Science Support Foundation.

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8. *Zr-Catalyzed cycloalumination of cycloalkynes and diynes with Et_3Al followed by treatment with CO_2, ClCOOEt, or $CO(OEt)_2$ (general procedure).* A glass reactor under a dry argon atmosphere at ambient temperature was charged under stirring with 10 ml of hexane, Cp_2ZrCl_2 (1 mmol), cycloalkyne (10 mmol) or cyclic diyne (5 mmol), and Et_3Al (30 or 60 mmol). The mixture was stirred for 4–6 h. Analysis of an aliquot by GLC indicated the formation of **3**, **4**, or **11**–**14** in 34–73% yields. After cooling the reaction mixture to 0 °C, CO_2 was slowly bubbled through via a gauge needle or ClCOOEt($CO(OEt)_2$) (36 or 72 mmol) was added at −78 °C and the mixture stirred overnight at ambient temperature. The reaction mixture was diluted with CH_2Cl_2 (15 ml) and quenched with 5% aqueous HCl (5 ml). The organic layer was washed with aqueous $NaHCO_3$ (10 ml), dried over $MgSO_4$, and concentrated. Chromatographic purification (haxane and then 5:1 hexane-EtOAc) afforded the target products **5**, **6**, or **15**–**18**.[2k,2j] Bicyclo[11.3.0]hexadec-1(13)-en-14-one (**6**): R_f = 0.56 (hexane–EtOAc, 5:1). IR: 1635 (C=O), 1691 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.91–2.62 (m, 8H), 0.89–1.93 (m, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.6, 21.9, 22.8, 23.5, 24.6, 24.8, 25.2, 25.4, 25.6, 27.9, 28.8, 29.1, 34.5, 140.0, 174.6, 210.7. MS, *m*/*z*: 234 (M$^+$). Anal. Calcd for $C_{16}H_{26}O$: C, 81.99; H, 11.18. Found: C, 81.78; H, 11.16.
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12. Bicyclo[12.3.$0^{1,14}$]heptadec-1(14)-en-7(8)-yn-15-one (**20**): Yield 59%. R_f = 0.52 (hexane–EtOAc, 5:1). IR: 771, 921, 1437, 1464, 1625 (C=O), 1674 (C=O), 1755 (C=O), 2846, 2960 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.49–2.51 (m, 2H, CH_2–C=), 2.45 (t, 2H, *J* = 7.2 Hz, CH_2–C=), 2.37–2.41 (m, 2H, CH_2–C=O), 2.16–2.26 (m, 6H, 3CH_2), 1.67–1.69 (m, 2H, CH_2), 1.39–1.62 (m, 10H, 5CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 17.9, 18.4, 23.2, 26.3, 26.6, 27.1, 27.3, 28.3, 28.3, 29.1, 34.2, 80.2, 81.3, 140.3, 174.1, 210.4. MS, *m*/*z*: 244 (M$^+$). Anal. Calcd for $C_{17}H_{24}O$: C, 83.55; H, 9.90. Found: C, 83.35; H, 9.88.