PART B

Regioselective monobromination of least reactive alkanes and cycloalkanes
VIB. 1. NaBr/98% H₂SO₄: AN EFFICIENT REAGENT FOR THE REGIOSELECTIVE MONOBROMINATION OF LEAST REACTIVE ALKANES AND CYCLOALKANES

VIB. 1.1. INTRODUCTION

Most of these reagents available for brominating are complex with potential environmental problems due to the generation of hazardous waste and handling of molecular Br₂ is generally found to be difficult. However, each example has its own specific set of conditions, hence the reagents have their own advantages and limitations. Therefore, there is a need for the development of alternative methods for the bromination of least reactive acyclic and cycloalkanes using simple reagents. We in our work suggest that, the combination of NaBr and 98% H₂SO₄ could allow the bromination of deactivated alkanes and cyclic hydrocarbons. This combination indeed acts as a very effective reagent for bromination of the saturated hydrocarbons by easy to handle, economically viable NaBr and 98% H₂SO₄. This method gives the products in good yields within short reaction duration (Scheme VIB.1, 2).

\[
\begin{align*}
H_n & \xrightarrow{\text{NaBr/98% H}_2\text{SO}_4} \text{Br} \\
n = 1, 2, 3 & \text{40-65 °C, 15-35 min}
\end{align*}
\]

Scheme VIB.1.

\[
\begin{align*}
\text{C}_{5}H_{n} & \xrightarrow{\text{NaBr/98% H}_2\text{SO}_4} \text{Br} \\
n = 1, 2, 3 & \text{40-65 °C, 15-35 min}
\end{align*}
\]

Scheme VIB.2.

VIB. 1.2. RESULTS AND DISCUSSION

Previous work from our laboratory describes the nuclear monohalogenation (bromination and iodination) of electron rich arenes by tetraalkylammonium halides or alkali metal halides in presence of conc. H₂SO₄.[13–15] In continuation of our work on bromination reactions, we are
reporting a simple and convenient method of bromination of unactivated acyclic and cyclic alkanes by NaBr / 98% H₂SO₄ at 40–65 °C. This is a new protocol, the yields are high and the reactions go to completion within 15–35 min.

The present reaction is expected to proceed by the in situ generation and reaction of the bromine molecule[13–14] formed from NaBr and 98% H₂SO₄ at 40–65 °C (which can be made out from appearance and disappearance of bromine color), and is regioselective, in the sense, more substituted bromide is formed from acyclic alkanes as shown in (Scheme VIB.3).

\[
\begin{align*}
\text{NaBr} + \text{H}_2\text{SO}_4 & \rightarrow \text{NaHSO}_4 + \text{HBr} \\
2 \text{HBr} + \text{H}_2\text{SO}_4 & \rightarrow \text{Br}_2 + 2 \text{H}_2\text{O} + \text{SO}_2 \\
\text{Br}_2 + \begin{array}{c}n \\
\text{H}
\end{array} & \rightarrow \begin{array}{c}n \\
\text{Br}
\end{array}
\end{align*}
\]

Scheme VIB.3.

A series of hydrocarbons were subjected to bromination by NaBr/98% H₂SO₄ in order to find the applicability of the reagent system. The results of this study are listed in Table VIB.1.
Table VIB.1: Bromination of alkanes and cycloalkanes by NaBr/98% H₂SO₄

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Reaction Temp (°C)</th>
<th>Reaction time (min)</th>
<th>Producta</th>
<th>Yield (%)b</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>n-Pentane</td>
<td>45</td>
<td>30</td>
<td>2-Bromopentane</td>
<td>78</td>
</tr>
<tr>
<td>2</td>
<td>n-Hexane</td>
<td>55</td>
<td>30</td>
<td>2-Bromohexane</td>
<td>75</td>
</tr>
<tr>
<td>3</td>
<td>n-Heptane</td>
<td>50</td>
<td>30</td>
<td>2-Bromoheptane</td>
<td>85</td>
</tr>
<tr>
<td>4</td>
<td>Cyclopentane</td>
<td>65</td>
<td>20</td>
<td>Cyclobromopentane</td>
<td>72</td>
</tr>
<tr>
<td>5</td>
<td>Cyclohexane</td>
<td>65</td>
<td>15</td>
<td>Cyclobromohexane</td>
<td>75</td>
</tr>
<tr>
<td>6</td>
<td>Cycloheptane</td>
<td>65</td>
<td>20</td>
<td>Cyclobromoheptane</td>
<td>70</td>
</tr>
</tbody>
</table>

a Characterized by IR, 1H NMR or GC-mass spectral analysis and by comparison with authentic samples. b Isolated yields.

VIB. 1.3. EXPERIMENTAL

Cyclopentane was prepared from cyclopentanone by Clemmensen reduction. All the solvents used and other alkanes were commercially available and distilled before use. Reactions were monitored on TLC and by GC with reference samples. Yields refer to the isolated yields of the products after purification by column chromatography (light petrol). IR, 1H NMR and GC-MS spectra were recorded on Nicolet 400D FT-IR Spectrophotometer, 300 MHz Brucker Spectrometer and SHIMADZU GC-MS QP 5050A instrument equipped with a 30 m long and 0.32 mm dia BP-5 column with the column temperature programme 80–15–250 °C respectively.

VIB. 1.4. GENERAL PROCEDURE FOR THE BROMINATION OF n-HEXANE

In a typical experiment, NaBr (1.03 g, 10 mmol) and 98% H₂SO₄ (1.96 g, 20 mmol) were treated with n-hexane (1.72 g, 20 mmol) and the contents were heated with constant stirring in an oil bath at 40–65 °C. After completion of the reaction (15 min, GC), the reaction was quenched with water (10 ml) and the organic layer was extracted with ether (3 × 10 mL), the combined ethereal extract was washed with saturated sodium bicarbonate solution, water and dried over anhydrous

Monobromonation of least reactive alkanes and cycloalkanes

229
sodium sulphate and the solvent was evaporated. The product after drying under vacuum was identified to be 2-bromohexane by the IR, $^1$H NMR, and mass spectral analysis.

**VIB. 1.5. CONCLUSIONS**

In conclusion, a novel approach to regioselective bromination of alkanes and cycloalkanes by NaBr/98% H$_2$SO$_4$ has been described. The reactions involve simple workup, use of commercial, readily available and inexpensive chemicals and high yields of the product make this procedure a useful alternative to the currently available methods.
VIB. 1.6. SPECTRAL DATA

**2-Bromopentane (1a)**

IR (neat) ν: 2996, 2936, 2875, 2733, 1468, 1466, 1430, 1380, 1302, 1297, 1263, 1202, 1149, 1071, 1028, 980, 872, 844, 638, 818 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz): δ 0.99–0.96 (m, 3H, CH₃), 1.40–1.6 (m, 2H, CH₂), 1.78–1.70 (m, 2H, CH₂), 1.79 (m, 3H, CH₃), 3.6 (m, 1H, CH) ppm; MS (70 ev), m/Z: 151 [M⁺]

**2-Bromohexane (2a)**

IR (neat) ν: 2961, 2931, 2874, 2862, 2835, 2734, 1467, 1378, 1345, 1303, 1290, 1238, 1194, 1045, 1007, 980, 885, 800, 750, 620, 532 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz): δ 0.93–0.86 (m, 3H, CH₃), 1.24–1.18 (m, 2H, CH₂), 1.36–1.26 (m, 2H, CH₂), 1.7 (m, 3H, CH₃), 3.5 (m, 1H, CH) ppm; MS (70 ev), m/Z: 165 [M⁺]

**2-Bromoheptane (3a)**

IR (neat) ν: 2966, 2930, 2872, 2828, 2737, 1465, 1430, 1380, 1300, 1292, 1286, 1260, 1200, 1149, 1080, 1076, 1025, 990, 927, 875, 845, 613 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz): δ 0.9–0.87 (m, 3H, CH₃), 1.24–1.21 (m, 2H, CH₂), 1.31 (m, 2H, CH₂), 3.48 (m, 1H, CH) ppm; MS (70 ev), m/Z: 179 [M⁺]

**Bromocyclopentane (4a)**

IR (neat) ν: 3445, 2923, 2828, 2789, 2675, 1463, 1460, 1459, 1448, 1370, 1332, 1299, 1206, 1189, 1152, 1085, 1084, 1044, 980, 886, 810, 682, 462 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz): δ 1.52 (t, J = 48 Hz, 2H, CH₂), 2.10 (m, 2H, CH₂), 3.45–3.5 (m, 1H, CH) ppm; MS (70 ev), m/Z: 149[M⁺]

**Bromocyclohexane (5a)**

IR (neat) ν: 3448, 2933, 2848, 2796, 2670, 1463, 1460, 1448, 1370, 1336, 1299, 1206, 1191, 1152, 1085, 1048, 989, 886, 810, 687, 464 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz): δ 1.3 (t, J = 9.6 Hz, CH₂), 2.18–2.14 (d, J = 16.2 Hz, 2H, CH₂), 4.24–4.16 (m, 1H, CH) ppm; MS (70 ev), m/Z: 163 [M⁺]

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Monobromonation of least reactive alkanes and cycloalkanes

231
Bromocycloheptane (6a)

IR (neat) ν: 3440, 2932, 2858, 2793, 2671, 1453, 1448, 1371, 1330, 1297, 1206, 1191, 1150, 1083, 1040, 989, 880, 810, 685, 463 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz): δ 1.34–1.24 (t, J = 10 Hz, 2H, CH₂), 1.7 (m, 2H, CH₂), 3.42 (m, 1H, CH) ppm; MS (70 ev), m/z: 177 [M⁺]
Fig. VIB.1. $^1$H NMR spectrum of 2-Bromohexane

Fig. VIB.1. $^1$H NMR spectrum of 2-Bromoheptane

Monobromonation of least reactive alkanes and cycloalkanes