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ALKOXIDE-MEDIATED OXIDATIVE RING EXPANSION OF BENZOCYCLOBUTENES. A NEW ROUTE TO 3,4-DIHYDROISOCOUMARINES†

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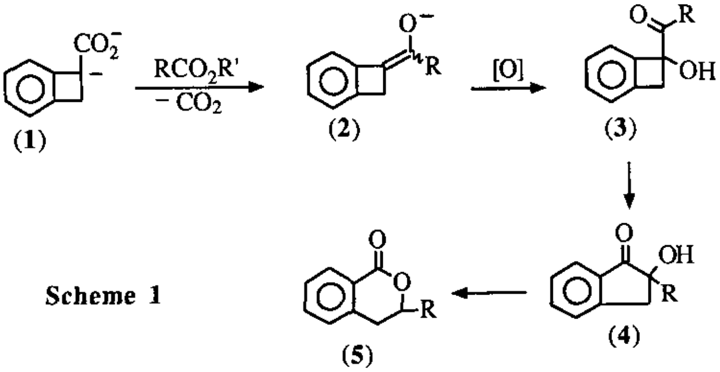
Abstract---Sequential treatment of the dianion of **6** with a variety of esters (**10**) and MoO_5·pyridine·HMPA complex provided the rearranged 2-hydroxy-1-indanones (**7**) along with the 1-acylbenzocyclobutenes (**8**), which were easily converted to **7**. Transformation of **7** to the 3,4-dihydroisocoumarines (**9**) was achieved by oxidative cleavage followed by reduction and acid treatment.

In the context of our studies about the development of novel and valuable transformations utilizing benzocylobutenes,[1] we were interested in the ring expansion reaction of the four-membered ring.[2] It has been demonstrated that benzocyclobutenol[3] and the 1-vinylbenzocyclobutenols[4] were converted by basic treatment to o-tolualdehyde and the annelated products, respectively. We reasoned that acylation[5] of the dianion (**1**) with the appropriate esters would, after spontaneous decarboxylation, give the enolate (**2**), which would be oxidized to provide the α-hydroxy ketone (**3**). The alkaline metal salt of **3** should readily rearrange regioselectively[2-4] to α-hydroxyindanone (**4**), which would be converted by standard manipulations to 3,4-dihydroisocoumarines (**5**),[6] one of the important frameworks of natural products.[7] (Scheme 1)



Scheme 1

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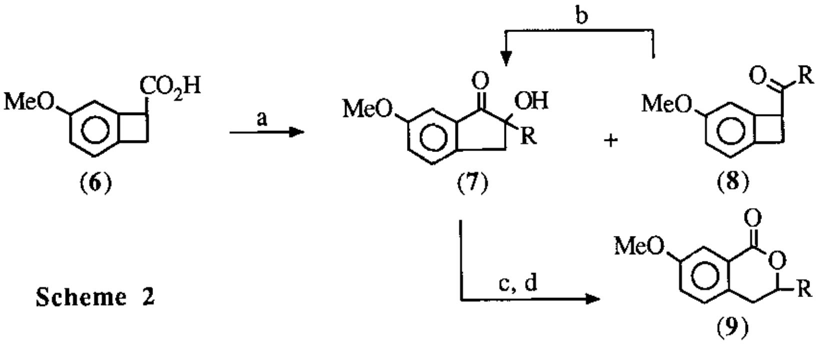
† This paper is dedicated to the memory of the Professor Tetsuji Kametani.

Thus, as shown in Scheme 2, the dianion, generated by treatment of 5-methoxybenzocyclobutene-1-carboxylic acid **(6)**[8] with 2.2 eq. of LDA, was reacted at 0 °C with the methyl ester **(10)** followed by oxidation with MoO_5·pyridine·HMPA (MoOPH)[10] complex at 0 °C to room temperature to provide a chromatographically easily separable mixture of two products. In most of the cases, the major product was the rearranged 2-hydroxy-1-indanone **(7)**[11,12] which might be conceived as being derived from the alkoxide-mediated regioselective 1,2-shift[13] of the incipient α-hydroxy ketone. On the other hand, the minor product was assigned as the 1-acylbenzocyclobutene **(8)** which could be efficiently converted to **7** by treatment with LDA and MoOPH. The yields for these transformations range from modest to good as can be seen from inspection of the examples collected in Table 1. It is noteworthy that in cases where there are no α-hydrogens for deprotonation in the ester **(10)**, such as **(10e-g)**, or where the α-position is sterically hindered, such as **(10c, d)**, *we observed higher yields of the products (7 + 8).*



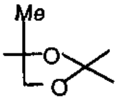
Scheme 2

Reagents a, LDA (2.2 eq), RCO_2Me (**10**), then MoOPH; b, LDA, MoOPH; c, H_5IO_6; d, $NaBH_4$ then H^+.

Transformation of **7** to the 3,4-dihydroisocoumarine **(9)** was achieved by a simple two-step sequence. Treatment of **7** with periodic acid provided the keto acid which was immediately reduced with sodium borohydride followed by acid treatment in a one-pot operation to afford **9** in the yields indicated in Table 1.

While there remains a problem of lower yields for the introduction of primary alkyl groups, the transformation datailed here provides a novel and simple methodology for the synthesis of both 2-hydroxy-1-indanones and 3,4-dihydroisocoumarines.

Table 1 Syntheses of 2-Hydroxy-1-indanones (7) and 3,4-Dihydroisocoumarines (9)

	R in **10**	yield, %[c] (**7**)	(**8**)	Conversion, %[c] (**8**) ⟶ (**7**)	Yield, %[c] (**9**)
a	Et	26	13	48[b]	47
b	p-$MeOC_6H_4(CH_2)_2$	11	12	93[b]	73
c	^{i}Pr	53	12	93	64
d	cyclohexyl	33	25	97[b]	63
e	^{t}Bu	58	8	97	48
f		68[a]	15[a]	74[b]	54[a]
g	Ph	75	0	91	74

a, mixture of two diastereoisomers
b, based on the consumed starting ketone (**3**)
c, not optimized

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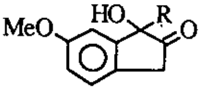
out by the successful transformation of **7** to **9** whose structure was rigorously confirmed by the 500 MHz ^{1}H-nmr decoupling experiments.



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