



# *N*-Bromosuccinimide-dibenzoyl peroxide/azobisisobutyronitrile: a reagent for *Z*- to *E*-alkene isomerization<sup>☆</sup>

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Received 25 April 2003; revised 13 June 2003; accepted 3 July 2003

Dedicated to Dr B. G. Hazra, OCS, NCL, Pune

**Abstract**—*N*-Bromosuccinimide-dibenzoyl peroxide/azobisisobutyronitrile is used to carry out several types of *Z*- to *E*-alkene isomerizations. The NBS-bromination conditions are sufficient for both allylic bromination and alkene isomerization. When the allylic hydrogens are not available in substrates, only the isomerization of the alkene takes place. The present conditions for isomerization of carbon–carbon double bonds are mild and efficient.

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## 1. Introduction

The generation of carbon–carbon double bonds in geometrically pure form is one of the most important reactions in synthetic organic chemistry<sup>1</sup> and many elegant methods are known in the literature.<sup>2</sup> However, in some of the reactions mixtures of *Z*- and *E*-alkenes are also formed<sup>2,3</sup> and radical<sup>4</sup> or photochemical<sup>5</sup> reactions have been used to transform the *Z*-isomers to the corresponding *E*-isomers. Isomerization of (*Z*)-stilbene to the *E*-isomer and dimethyl maleate to dimethyl fumarate are usually catalyzed by bromine via the reversible addition of a bromine radical to the double bond.<sup>6</sup> Very recently Spencer et al. have demonstrated<sup>7</sup> a facile palladium(II)-catalyzed isomerization of *Z*-arylalkenes to *E*-arylalkenes. The provision of a new method for isomerization of *Z*-olefins to *E*-olefins is a challenging task of current interest and in this context, we herein report an easy access to several types of geometrically pure *E*-olefins using *N*-bromosuccinimide-dibenzoyl peroxide/azobisisobutyronitrile (NBS-DBP/AIBN) reagent.

## 2. Results and discussion

In our on going studies<sup>8</sup> on the synthesis of recently isolated bioactive natural products, we carried out the reaction of dimethyl methylmaleate with NBS-AIBN and obtained

dimethyl bromomethylfumarate in 85% yield. Both allylic bromination and isomerization of the carbon–carbon double bond took place in one-pot via an in situ addition–elimination of the bromine radical, which was further confirmed by obtaining the same product from dimethyl methylfumarate (Table 1, Entry 3). On the basis of this observation,<sup>9</sup> we prepared a systematic plan to study the NBS-DBP/AIBN induced *Z*- to *E*- carbon–carbon double bond isomerization with several types of olefins having a variety of substituents. The results are presented in Scheme 1 and Table 1. Maleic acid, on treatment with NBS-DBP in refluxing acetic acid, gave fumaric acid in 90% yield, while dimethyl maleate, on treatment with NBS-AIBN in refluxing CCl<sub>4</sub> gave dimethyl fumarate in 98% yield (Entries 1 and 2). The process of carbon–carbon double bond isomerization was found to be slow in tetrasubstituted dimethyl dimethylmaleate using 1.1 equiv. of NBS while the use of 2.5 equiv. of NBS gave a 1:1 mixture of dimethyl dibromomethylmaleate and dimethyl dibromomethylfumarate in 96% yield (Entry 4). Interestingly, dimethyl methoxymaleate, on treatment with NBS-DBP in refluxing CCl<sub>4</sub>, did not show any reaction. On the contrary, the corresponding dimethyl methoxyfumarate underwent very smooth carbon–carbon double bond isomerization to yield dimethyl methoxymaleate in 92% yield, revealing that the *E*-isomer is thermodynamically more stable than the *Z*-isomer (Entries 5 and 6). Methyl maleanilate and methyl *Z*-cinnamate, under similar reaction conditions, gave the corresponding *E*-products in 90% and 96% yields respectively (Entries 7 and 8). As expected, methyl *Z*-oleate on treatment with NBS-DBP in refluxing CCl<sub>4</sub> gave the methyl *E*-dibromooleate in 95% yield, while under the same set of reaction conditions *Z*-stilbene was transformed into *E*-stilbene in ~100% yield (Entries 9 and 10).

<sup>☆</sup> NCL Communication No. 6645.

**Keywords:** isomerization; NBS-bromination; carbon–carbon double bonds.

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**Table 1.** NBS-DBP/AIBN induced carbon–carbon double bond isomerizations

Entry	Starting material <sup>a</sup>	Reaction conditions	Product	Yield (%)
1		NBS (2.0 equiv.), DBP, AcOH, reflux, 6 h		90
2		NBS (1.1 equiv.), AIBN, CCl4, reflux, 1 h		98
3		NBS (1.5 equiv.), AIBN, CCl4, reflux, 12 h		85
4		NBS (2.5 equiv.), DBP, CCl4, reflux, 2 h		46 <sup>b</sup>
5		NBS (2.0 equiv.), DBP, CCl4, reflux, 8 h	No Reaction	0
6		NBS (2.0 equiv.), DBP, AcOH, reflux, 8 h		92
7		NBS (4.0 equiv.), DBP, CCl4, reflux, 10 h		90
8		NBS (1.1 equiv.), AIBN, CCl4, reflux, 2 h		96
9		NBS (2.5 equiv.), DBP, CCl4, reflux, 4 h		95
10		NBS (2.0 equiv.), DBP, CCl4, reflux, 3 h		~100
11		NBS (1.1 equiv.), DBP, CCl4, reflux, 2 h		60 <sup>c</sup>

<sup>a</sup> The *Z*-alkenes and geometric mixtures of alkenes were prepared by using known literature procedures.<sup>7,12</sup>

<sup>b</sup> 50% Dimethyl dibromomethylmaleate was also formed.

<sup>c</sup> 10–15% Mixture of ring brominated products was also obtained. Ar=3,5-dimethoxyphenyl; Ar'=p-methoxyphenyl.

*Z*-Trimethoxystilbene, on treatment with NBS (1.1 equiv.) and DBP (catalytic) in refluxing CCl<sub>4</sub> gave the trimethoxy derivative of bioactive resveratrol<sup>11</sup> in 60% yield and due to the mesomeric effect of the –OMe groups, we also observed 10–15% formation of mixtures of ring brominated *E*-trimethoxystilbene derivatives (Entry 11). As indicated in Table 1, we could isomerize different types of olefins with a variety of substituent patterns from *Z*- to *E*- forms using NBS-DBP/AIBN and the present method is simple and efficient.

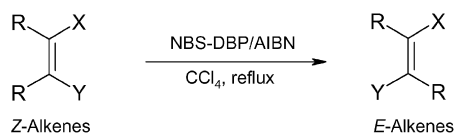
### 3. Conclusion

In summary, we have demonstrated that the reagent NBS-DBP does both allylic bromination and several types of *Z*- to *E*- carbon–carbon double bond isomerization. The *Z*-alkenes without allylic hydrogens in pure form or mixtures of geometric isomers can be easily transformed into the corresponding *E*-alkenes using NBS-DBP/AIBN in quantitative yields. The present studies also provide a useful caution mark to the chemists attempting allylic bromination of *Z*-alkenes.

### 4. Experimental

#### 4.1. General

Melting points are uncorrected. Column chromatographic separations were carried out on silica gel (60–120 mesh). Commercially available *N*-bromosuccinimide, dibenzoyl peroxide, azobisisobutronitrile, maleic acid, dimethyl maleate and ethyl *Z*-oleate were used. The *Z*-alkenes and



R = H, CO<sub>2</sub>H, CO<sub>2</sub>Me; X/Y = H, Me, Alkyl, CH<sub>2</sub>Br, CHBr<sub>2</sub>, Ph, Aryl, CO<sub>2</sub>Me, CONHAr

**Scheme 1.**

geometric mixtures of alkenes were prepared by using known literature procedures.<sup>7,12</sup>

#### 4.2. General procedure for the isomerization of *Z*-alkenes to *E*-alkenes

A mixture of *Z*-alkene, *N*-bromosuccinimide and catalytic amount of DBP/AIBN (10 mol%) in carbon tetrachloride (5–10 mL per mmol of substrate) was gently refluxed (see Table 1). The mixture was allowed to cool to room temperature and then filtered. The residue was washed with CCl<sub>4</sub> and the combined organic layer was washed with water, brine, dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated in vacuo. The obtained residue was purified by silica gel column chromatography using petroleum ether/ethyl acetate as an eluent to obtain the desired *E*-alkene.

**4.2.1. Fumaric acid.** 90% Yield; crystalline solid; mp 298–300°C (sublimes) [lit.<sup>13</sup> mp 299–300°C (sublimes)]. Spectroscopic data are identical to that reported in the literature.<sup>14</sup>

**4.2.2. Dimethyl fumarate.** 98% Yield; crystalline solid; mp 100–101°C (lit.<sup>13</sup> mp 103–104°C). Spectroscopic data are identical to that reported in the literature.<sup>14</sup>

**4.2.3. Dimethyl bromomethylfumarate.** 85% Yield; thick oil. Spectroscopic data are identical to that reported in the literature.<sup>8a</sup>

**4.2.4. Dimethyl dibromomethylmaleate.** 50% Yield; thick oil. Spectroscopic data are identical to that reported in the literature.<sup>2f</sup>

**4.2.5. Dimethyl dibromomethylfumarate.** 46% Yield; thick oil. Spectroscopic data are identical to that reported in the literature.<sup>2f</sup>

**4.2.6. Dimethyl methoxymaleate.** 92% Yield; thick oil. Spectroscopic data are identical to that reported in the literature.<sup>12b</sup>

**4.2.7. Methyl fumaranilate.** 90% Yield; mp 164–165°C; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz) δ 3.83 (s, 3H), 6.85–7.65 (m, 7H), 7.90–8.20 (m, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 125 MHz) δ 52.3, 120.1, 121.6, 125.2, 129.2, 132.2, 137.3, 161.5, 165.9; IR (CHCl<sub>3</sub>) ν<sub>max</sub> 3325, 1717, 1684, 1659 cm<sup>-1</sup>. Anal. calcd for C<sub>11</sub>H<sub>11</sub>NO<sub>3</sub>: C, 64.38; H, 5.40. Found: C, 64.42; H, 5.37.

**4.2.8. Methyl *E*-cinnamate.** 96% Yield; mp 36–38°C (lit.<sup>13</sup> mp 36–38°C). Spectroscopic data are identical to that reported in the literature.<sup>14</sup>

**4.2.9. Ethyl 9(*E*)-8,11-dibromo-octadecenoate.** 95% Yield; thick oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz) δ 0.88 (t, *J*=6 Hz, 3H), 1.26 (m, 21H), 1.50–2.00 (m, 4H), 2.29 (t, *J*=8 Hz, 2H), 4.13 (q, *J*=8 Hz, 2H), 4.40–4.90 (m, 2H), 5.70–6.00 (m, 2H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 125 MHz) δ 14.0, 14.2, 21.0 (2-CH<sub>2</sub>), 22.6, 24.8, 29.1–29.6 (8-CH<sub>2</sub>), 31.9, 34.3, 60.0, 128.3 (2-CH<sub>2</sub>), 173.8; IR (neat) ν<sub>max</sub> 1730, 1462, 1373, 1180, 1034, 962 cm<sup>-1</sup>. Anal. calcd for C<sub>20</sub>H<sub>36</sub>Br<sub>2</sub>O<sub>2</sub>: C, 51.30; H, 7.75. Found: C, 51.25; H, 7.83.

**4.2.10. *E*-Stilbene.** ~100% Yield; crystalline solid; mp 122–123°C (lit.<sup>13</sup> mp 122–124°C). Spectroscopic data are identical to that reported in the literature.<sup>14</sup>

**4.2.11. *E*-4-Methoxy-3',5'-dimethoxystilbene.** 60% Yield; crystalline solid; mp 78°C. Spectroscopic data are identical to that reported in the literature.<sup>7</sup>

#### Acknowledgements

M. M. B. and A. K. thank CSIR, New Delhi, for the award of a research fellowship. N. P. A. thanks the Department of Science and Technology, New Delhi, for financial support. We thank Dr K. N. Ganesh, Head, Division of Organic Chemistry (Synthesis) for constant encouragement.

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