JOC*Note*

First Tandem Free-Radical Cyclization Reaction of Alkylenecyclopropanes: A Novel and Efficient Method for the Preparation of 2-(3,4-Dihydronaphthalen-2-yl)malonic Acid Diethyl Esters

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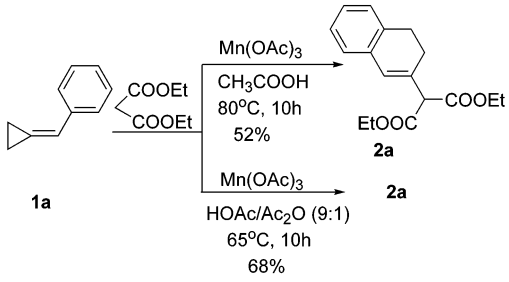
Abstract: Alkylidenecyclopropanes undergo $Mn(OAc)_3$-mediated addition with malonate, leading to dihydronaphthalene derivatives in moderate yields.

During the past decades, methylenecyclopropanes (MCPs) have been extensively studied because the relief of ring strain provides a potent thermodynamic driving force.[1] Recently, increasing attention has been paid to the transition-metal-mediated reactions of MCPs, which have been usually employed for the construction of complex and interesting organic molecules.[2]

Radical cyclization of alkenes has become a valuable method for the synthesis of cyclic compounds during the past 30 years.[3] Usually oxidative termination of radical cyclizations is advantageous over reductive terminations because more highly functionalized, versatile products are produced.[4a] Manganese(III)-mediated oxidative free-radical cyclizations of alkenes with 1,3-dicarbonyl compounds, which is a very useful method for the construction of new C−C bonds and functionalized cyclic compounds,[4] have been well reported.[5] However, to the best of our knowledge, manganese(III)-mediated free-radical cyclizations of MCPs is not documented.

SCHEME 1



During our study of MCPs, we have observed the interesting and unique reactivity of the cyclopropane ring of MCPs,[6] which stimulated us to further investigate the $Mn(OAc)_3$-mediated reaction of MCPs with malonic acid diethyl ester.

As a first attempt, we examined the reaction of benzylidenecyclopropane (**1a**) with 2 equiv of $Mn(OAc)_3 \cdot 2H_2O$ and 1 equiv of malonic acid diethyl esters in acetic acid at 80 °C. Fortunately, 2-(3,4-dihydronaphthalen-2-yl)malonic acid diethyl ester (**2a**) was isolated in 52% yield after heating for 10 h. Further screening demonstrated that HOAc/Ac_2O (9:1) was the better reaction medium, and the reaction could be carried out at a lower temperature (65 °C), affording **2a** in 68% yield (Scheme 1).

With this result in hand, a series of alkylidenecyclopropanes[7] were chosen as substrates to afford 2-(3,4-dihydronaphthalen-2-yl)malonic acid diethyl ester highly selectively in moderate yields (Table 1).

Furthermore, we examined the reaction of 1-(2-cyclopropylidenepropyl)-4-methoxybenzene (**1i**) with malonic acid diethyl ester in the presence of $Mn(OAc)_3$ for the synthesis of 2-(3-methoxy-8-methyl-6,9-dihydro-5*H*-benzocyclohepten-7-yl)malonic acid diethyl ester (**2i**). However, only 2-[3-(4-methoxy-phenyl)-2-methyl-1-vinyl- propenyl]malonic acid diethyl ester (**2j**) was isolated in 41%

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(7) The substituted MCPs **1** are readily available by the reaction of aldehydes/ketones with 3-bromopropylphosphonium bromide. It should be noted that the aryl-substituted MCPs are rather stable at −15 °C. For the synthesis of MCPs, see: Utimoto, K.; Tamura, M.; Sisido, K. *Tetrahedron* **1973**, *14*, 1169.

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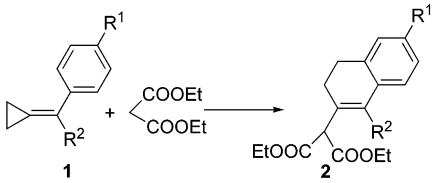
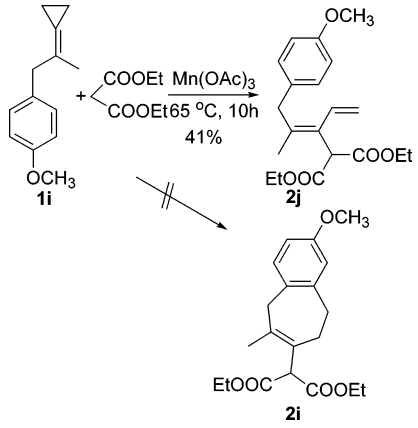
TABLE 1. Synthesis of (*Z*)-2,4-Dihalobutenes



entry	R^1	R^2	time (h)	product (yield %)[a]
1	H	H (**1a**)	10	**2a** (68)
2	CH_3	H (**1b**)	8	**2b** (70)
3	H	Ph (**1c**)	10	**2c** (72)
4	H	CH_3 (**1d**)	12	**2d** (59)
5	CH_3O	H (**1e**)	8	**2e** (64)
6	Cl	H (**1f**)	10	**2f** (60)
7	Br	H (**1g**)	10	**2g** (67)
8	NO_2	H (**1h**)	20	0

[a] Isolated yields

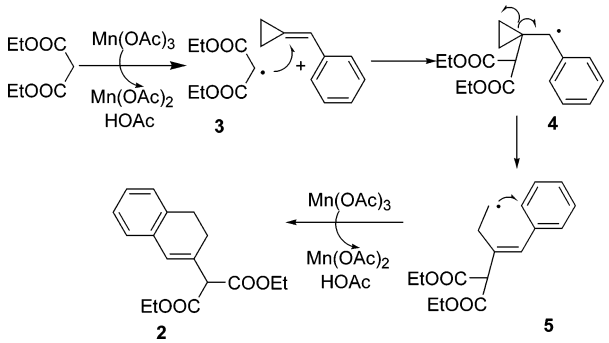
SCHEME 2



yield, indicating that the synthesis of a seven-membered cyclic compound is not easy (Scheme 2).

A plausible reaction mechanism was suggested as follows: the reaction of malonic acid diethyl ester with $Mn(OAc)_3$ would give radical **3**,[8] which adds to the C=C bond of MCP highly regioselectively to give intermediate **4**.[9] A β-scission of the C−C bond in the cyclopropane ring in **4** affords intermediate **5**,[10] in which the radical carbon

SCHEME 3



attacks the phenyl group intramolecularly to undergo cyclization reaction to produce **2** with the loss of a proton and oxidation in the presence of another molecule of $Mn(OAc)_3$ (Scheme 3).[5d]

In conclusion, we have developed a novel, convenient, and efficient method for the synthesis of 2-(3,4-dihydronaphthalen-2-yl)malonic acid diethyl esters, pivotal skeletons in many natural products with an unusual range of biological activities and useful building blocks in organic synthesis,[11] in moderate yield by the reaction of arylidenecyclopropanes and malonic acid diethyl ester in the presence of $Mn(OAc)_3$. The reaction mechanism and synthetic application of this methodology are being further studied in our laboratory.

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Supporting Information Available: Experimental procedures and spectral data for compounds prepared. This material is available free of charge via the Internet at http://pubs.acs.org.

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