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An efficient protocol for the synthesis of brominated norbornene, norbornadiene, and benzonorbornadiene

Selçuk EŞSİZ*
Department of Chemistry, Faculty of Science, Atatürk University, Erzurum, Turkey

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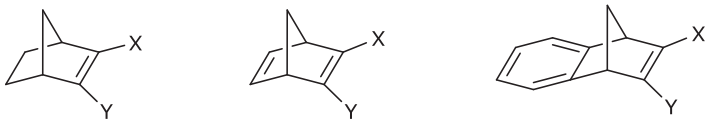
Abstract: An efficient protocol for the synthesis of 2-bromonorbornene, 2-bromonorbornadiene, 2-bromoben- zonorbornadiene, 2,3-dibromonorbornene, 2,3-dibromonorbornadiene, and 2,3-dibromobenzonorbornadiene in good yields has been developed. 1,2-Dibromotetrachloroethane is used as the brominating agent for these reactions. The results are discussed in comparison with alternative methods in the literature.

Key words: 2,3-Dibromonorbornene, 2,3-dibromonorbornadiene, 2,3-dibromobenzonorbornadiene, 1,2-dibromotetrachloroethane

1. Introduction

The reactivity of bicyclo[2.2.1]alkenes is higher than that of other alkenes because they have a unique geometry, and they are important compounds in synthetic organic chemistry (Figure). The photoisomerization reaction of norbornadiene derivatives to quadricyclanes is reported to be of potential use for molecular solar-thermal energy storage systems and molecular photoswitches.[1–3] The traditional method for forming substituted bicycles involves the Diels–Alder reaction, but this method is limited. Therefore, many groups have investigated alternative methods for the synthesis of substituted bicyclo[2.2.1]alkenes.[4–6] Bicyclo[2.2.1]alkenes have found a wide range of applications in science.[7–14] One of the easiest ways to derivatize bicyclo[2.2.1]alkenes is to use their brominated derivatives. Therefore, in this work, we aimed to efficiently synthesize 2-bromobicyclo[2.2.1]alkenes using a mixture of t-BuOK/n-BuLi and 1,2-dibromotetrachloroethane (DBTCE) and 2,3-dibromobicyclo[2.2.1]alkenes using lithium diisopropylamide (LDA) and DBTCE.



1, X=Y=H
2, X=Br, Y=H
3, X=Y=Br

4, X=Y=H
5, X=Br, Y=H
6, X=Y=Br

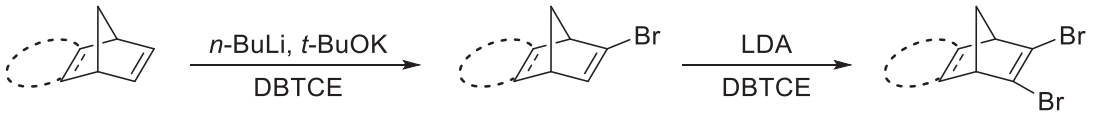
7, X=Y=H
8, X=Br, Y=H
9, X=Y=Br

Figure. Structure of bicyclics.

*Correspondence: sessiz@atauni.edu.tr

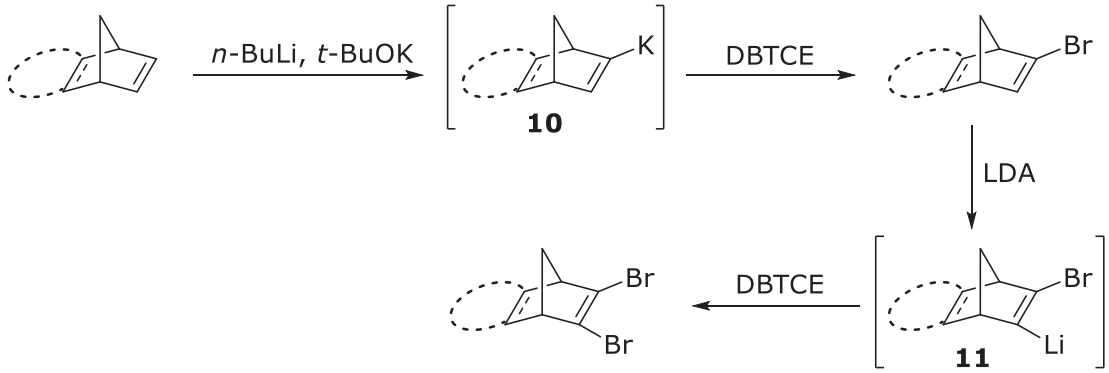
2. Results and discussion

Our strategy, which involves trapping of metallated bicyclics with DBTCE, leads to the formation of 2-bromo or 2,3-dibromobicyclics (Scheme 1). In the first step, a synthetic procedure modified from that reported by Szeimies was used.[15] To obtain monobromides **2**,[14,16] **5**,[15–17] and **8**,[16,18] *n*-BuLi was added to a solution of the alkene and *t*-BuOK in THF, followed by trapping with DBTCE. In a further step, to deprotonate monobromides, LDA was added to a solution of monobromide in THF and the solution was treated with DBTCE to give dibromides **3**,[14,16] **6**,[15–17,19] and **9**[16] (Scheme 1).



Scheme 1. Synthesis of 2- and 2,3-brominated bicyclo[2.2.1]alkenes.

To deprotonate the alkenes (Scheme 2), in the first step, *n*-butyl lithium was slowly added to a solution of alkenes and potassium *tert*-butoxide in THF to give a yellow solution of the potassium coordinated bicyclic alkenes **10**. When the solution of **10** was reacted with DBTCE in THF, the desired monobromides **2**, **5**, and **8** were successfully obtained in 52%, 56%, and 45% yields, respectively. Similarly, in the second step, monobromoalkenes were added to the solution of LDA, which is easily prepared by addition of *n*-BuLi to the solution of diisopropylamine in THF, and to the obtained solution of the lithium coordinated deprotonated bicyclic alkenes **11** was added a solution of DBTCE in THF. Dibromides **3**, **6**, and **9** were obtained in 75%, 77%, and 85% yields, respectively.



Scheme 2. Reaction steps.

Tam et al. and Moth-Poulsen et al. reported that the yield of 2,3-dibromonorbornadiene (**6**) based on *t*-BuOK was 65%[17] and 37%[19] and based on norbornadiene (**4**) was 16%[17] and 15%,[19] respectively. In this study, the yield of 2,3-dibromonorbornadiene (**6**) is 43% for two steps. In a previous study, the starting material, norbornadiene (**4**), was also used over stoichiometric amounts. The bromination reaction of norbornadiene (**4**) to obtained 2,3-dibromonorbornadiene resulted in formation of 2-bromonorbornadiene (**5**) and 2,3-dibromonorbornadiene (**6**).[17] The synthesis of brominated norbornene and benzonorbornadiene was limited via this strategy in the literature. Ryu et al. also reported that DBTCE was an excellent brominating agent compared to Br_2 and NBS and employed it as an electrophile for α-bromination reaction of ketones.[20]

In conclusion, in the present study, the yield of products is high compared to the previously published procedure. The advantages of this methodology are that it has prevented the use of overstoichiometric amounts

of alkene, it represented relatively good yields, and it obtained a single product for dibromides compared to previous methods. An alternative method has been developed for the synthesis of brominated norbornenes and benzonorbornadienes. This method can be also applied for bromination of other bicyclics to their corresponding bromides.

3. Experimental

All reactions were carried out under argon using Schlenk techniques. The reaction flask was heated at reduced pressure with a heat gun and flushed with argon. All solvents were dried and distilled before use. Column chromatography was performed using silica gel 60 (Merck) and chromatography was carried out using petroleum ether as eluent. All analytical data were consistent with those of previous reports.

3.1. General method for monobromides

A 50-mL well-dried Schlenk flask was charged with argon through a Schlenk line. To a solution of alkenes (20.0 mmol) and KOt-Bu (2.5 g, 22.3 mmol) in THF (20 mL), $n-$BuLi in hexane (2.5 M, 8.8 mL, 22.0 mmol) was added dropwise at –78 °C over 1 h. The mixture was stirred at –40 °C for 1 h and cooled again to –78 °C. A solution of DBTCE (6.51 g, 20.0 mmol) was added over 15 min and the mixture was stirred at –60 °C for 1 h. The reaction mixture was allowed to come to RT and stirred for 2 h. The reaction mixture was quenched with saturated ammonium chloride (20 mL), the aqueous layer was extracted with diethyl ether (3 ×20 mL), and the combined organic layers were washed with brine (25 mL), dried over Na_2SO_4, and concentrated under vacuum. The residue was purified by column chromatography (silica gel, 50 g, petroleum ether) to give the product.

2-Bromonorbornene (**2**): ^{1}H NMR (400 MHz, $CDCl_3$)δ = 6.01 (d, J = 3.0 Hz, 1H), 2.87–2.91 (m, 2H), 1.65–1.69 (m, 2H), 1.60 (m, 1H), 1.10–1.20 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$)δ = 134.8, 125.6, 50.4, 48.1, 44.0, 25.9, 24.3.

2-Bromonorbornadiene (**5**): ^{1}H NMR (400 MHz, $CDCl_3$)δ = 6.89 (dd, J = 5.2 and 2.9 Hz, A part of AB system, 1H), 6.77 (dd, J = 5.2 and 2.9 Hz, A part of AB system, 1H), 6.64 (d, J = 3.3 Hz, 1H), 3.61 (m, 1H), 3.48 (m, 1H), 2.26 (dt, J = 6.0 and 1.5 Hz, A part of AB system, 1H), 2.07 (dt, J = 6.0 and 1.8 Hz, A part of AB system, 1H). ^{13}C NMR (100 MHz, $CDCl_3$)δ = 143.1, 142.0, 139.8, 136.9, 74.1, 58.5, 51.8.

2-Bromobenzonorbornadiene (**8**): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.33 (dd, J = 6.0 and 2.0 Hz, 1H), 7.22 (dd, J = 6.0 and 2.0 Hz, 1H), 7.04–6.91 (m, 2H), 6.48 (d, J = 3.5 Hz, 1H), 3.92 (s, 1H), 3.71 (s, 1H), 2.57 (d, J = 6.5 Hz, 1H), 2.32 (d, J = 6.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$)δ 150.3, 149.5, 148.4, 135.6, 125.2, 124.6, 122.1, 121.6, 68.8, 56.7, 50.7.

3.2. General method for dibromides

A 50-mL well-dried Schlenk flask was charged with argon through a Schlenk line. A solution of n-BuLi in hexane (2.5 M, 4.4 mL, 11.0 mmol) was added to a solution of dry diisopropylamine (1.55 mL, 11.1 mmol) in dry THF (10 mL) at 0 °C and cooled at –78 °C. A solution of monobromides (10.0 mmol) in dry THF (10 mL) was added over 15 min and the mixture was stirred at the same temperature for 1 h. A solution of DBTCE (3.3 g, 10.1 mmol) in dry THF (10 mL) was added dropwise and the temperature was left to rise to RT overnight. The reaction mixture was quenched with saturated ammonium chloride (20 mL), the aqueous layer was extracted with diethyl ether (3 ×20 mL), and the combined organic layers were washed with brine (25 mL), dried over

Na_2SO_4, and concentrated under vacuum. The residue was purified by column chromatography (silica gel, 50 g, petroleum ether).

2,3-Dibromonorbornene (**3**): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.98–3.03 (m, 2H), 1.78 (dt, J = 8.2 and 1.6 Hz, A part of AB system, 1H), 1.69 (AA' part of AA'BB' system, 2H), 1.32 (BB' part of AA'BB' system, 2H), 1.21 (dt, J = 8.2 and 1.8 Hz, A part of AB system, 1H). ^{13}C NMR (100 MHz, $CDCl_3$)δ = 125.4, 51.6, 47.0, 25.7.

2,3-Dibromonorbornadiene (**6**): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.89 (t, J = 1.9 Hz, 2H), 3.63 (p, J = 1.8 Hz, 2H), 2.46 (dt, J = 6.3 and 1.8 Hz, A part of AB system, 1H), 2.17 (dt, J = 6.3 and 1.8 Hz, A part of AB system, 1H). ^{13}C NMR (100 MHz, $CDCl_3$)δ = 143.3, 135.1, 60.7, 28.9.

2,3-Dibromobenzonorbornadiene (**9**): ^{1}H NMR (400 MHz, $CDCl_3$)δ = 7.36–7.30 (AA' part of AA'BB' system, 2H), 7.27–6.99 (BB' part of AA'BB' system, 2H), 3.92–3.95 (m, 2H), 2.77 (dt, J = 7.4 and 1.6 Hz, A part of AB system, 1H), 2.40 (dt, J = 7.4 and 1.8 Hz, A part of AB system, 1H). ^{13}C NMR (100 MHz, $CDCl_3$)δ = 149.9, 135.8, 127.5, 124.1, 69.2, 60.8.

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