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Acetoxylation and Hydroxylation of Diarylmethylenecycloalkanes via Radical Approach

Min Jiang, Yin Wei,* and Min Shi*

State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Lu, Shanghai 200032, China

mshi@mail.sioc.ac.cn

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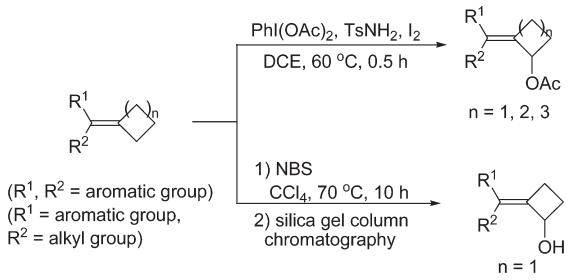

Diarylmethylenecycloalkanes were acetoxylated under the radical reaction conditions with PhI(OAc)$_2$, I_2, and $TsNH_2$. Moreover, upon treating the products from the reactions of methylenecyclobutanes with *N*-bromosuccinimide (NBS) through silica gel column chromatography, the corresponding substituted methylenecyclobutanols were obtained in moderate to good yields. The plausible mechanisms have been proposed on the basis of the control experiments.

Introduction

The functionalization of an allylic C−H bond in an olefin is of fundamental importance in organic synthesis due to the broad synthetic potential of these alkene derivatives including enantioenriched ones obtained for the preparation of complex molecules.[1] The practical utility of such reactions for complex molecule synthesis is governed by their ability to operate with predictable and high levels of chemoselectivity, stereoselectivity, regioselectivity, and site selectivities. Recently transition metal-catalyzed functionalization of allylic C−H bonds has been well developed and widely used in organic synthesis.[2,3] In these processes, transition metal complexes of rhodium, ruthenium, manganese, silver, copper, palladium, cobalt, and iron as catalysts are essential.[4] Meanwhile, the *transition metal-free* intermolecular acetoxylation and amination methods for saturated C−H bonds, which are more environmentally benign processes,[5] have also been developed and have attracted much attention. During our ongoing investigation on the chemical reactivity of highly strained small rings, we found that it is necessary to find a simple and direct method to functionalize the allylic C−H bond of methylenecycloalkanes. Moreover, we also found that methylenecycloalkanes having a four-, five-, or six-membered ring such as methylenecyclobutanes (MCBs) and methylenecyclopentanes as well as methylenecyclohexanes, a

*To whom correspondence should be addressed. Fax: 86-21-64166128.

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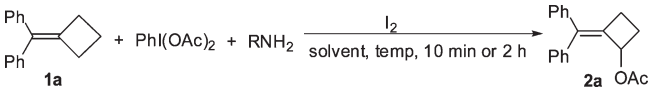
TABLE 1. Optimization of the Reaction Conditions for the Acetoxylation of MCB 1a



entry[a]	RNH_2	1/$PhI(OAc)_2$/RNH_2/I_2	solvent	temp (°C)	yield (%)[b] of **2a**
1	$TsNH_2$	1.0/2.5/1.0/1.0	DCE	60	58
2	$TsNH_2$	1.0/2.5/0/1.0	DCE	60	0
3	$TsNH_2$	1.0/1.5/1.0/0	DCE	60	0
4	$TsNH_2$	1.0/1.0/1.0/0.3	DCE	60	27
5	$TsNH_2$	1.0/1.0/0.3/0.3	DCE	60	54
6	$TsNH_2$	1.0/1.5/0.3/0.3	DCE	60	63
7	$TsNH_2$	1.0/2.0/0.3/0.3	DCE	60	72
8	$TsNH_2$	1.0/2.0/0.3/0.3	DCE	rt[c]	0
9	$PhSONH_2$	1.0/1.5/1.5/1.5	DCE	60[c]	NR
10	$TsNHNH_2$	1.0/1.5/1.5/1.5	DCE	60[c]	NR
11	$PhCH_2NH_2$	1.0/1.5/1.5/1.5	DCE	60[c]	NR
12	$BocNH_2$	1.0/1.5/1.5/1.5	DCE	60[c]	trace
13	$TsNH_2$	1.0/2.0/0.3/0.3	CH_3CN	60	65
14	$TsNH_2$	1.0/2.0/0.3/0.3	THF	60[c]	NR
15	$TsNH_2$	1.0/2.0/0.3/0.3	toluene	60[c]	32
16	$TsNH_2$	1.0/2.0/0.3/0.3	DCE, toluene (1:1)	60	78
17	$TsNH_2$	1.0/2.0/0.3/0.3 (NBS)	DCE	60	0
18	$TsNH_2$	1.0/2.0/0.3/0.3 (NCS)	DCE	60	complex
19	$TsNH_2$	1.0/2.0/0.3/0.3 (NIS)	DCE	60	trace

[a]Reaction conditions: **1a** (0.2 mmol), $PhI(OAc)_2$ (1.0−2.5 mmol), RNH_2 (0−1.5 mmol), I_2 (0−1.5 mmol), and solvent (2.0 mL) were employed; the reactions were carried out at various temperatures within 10 min. Iodine was added into the reaction mixtures two times (at the first minute and the fifth minute). [b]Isolated yields. [c]The reaction time is 2 h.

class of moderately strained alkenes, have been seldom used as substrates in organic synthesis. For example, as for MCBs, it has been only known that they could be easily oxidized to the corresponding cyclopentanone or cyclobutylmethanone derivatives in good yields under mild reaction conditions.[6a−f] Previously, we reported that the reactions of MCBs with acyl chlorides produced the corresponding substituted cyclopentene derivatives in moderate to high yields via ring enlargement in the presence of aluminum chloride under mild conditions.[6g] Herein, we wish to report the interesting acetoxylation and hydroxylation methods of diarylmethylenecycloalkanes via the free radical reaction processes.

Results and Discussion

The reaction of MCB **1a** with iodobenzene diacetate, amine, and iodine was initially investigated for seeking the optimal reaction conditions. The results are summarized in Table 1. As shown in Table 1, it was found that using $PhI(OAc)_2$ (2.5 equiv), $TsNH_2$ (1.0 equiv), and I_2 (1.0 equiv) to react with **1a** afforded acetoxylation product **2a** in 58% yield at 60 °C in 1,2-dichloroethane (DCE) within 10 min (Table 1, entry 1). Prolongation of reaction time led to the low yield. If the reactions were carried out in the absence of $TsNH_2$ or I_2, no product **2a** was obtained (Table 1, entries 2 and 3). Varying the ratio of **1a**/$PhI(OAc)_2$/$TsNH_2$/I_2 to 1.0/1.0/1.0/0.3 or 1.0/1.0/0.3/0.3 provided **2a** in 27% and 54% yield, respectively (Table 1, entries 4 and 5). Thus we found that the lesser amount of $TsNH_2$ gave the better result. Increasing the amount of $PhI(OAc)_2$ to 2.0 equiv led to the higher yield of **2a** (Table 1, entries 6 and 7). However, upon decreasing the temperature to room temperature (20 °C), the product **2a** was not obtained (Table 1, entry 8). If $TsNH_2$ was replaced by other amines such as $PhSONH_2$, $TsNHNH_2$, or $PhCH_2NH_2$, no reactions occurred (Table 1, entries 9−11) and only a trace amount of acetoxylation product was acquired if $BocNH_2$ was employed. Further examination of solvent effects revealed that in acetonitrile (CH_3CN), tetrahydrofuran (THF), and toluene, **2a** was obtained in 65%, 0%, and 32% yield at 60 °C, respectively (Table 1, entries 13−15). It was observed that using toluene as solvent led to the formation of **2a** in 32% yield in a very clean reaction within 2 h and the abundant substrate **1a** was recovered after workup. The highest yield was achieved (78%, Table 1, entry 16) with the mixed solvents of DCE and toluene (1:1). When I_2 was changed to NBS, NCS, or NIS, almost no desired product was obtained (Table 1, entries 17−19). Thus, the ratio of 1.0/2.0/0.3/0.3 for **1a**/$PhI(OAc)_2$/$TsNH_2$/I_2 is the best one for this reaction to give **2a** in good yield at 60 °C, employing DCE and toluene as mixed solvents.

Under these optimal reaction conditions, we next carried out the reactions of a variety of diarylmethylenecycloalkanes **1** including diarylmethylenecyclobutanes (n = 1), diarylmethylenecyclopentanes (n = 2), and diarylmethylenecyclohexanes (n = 3) with iodobenzene diacetate in the presence of $TsNH_2$ and iodine to examine the scope and limitations. We found that the corresponding products **2** were obtained in moderate to good yields within 10 min in spite of **1** (n = 1, 2, 3) bearing electron-rich, electron-neutral, and electron-poor substituents on the benzene rings (Table 2). For aryl-substituted MCBs **1b**−**d** (n = 1) having an electron-poor substituent at the para-position of the benzene ring, the corresponding products **2b**−**d** were obtained in 69−76% yields (Table 2, entries 1−3). However, for MCBs **1e** and **1f** having an electron-rich substituent at the ortho-, meta-, and para-positions of the benzene ring, the corresponding products **2e**

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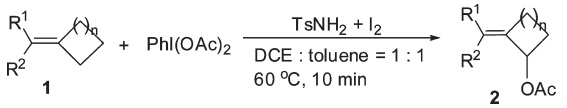
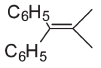
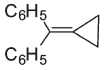
TABLE 2. Scope and Limitations of the Acetoxylation Reaction of Diarylmethylenecycloalkanes 1



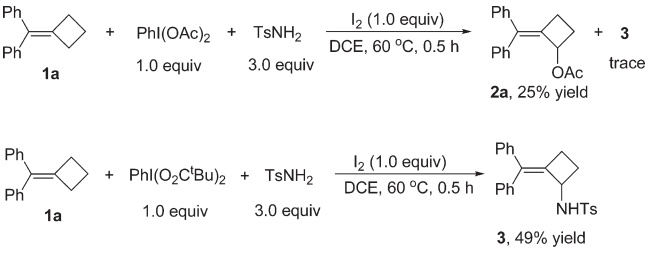
entry[a]	1 (R^1/R^2)	n	yield (%)[b] 2
1	**1b**, (*p*-ClC$_6$H$_4$/*p*-ClC$_6$H$_4$)	1	**2b**, 76
2	**1c**, (*p*-ClC$_6$H$_4$/C$_6$H$_5$)	1	**2c**, 71 (1.0:1.0)[c]
3	**1d**, (*p*-FC$_6$H$_4$/C$_6$H$_5$)	1	**2d**, 69 (1.0:1.0)[c]
4	**1e**, (*o,m*-Me$_2$C$_6$H$_3$/C$_6$H$_5$)	1	**2e**, 74 (1.0:1.0)[c]
5	**1f**, (*m,p*-Me$_2$C$_6$H$_3$/C$_6$H$_5$)	1	**2f**, 71 (1.0:1.0)[c]
6	**1g**, (C$_6$H$_5$/C$_6$H$_5$)	2	**2g**, 86
7	**1h**, (*p*-ClC$_6$H$_4$/*p*-ClC$_6$H$_4$)	2	**2h**, 81
8	**1i**, (*p*-MeC$_6$H$_4$/*p*-MeC$_6$H$_4$)	2	**2i**, 76
9	**1j**, (C$_6$H$_5$/C$_6$H$_5$)	3	**2j**, 81
10	**1k**, (*p*-ClC$_6$H$_4$/*p*-ClC$_6$H$_4$)	3	**2k**, 77
11	**1l**, (*p*-BrC$_6$H$_4$/Me)	1	**2l**, complex mixtures
12	**1m**, 	-	**2m**, 45
13	**1n**, 	0	**2n**, complex mixtures

[a]Reaction conditions: **1** (0.2 mmol), PhI(OAc)$_2$ (0.2 mmol), TsNH$_2$ (0.06 mmol), I$_2$ (0.06 mmol) in mixed solvent [DCE (1.0 mL) and toluene (1.0 mL)]; the reactions were carried out at various temperatures within 10 min. Iodine was added two times (at the first minute andthe fifth minute). [b]Isolated yields. [c]The ratios of cis and trans isomers were determined by ^{1}H NMR spectroscopic data.

and **2f** were obtained in 74% and 71% yield, respectively (Table 2, entries 4 and 5). Using methylenecyclopentanes **1g**−**i** (n = 2) and the methylenecyclohexanes **1j**−**k** (n = 3) as the substrates afforded the corresponding products **2g**−**k** in 76−86% yields under the standard conditions (Table 2, entries 6−10). Unfortunately, when using aliphatic substituted MCB **1*l*** as the substrate, the reaction yielded unknown complex mixtures without the desired product **2*l***, suggesting that an aromatic group is required in this transformation (Table 2, entry 11). When compound **1m** was used as substrate, the expected product **2m** was isolated in 45% yield (Table 2, entry 12). Furthermore, using methylenecycloproane **1n** as substrate provided complex product mixtures, indicating that a higher yield of the desired product could be obtained for these methylenecycloalkanes having a four-, five-, or six-membered ring (Table 2, entry 13).

The amination of MCB **1a** was also carried out with use of a large excess of TsNH$_2$ (**1a**/PhI(OAc)$_2$/TsNH$_2$/I$_2$ = 1.0/1.0/3.0/1.0) under the standard conditions, but affording the corresponding product **3** in trace and **2a** in 25% yield. With use of PhI(OOC^{t}Bu)$_2$[7] instead of PhI(OAc)$_2$, the corresponding amination product **3** was isolated in 49% yield when the ratio of **1a**/PhI(OOC^{t}Bu)$_2$/TsNH$_2$/I$_2$ was also changed to 1.0/1.0/3.0/1.0 (Scheme 1).

SCHEME 1. The Reaction of MCB 1a with PhI(OAc)$_2$ or PhI(O$_2$C^{t}Bu)$_2$, TsNH$_2$, and I$_2$



As a proposed mechanism for the PhI(OAc)$_2$/I$_2$-mediated amination reactions by Fan's group,[8] a plausible reaction has been shown in the Supporting Information (Scheme SI-1).

On the other hand, *N*-bromosuccinimide (NBS) is extensively used in allylic and benzylic brominations[9] which have been generally described as a free radical chain reaction involving succinimidyl radical.[10] Allylic bromination, as a common synthetic method for introducing a substituent in the organic compound, has resulted in a steadily growing interest in organic chemistry and has proved to be a powerful synthetic tool with numerous applications in organic chemistry and pharmaceutical chemistry.[11] Bergman's group recently also reported that cyclopropyl methyl ketone can be transformed into methylenecyclobutane through halogenation along with the acetoxylation of 2-bromo-1-methylenecyclobutane.[12] Moreover, the hydroxylation at the "allylic position" of an olefin is also essential in organic synthesis. However, hydroxylation of the allylic position is mainly carried out by the action of oxygen. It is necessary to find other facile synthetic methods to achieve the hydroxylation at the "allylic position" of an olefin without oxygen.

We next investigated the allylic bromination reactions of MCBs using NBS as free radical reagent. Surprisingly we found that the desired bromination products were readily converted into the corresponding methylenencyclobutanol in moderate to good yields during purification of the bromination products through silica gel column chromatography.

Subsequent examinations with diphenylmethylenecyclobutane **1a** as the substrate to react with *N*-bromosuccinimide (NBS) (1.0−2.0 equiv) in carbon tetrachloride (CCl_4) were aimed at determining the optimal conditions and the results are summarized in Table 3. The reaction of **1a** with NBS (**1a**/NBS = 1/1.5) was carried out at 70 °C for 10 h and then the solvent was removed under reduced pressure and the residue was purified by Huang Hai silica gel column chromatography (SiO_2 with 300−400 mesh). It was found that 2-(diphenylmethylene)cyclobutanol **4a** was obtained in 70% yield (Table 3, entry 1). Increasing the amounts of NBS to 2.0 equiv, the reaction became disordered, affording

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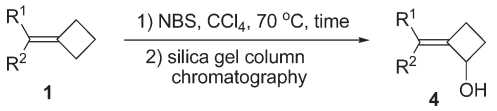
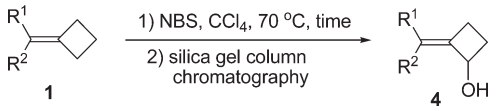
TABLE 3. Optimization of the Reaction Conditions



entry[a]	halogen	1a/halogen	additive	solvent	temp (°C)	yield (%)[b] of 4a
1	NBS	1/1.5		CCl_4	70	70
2	NBS	1/2		CCl_4	70	complex[d]
3	NBS	1/1		CCl_4	70	42
4	NBS	1/1.5		CCl_4	rt	NR
5	NBS	1/1.5		CCl_4	70	65[e]
6	NBS	1/1.5	AIBN[c]	CCl_4	70	21
7	NBS	1/1.5	BPO[c]	CCl_4	70	30
8	NBS	1/1.5	TEMPO[c]	CCl_4	70	NR
9	Br_2	1/1.5		CCl_4	70	25
10	NCS	1/1.5		CCl_4	70	NR
11	NIS	1/1.5		CCl_4	70	trace
12	I_2	1/1.5		CCl_4	70	complex[d]
13	NBS	1/1.5		CH_3CN	70	trace
14	NBS	1/1.5		DMF	70	complex[d]
15	NBS	1/1.5		toluene	70	36
16	NBS	1/1.5		DCE	70	trace

[a]Reaction conditions: **1a** (0.2 mmol), halogen (*x* mmol), solvent (2.0 mL); the reactions were carried out at various temperatures. Then, the solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography. [b]Isolated yields. [c]Additive (0.02 mmol). [d]The reactions were complex during the bromide steps. [e]The residue was purified by neutral aluminum oxide column chromatography (Al_2O_3).

TABLE 4. Scope and Limitations of the Reactions of MCBs with NBS



entry[a]	1 (R^1/R^2)	1/NBS	time (h)	yield (%)[b] 4
1	**1b**, (*p*-ClC_6H_4/*p*-ClC_6H_4)	1/1.5	12	**4b**, 71
2	**1c**, (*p*-ClC_6H_4/C_6H_5)	1/1.5	12	**4c**, 73[c]
3	**1d**, (*p*-FC_6H_4/C_6H_5)	1/1.5	12	**4d**, 74[c]
4	**1o**, (*p*-FC_6H_4/*p*-FC_6H_4)	1/1.5	12	**4e**, 71
5	**1p**, (*p*-MeC_6H_4/C_6H_5)	1/3	3	**4f**, 84 (1.7:1.3)[d]
6	**1f**, (*m*,*p*-$Me_2C_6H_3$/C_6H_5)	1/3	3	**4g**, 81 (1.0:1.0)[d]
7	**1e**, (*o*,*p*-$Me_2C_6H_3$/C_6H_5)	1/3	3	**4h**, 81 (2.0:1.0)[d]
8	**1q**, (*p*-MeC_6H_4/*p*-MeC_6H_4)	1/3	3	**4i**, 79
9	**1r**, (C_4H_9/C_4H_9)	1/1.5	1	**4j**, complex
10	**1s**, Ph-	1/1.5	12	**4k**, complex
11	**1m**, (*p*-BrC_6H_4/Me)	1/1.5	12	**4l**, 54
12	**1t**, (*p*-BrC_6H_4/H)	1/1.5	12	**4m**, complex

[a]Reaction conditions: **1** (0.2 mmol), NBS (0.4 or 0.9 mmol), CCl_4 (2.0 mL); the reactions were carried out at 70 °C. Then, the solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography to give the corresponding products **4** in moderate to good yields. [b]Isolated yields. [c]The ratios could not be determined by NMR spectroscopic data. [d]The ratios were determined by ^{1}H NMR spectra.

complex product mixtures (Table 3, entry 2). Reducing the amounts of NBS to 1.0 equiv, the yield of **4a** was only 42% (Table 3, entry 3). Thus, the best ratio of **1a**:NBS was 1:1.5. The reaction did not take place at room temperature (20 °C) within 10 h (Table 3, entry 4). Product **4a** could also be obtained in 65% yield after purification with neutral aluminum oxide column chromatography (Al_2O_3) (Table 3, entry 5). Adding 2,2-azobisisobutyronitrile (AIBN) or benzoyl peroxide (BPO) as the radical initiator produced **4a** in 21% and 30% yield, respectively (Table 3, entries 6 and 7). In the presence of a radical inhibitor such as 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO), no reaction occurred, rendering likely the intervention of a radical pathway (Table 3, entry 8). With Br_2 instead of NBS, **4a** was obtained in 25% yield under identical conditions (Table 3, entry 9). When *N*-chlorosuccinimide (NCS), *N*-iodosuccinimide (NIS), or I_2 was used to replace NBS in the reaction with MCB **1a**, either no reaction was observed or a trace amount of **4a** and complex mixtures were obtained (Table 3, entries 10−12). The examination of the solvent effects revealed that CCl_4 was the best one for this transformation. Using toluene as the solvent afforded **4a** in 36% yield under the standard conditions. However, in acetonitrile or 1,2-dichloroethane (DCE), **4a** was formed in a trace amount, and in *N*,*N*-dimethylformamide (DMF), the reaction became disordered, affording complex product mixtures with many unidentified byproducts (Table 3, entries 13−16). Therefore, the best conditions are to carry out the reaction in CCl_4 at 70 °C with 1.0 equiv of **1a** and 1.5 equiv of NBS as the starting materials.

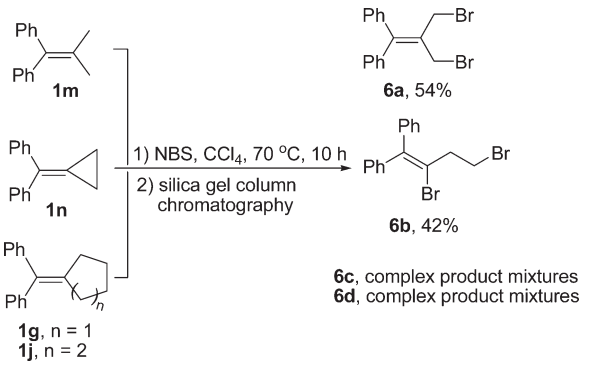
To confirm the structure of product **4a**, we further transferred **4a** to the corresponding ester product **5** with 4-nitrobenzoic acid as a colorless solid (see Scheme SI-2 in the Supporting Information). The X-ray crystal structure of **5** has been unambiguously determined and its CIF data are presented in the Supporting Information (Figure SI-1).[13]

With these optimal conditions in hand, we next carried out the reactions of a variety of MCBs **1** with NBS to examine the scope and limitations and the results of these experiments are shown in Table 4. It can be seen from Table 4, as for symmetrical MCBs **1b** and **1o** bearing electron-poor substituents on the benzene ring, the corresponding products **4b** and **4e** were obtained in 71% and 71% yield, respectively, after purification with silica gel column chromatography (Table 4, entries 1 and 4). In the case of unsymmetrical MCBs **1c** and **1d**, **4c** and **4d** were obtained in 73% and 74% yield, respectively, as isomeric mixtures (Table 4, entries 2 and 3). The isomeric ratios of **4c** and **4d** were determined after they were transformed to the compounds **2c** and **2d** by acetyl chloride in the presence of triethylamine (1.2 equiv) and DMAP (0.1 equiv) because the isomeric ratios of **2c** and **2d** could be determined by ^{1}H NMR spectroscopic data (see Scheme SI-3 in the Supporting Information).

As for MCBs **1p**, **1e**, **1f**, and **1q** bearing electron-rich substituents on the benzene ring, we found that a portion of starting materials **1** were recoverd under the standard conditions. Increasing the employed amount of NBS to 3.0 equiv afforded the corresponding products **4f**−**i** in 79−84% yields within 3 h after purification by silica gel column

(13) The crystal data of **5** have been deposited with the Cambridge Crystallographic Data Centre; deposition no. 687450. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre, 12 Union Rd., Cambridge CB2 1EZ, UK or via www.ccdc.cam.ac.uk/conts/retrieving.html. Empirical formula, $C_{24}H_{19}NO_4$; formula weight, 385.40; crystal color/habit, colorless/prismatic; crystal dimensions, 0.432 × 0.411 × 0.128 mm^3; crystal system, monoclinic; lattice type, primitive; lattice parameters, a = 18.083(2) Å, b = 13.6403(15) Å, c = 7.8790(9) Å, α = 90°, β = 97.809(2)°, γ = 90°, V = 1925.4(4)Å^3; space group, $P2(1)/c$; Z = 4; D_{calc} = 1.330 g/cm^3; F_{000} = 808; diffractometer, Rigaku AFC7R; residuals, R/Rw 0.0664/0.1729.

SCHEME 2. Reaction of 1 (0.2 mmol) with NBS (0.3 mmol) and Then Separation of Products by Silica Gel Column Chromatography

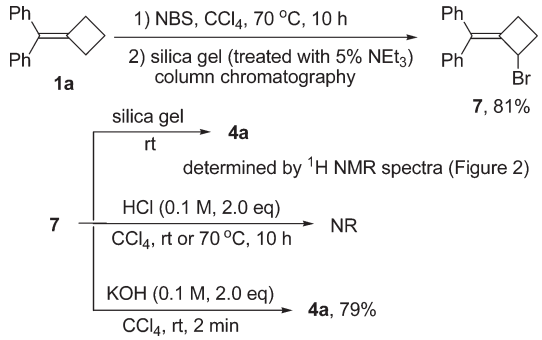


chromatography (Table 4, entries 5−8). Unfortunately, as for aliphatic MCBs **1r** and **1s**, complex reaction products were formed without the expected products **4j** and **4k** under the standard conditions (Table 4, entries 9 and 10). Furthermore, employing MCB **1m** with an aromatic substitute (R^1) and a methyl group (R^2) as the substrate gave the corresponding cyclobutanol **4*l*** in 54% yield (Table 4, entry 11). However, for MCB **1t** in which R^1 is an aromatic group and R^2 is a proton, the reaction became disordered and a complex product mixture was formed (Table 4, entry 12). The product structures of **4b**−**i** and **4*l*** were determined by NMR spectroscopic data, mass, HRMS, and microanalyses (see the Supporting Information).

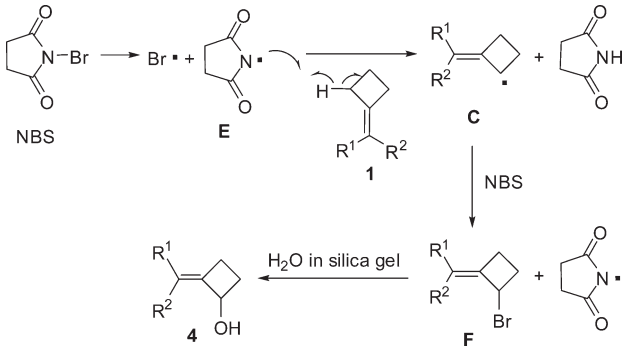
Under these optimal conditions, we further investigated the reaction of 2-methyl-1,1-diphenylpropene **1m** and diphenylmethylenecycloalkanes **1n**, **1g**, and **1j** with NBS. It was found that these reactions did not give the hydroxylation products (Scheme 2). In the case of **1m**, the corresponding dibrominated compound **6a**, derived from a radical reaction pathway, was obtained in 54% yield. Using diphenylmethylenecyclopropane **6b** as the substrate afforded the ring-opening product **6b** in 42% yield along with the recovery of the starting materials.[14] But by using diphenylmethylenecyclopentane **1g** and diphenylmethylenecyclohexane **1j** as the substrates under the standard conditions, the reactions became disordered, forming the complex product mixtures. Thus, the cyclobutane ring plays an important role in this transformation.

We found that if using the deactivated silica gel column chromatography to purify the product after reaction,[15] the brominated product **7** was obtained in 81% yield rather than **4a** (Scheme 3). Adding silica gel into the brominated product **7** in a ^{1}H NMR tube, we found that the cyclobutanol **4a** was produced after 10 min on the basis of ^{1}H NMR spectroscopic data shown in Figure SI-2 (Supporting Information). By stirring product **6** with 2.0 equiv of aqueous hydrochloric acid solution (0.1 M) in CCl_4 at 70 °C, no reaction occurred (Scheme 3). However, with use of aqueous potassium hydroxide solution (0.1 M) instead of aqueous hydrochloric acid

SCHEME 3. Control Experiments



SCHEME 4. A Proposed Reaction Mechanism



solution, we found that **6** could be transformed to **4a** within 2 min (Scheme 3).

To confirm the mechanism of this reaction, we performed deuterium-labeling studies using deuterated silica gel to purify the product.[16] Under the standard reaction conditions, the cyclobutanol **4a**-*d* with deuterated hydroxyl group (OD) was separated in 79% yield on the basis of the corresponding ^{1}H NMR spectroscopic data (see Figure SI-2 in the Supporting Information).

On the basis of the above experimental results, it is clear that the transformation of brominated compound **7** to **4a** can take place easily in silica gel, neutral aluminum oxide, and aqueous potassium hydroxide solution, suggesting that the hydroxylation of **7** by water could be assisted by silica gel and neutral aluminum oxide due to its particular structure. The detailed mechanistic investigation is underway on the basis of DFT calculation.

A plausible mechanism for the formation of cyclobutanols **4** is outlined in Scheme 4 based on the above deuterium labeling and control experiments. We proposed that the reaction proceeded through the Wohl−Ziegler reaction pathway.[17] The bromine radical Br and succinimidyl radical **E** are first produced by thermal cleavage of NBS.[18] The radical **E** abstracts a proton from the allylic position of MCB **1** to give radical **C** and succinimide. The radical **C** abstracts the bromo atom from NBS to afford the brominated product

(14) (a) Shao, L. X.; Zhao, L. J.; Shi, M. *Eur. J. Org. Chem.* **2004**, *23*, 4894–4900. (b) Zhou, H. W.; Huang, X.; Chen, W. L. *Synlett* **2003**, *13*, 2080–2082.

(15) The silica gel was stirred in petroleum ether with 5% NEt_3 for 24 h, then it was dried for 2 h at 120 °C.

(16) The silica gel was stirred in deuterium oxide (D_2O) for 48 h, then it was dried for 10 h at 120 °C.

(17) Wohl, A. *Ber. Dtsch. Chem. Ges.* **1919**, *52*, 51.

(18) For eamples for similar bromination reaction, see: (a) Kim, S. S.; Choi, S. Y.; Kang, C. H. *J. Am. Chem. Soc.* **1985**, *107*, 4234–4237. (b) Heasley, V. L.; Louie, T. J.; Luttrull, D. K.; Millar, M. D. *J. Org. Chem.* **1988**, *53*, 2199–2204. (c) Buckles, R. E.; Johnson, R. C. *J. Org. Chem.* **1957**, *22*, 55–59.

F ($R^1 = R^2 =$ Ph, product **F** = product **7**). Purification of **F** with the silica gel column chromatography produces the cyclobutanol **4** through hydroxylation.

This is a very simple and convenient synthetic approach to obtain the methylenecyclobutanol compounds from methylenecyclobutanes without using other reagents except NBS under mild reaction conditions, although it is only limited to diarylmethylenecyclobutanes (both R^1 and R^2 = aromatic rings).

Conclusions

In summary, we have developed fairly efficient acetoxylation and hydroxylation reactions of diarylmethylenecycloalkanes with $PhI(OAc)_2$, I_2, $TsNH_2$, and NBS respectively upon heating through radical process to produce the corresponding products in moderate to good yields under mild conditions. In the case of methylenecyclobutanes, an unexpected transformation of methylenecyclobutanes to methylenecyclobutanols via bromination with *N*-bromosuccinimide and silica gel purification was discovered through a Wohl−Ziegler reaction pathway. These functionalized cyclo-compounds are a useful structural motif in the synthesis of many natural products and bioactive compounds.[19] Plausible mechanisms have been proposed. Clarification of the reaction mechanism and further application of this transformation are in progress.

Experimental Section

These olefin starting materials are not commercially available and they have been prepared according to previous literature.[20]

General Procedure for the Reactions. Preparation of the Products 2. Under ambient atmosphere, diarylmethylenecycloalkanes **1** (0.2 mmol) and $PhI(OAc)_2$ (0.3 mmol), $TsNH_2$ (0.06 mmol), and I_2 (0.03 mmol) were added into a Schlenk tube. The reaction mixture was stirred at 60 °C in DCE. After 5 min another sample of I_2 (0.03 mmol) was added into the reaction mixtures. The reaction was completed after 10 min. The solvent was removed under reduced pressure and the residue was purified by the 300−400 mesh silica gel column chromatography with ethyl acetate and petroleum ether (1:30) under room temperature (22−24 °C) to give the corresponding products **2** in moderate to good yields.

Preparation of the Products 4. Under ambient atmosphere, methylenecybutanes **1** (MCBs) (0.2 mmol) and NBS (0.3 mmol) were added into a Schlenk tube. The reaction mixture was stirred at 70 °C in CCl_4 until the reaction was complete. Then, the solvent was removed under reduced pressure and the residue was purified by 32 g of 300−400 mesh silica gel column chromatography with ethyl acetate and petroleum ether (1:10) at room temperature (22−24 °C) to give the corresponding products **4** in moderate to good yields.

2-(Diphenylmethylene)cyclobutyl acetate (2a): olorless oil; IR (CH_2Cl_2) ν 3055, 2951, 1737, 1599, 1370, 1072, 1033, 939, 769, 700, 633 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 1.72 (3H, s, CH_3), 2.09−2.16 (1H, m, CH_2), 2.46−2.53 (1H, m, CH_2), 2.70 (1H, ddd, J = 16.0, 8.0, 8.0 Hz, CH_2), 2.94−3.01 (1H, m, CH_2), 5.90−5.94 (1H, m, CH), 7.17−7.33 (10H, m, ArH); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 20.7, 26.2, 27.1, 71.5, 126.8, 126.9, 127.8, 128.1, 128.5, 129.2, 137.1, 137.7, 139.2, 139.8, 169.9; MS (EI) m/z (%) 278 (40.88) [M^+], 236 (81.19), 218 (100.00), 203 (23.54), 178 (27.35), 129 (32.60), 115 (40.75), 91 (83.09); HRMS (EI) calcd for $C_{19}H_{18}O_2$ (M^+) requires 278.1307, found 278.1303.

2-(Diphenylmethylene)cyclobutanol (4a): colorless oil; IR (CH_2Cl_2) ν 3549, 3022, 2854, 1727, 1607, 1510, 1446, 1118, 1042, 820, 723 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 1.66 (1H, br s, OH), 1.99−2.08 (1H, m, CH_2), 2.37−2.45 (1H, m, CH_2), 2.62 (1H, ddd, J = 18.0, 9.0, 9.0 Hz, CH_2), 2.87−2.98 (1H, m, CH_2), 5.03−5.08 (1H, m, CH), 7.19−7.37 (10H, m, ArH); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 25.2, 28.7, 71.5, 128.5, 128.6, 129.8, 130.5, 132.8, 133.1, 133.4, 137.6, 138.2, 144.3; MS (EI) m/z (%) 236 (61.86) [M^+], 218 (81.84), 208 (63.99), 178 (46.28), 159 (45.66), 115 (47.65), 91 (100.00), 77 (33.86); HRMS (EI) calcd for $C_{17}H_{16}O$ (M^+) requires 236.1201, found 236.1202.

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Supporting Information Available: Spectroscopic data (^1H, ^{13}C spectroscopic data), HRMS of the compounds shown in the tables, the X-ray crystal structure of compound **7**, along with the detailed description of experimental procedures. This material is available free of charge via the Internet at http://pubs.acs.org.

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