Pergamon

Tetrahedron Letters 39 (1998) 4321–4324

TETRAHEDRON LETTERS

Cross Coupling-Conjugate Addition Reaction of Zirconacyclopentadienes with 3-Iodopropenoates

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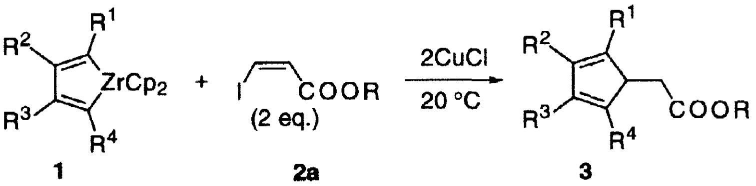
Received 2 March 1998; revised 6 April 1998; accepted 7 April 1998

Abstract: Copper-mediated reaction of zirconacyclopentadienes with iodopropenoates afforded penta- and hexasubstituted cyclopentadienes.

Direct transformation of metallacycles to carbocyclic compounds is of general synthetic interest,[1] and special attention has been devoted to the preparation of cyclopentadiene derivatives that find extensive use not only in organic synthesis but also in polymer chemistry using metallocenes. Despite the existence of a number of synthetic methods affording cyclopentadienes, the most attractive one seems to be the direct transformation of five-membered metallacycles that are readily prepared by the reaction of low-valent transition metals with alkynes and/or alkenes. In this regard especially attractive are zirconacycles, which can be easily prepared bearing different substituents, that can participate in a number of cyclization reactions, including also the formation of cyclopentadienes.[2,3]

In this paper we would like to report a new procedure for the direct preparation of cyclopentadienes from zirconacyclopentadienes based on a *cross coupling-conjugate addition* reaction sequence. Our synthetic strategy was based on the following concepts: firstly, transmetallation of a zirconacyclopentadiene to a more reactive dimetallo-intermediate, and secondly, reaction of the transmetallated compound with a suitable substrate bearing two electrophilic sites that are able to participate in the tandem reaction sequence. As the reagent for the transmetallation of zirconacyclopentadienes was chosen CuCl, which has often been successfully used in many reactions involving organozirconium compounds.[4,5] As far as the tandem reaction was concerned, it was envisioned that a sequence of a cross-coupling reaction followed by an intramolecular conjugate addition would best serve the purpose. Examples of separate cross-coupling reactions of zirconacycles with vinyl or aryl iodides[4g,h] are known as well as the conjugate additions to unsaturated enones.[5] Suitable substrates bearing two electrophilic sites that are able to participate in the proposed tandem reaction are 3-iodopropenoates which, in turn, are easily prepared from alkynoic acid derivatives.[6]

On the basis of this idea it was found that the addition of **2a** (2 mmol) and CuCl (2 mmol) in this order to a solution of tetraethylzirconacyclopentadiene[7] **1a** (1 mmol) in THF (5 mL) at 20 °C resulted in a slightly exothermic reaction and the formation of the product **3a**[8] in 98% yield (GC) within 5 min (Scheme 1). Methyl (*Z*)-3-bromopropenoate gave similar results (98% GC), but extended reaction time was needed for the completion of the reaction (15min to 1h).



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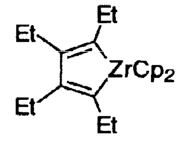
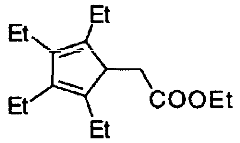
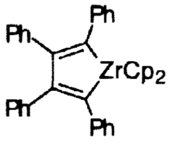
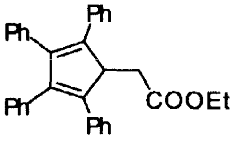
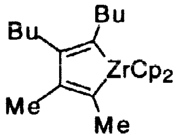
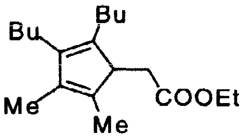
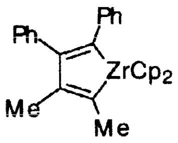
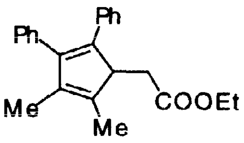
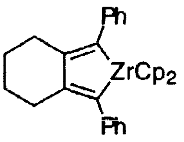
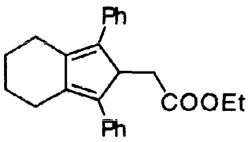
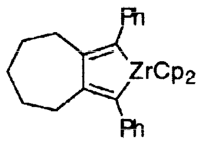
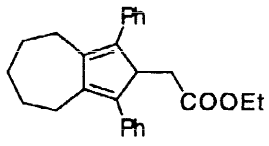
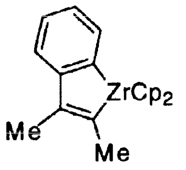
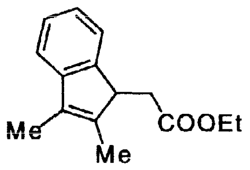
PII: S0040-4039(98)00762-X

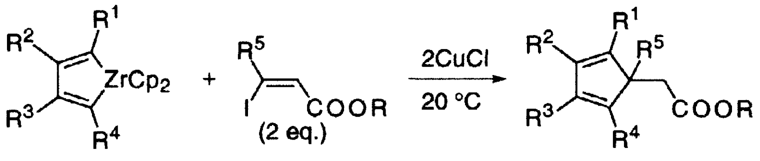
Further study involving the use of symmetrically and unsymmetrically substituted monocyclic as well as bicyclic zirconacyclopentadienes **1a-f** bearing alkyl and aryl groups resulted in all cases in the formation of cyclopentadiene products in high yields. Indenylzirconacyclopentadiene **1g** gave **3g** in 63% yield. Results are summarized in Table 1. Trimethylsilyl substituted zirconacyclopentadienes afforded the desired products only in low yields (10-20% isolated yields). Although 1 equiv. of iodopropenoate should be sufficient to give high yields of the desired products, 1.5-2 equiv. of iodopropenoate to zirconacyclopentadiene were found to be required to achieve satisfactory yields. The same concerns the amount of CuCl; 2 equiv. are necessary to get high yields of the products.

Table 1. CuCl-Mediated Reaction of Zirconacyclopentadienes with (*Z*)-3-Iodopropenoate **2a**.

Zirconacyclopentadiene		Product		Yield/% [a]
	**1a**		**3a**	97 (57)
	**1b**		**3b**	- (70)
	**1c**		**3c**	80 (40)
	**1d**		**3d**	98 (63)
	**1e**		**3e**	84 (54)
	**1f**		**3f**	65 (45)
	**1g**		**3g**	63 (41)

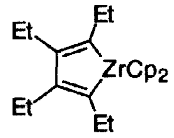
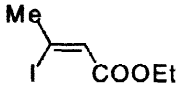
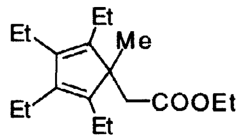
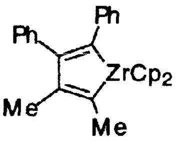
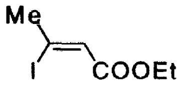
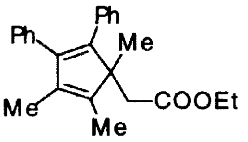
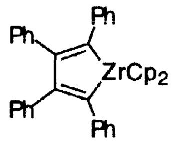
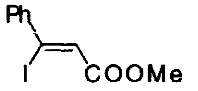
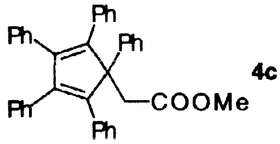
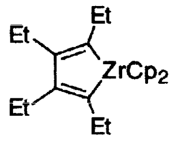
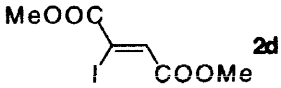
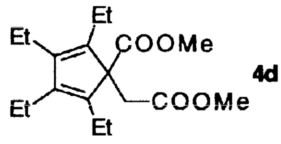
[a] GC yields. Isolated yields are given in parentheses.

In the next step were used 3-substituted-3-iodopropenoates. As expected, they also readily participated in this reaction, though longer reaction time was needed depending on the character of the substituent, and as products were obtained hexasubstituted cyclopentadienes. As representative examples were chosen methyl, phenyl,[6] and carboxymethyl[9] 3-substituted-3-iodopropenoates **2b-d**. In all cases the corresponding products were obtained in high yields. Results are summarized in Table II. The structure of the product **4c**[10] was confirmed by X-ray analysis.



1 2b-d 4 (2)

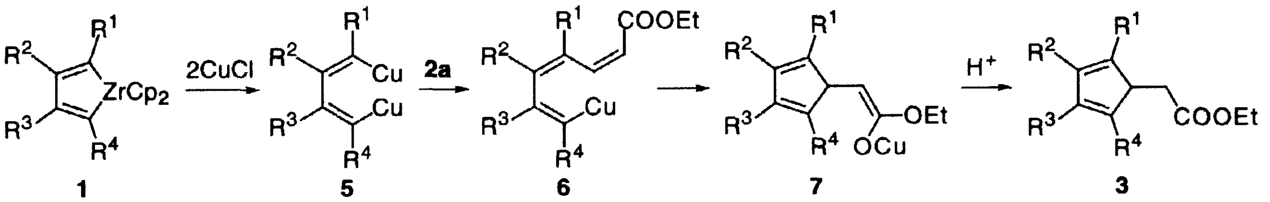
Table 2. CuCl-Mediated Reaction of Zirconacyclopentadienes with Iodopropenoates **2b-2d**.

Zirconacyclopentadiene		Propenoate		Reaction conditions T (°C)	Reaction conditions t (h)	Product		Yields (%)[a]
	**1a**		**2b**	20	3		**4a**	95 (54)
	**1d**		**2b**	20	3		**4b**	97 (58)
	**1b**		**2c**	20	1		**4c**	- (78)
	**1a**		**2d**	0	0.5		**4d**	97 (71)

[a] GC yields. Isolated yields are given in parentheses.

Thus, the idea of a combination of the tandem cross coupling-conjugate addition reaction proved to be useful, and we may conclude that the reaction mechanism is as follows (Scheme 1). Firstly, the zirconacyclopentadiene **1** undergoes transmetallation with CuCl to form the diorganocopper intermediate **5**. Secondly, the intermediate **5** reacts in the first step with 3-iodopropenoate **2** to give the intermediate **6**. However, the question remains whether this step proceeds indeed via a single-step cross-coupling reaction or via a multi-step Michael addition-elimination reaction. Nevertheless, the longer reaction time needed in the reaction with bromopropenoates in comparison with iodopropenoates indicates that this step should proceed via a cross-coupling reaction.[11] Finally, the intermediate **6** undergoes intramolecular Michael addition forming the enolate **7** which, after hydrolysis, gives the cyclopentadiene product **3**.

Scheme 1



1 5 6 7 3

We conclude that this reaction offers a new pathway to a variety of penta- and hexasubstituted cyclopentadienes. Moreover, the presence of an ester group in the side chain may potentially serve as the reaction center for further transformations and/or modifications.

References

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(8) **3a**: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 1.00 (t, $J = 7.6$ Hz, 6H), 1.03 (t, $J = 7.5$ Hz, 6H), 1.22 (t, $J = 7.1$ Hz, 3H), 2.07-2.16 (m, 2H), 2.21 (q, $J = 7.5$ Hz, 4H), 2.38 (d, $J = 6.4$ Hz, 2H), 2.36-2.45 (m, 2H), 3.26 (t, $J = 6.4$ Hz, 1H), 4.09 (q, $J = 7.1$ Hz, 2H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 14.12, 15.11 (2C), 15.36 (2C), 18.54 (2C), 19.35 (2C), 34.24, 47.37, 60.13, 140.88 (2C), 142.34 (2C), 172.74; IR (neat) 1737 cm^{-1}; HRMS calcd for $C_{17}H_{28}O_2$ 264.2087, found 264.2084.

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(10) **4c**: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 3.29 (s, 2 H), 3.56 (s, 3 H), 6.28-7.23 (m, 25H); ^{13}C NMR ($CDCl_3$, Me_4Si, 100 MHz) δ 36.56, 51.12, 64.38, 126.11, 126.49 (2C), 126.55 (2C), 126.81 (2C), 127.43 (4C), 127.53 (4C), 128.73 (2C), 129.80 (4C), 129.97 (4C), 135.52 (2C), 135.70 (2C), 138.54, 144.43 (2C), 149.63 (2C), 170.44; IR (neat) 1738 cm^{-1}. Anal. Calcd for $C_{38}H_{30}O_2$ C, 88.00; H, 5.83%. Found C, 87.93; H, 5.98%.

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