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INTRAMOLECULAR CYCLIZATION OF THE PRODUCT OF IODO-ALKOXYLATION WITH 3,4-DIHYDRO-2H-PYRANO DIMETHYLACETYLENE CARBINOL AND WITH ITS C_{SP}-SUBSTITUTED DERIVATIVES

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As a result of the research of the reaction of 3,4-dihydro-2H-pyrano-dimethylacetylene carbinol (also with its C_{sp}-substituted derivatives) of iodo-alkylation on clinoptilolite in the presence of $(NaK)_4CaAl_6Si_{30}O_{72}$ and crystalline iodine, 3-iodine-2-[(2-methyl-4-organyl-but-3-in-2-yl)oxy]oxane was prepared. This method of preparation of heterocyclic compounds allows the reaction to be carried out in the absence of solvents, which reduces the amount of reagents and allows obtaining a product with high purity and high yield (67.5%). It was established that the latter under the conditions of the Kucherov reaction turn into heterocyclic compounds. Thus, effective regioselective methods for the synthesis of dioxin derivatives have been developed. This fact is probably related and is obviously explained by the intramolecular cyclization of the resulting intermediate-ketohydroxyester, i.e. tandem hydrolysis of C−I and hydration of C≡C bonds of the reaction products. The yield of 2-benzyl-3,3-dimethylhexahydro-4aH-piran[2,3-b][1,4]dioxin-2-ol is higher than that of structural analogues. It should also be noted that the synthesized compounds have an increased reactivity, and are rich in nucleophilic centers. Based on experimental data, it was established that the compounds obtained in this way are stable and do not undergo hydrolysis. Some physicochemical properties of the synthesized compounds were given, their composition and structure were confirmed by elemental analysis data, and all synthesized compounds were identified by IR and NMR spectroscopy.

Keywords: 3,4-dihydro-2H-pyran, clinoptilolite, intramolecular cyclization, crystalline iodine, dimethylacetylene carbinol.

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Introduction

In recent years, extensive research has been carried out in the field of synthesis of propargyl β-iodesters, performed with the interaction of three-component systems consisting of olefin, propargyl alcohol and crystalline iodine in the presence of HgO [1−3]. Propargyl ethers have proved to be convenient starting substances in the synthesis of a number of promising compounds for practical use [4−6], and in organic synthesis [7−12]. Structural analogues of these compounds are of great interest and have a variety of practically useful properties [13], as well as in medicine [14].

Our goal was to obtain condensed bicyclic compounds by intramolecular cyclization of the alkoxyiodination product of 3,4-dihydro-2H-pyran with dimethylacetylenecarbinol and its C_{sp}-substituted derivatives and further hydration of the resulting compounds in one stage.

Results and discussion

Previously, we found that by single-stage synthesis of alkooxygalogenation of a double bond, heterocyclic compounds can be obtained by replacing HgO with a safer and low-toxic catalyst clinoptilolite $(NaK)_4CaAl_6Si_{30}O_{72}$ [15]. A similar reaction of alkoxy iodination in the presence of 3,4-dihydro-2H-pyran and crystalline iodine in the presence of clinoptilolite $(NaK)_4CaAl_6Si_{30}O_{72}$ proceeds regioselectivity by double

bond. This is evidenced by the ^{1}H NMR data of the acetyl proton doublet signal with a chemical shift at δ=4.87 ppm with a characteristic value J=4.6 Hz, as well as absorption bands characteristic of the acetyl bond (ν_{C-O}) of the middle band in the region of 1173 cm^{-1} are observed in the IR spectra. With further hydration, the products (I–V) turn into condensed bicyclic heterocycles (VI–X) (Scheme 1). Methyl groups are diastrophic at position 3 for compounds (I–X) and they exhibit different singlet signals at 1.04 s (3H, (CH_3)), 1.09 s (3H, (CH_3)) ppm.

The formation of the latter is obviously explained by the intramolecular cyclization of the resulting intermediate, ketohydroxyester, i.e. tandem hydrolysis of C–I and hydration of C≡C bonds of reaction products (I–V) (Scheme 2). It should be noted that with an increase in the volume of the C_{sp} substituent, the yields of the reaction products increase.

Under these conditions, according to the GC data [16], the reaction is completed in 2–3 hours and leads to the formation of reaction products with a yield of up to 68.2%. The resulting compounds (VI–X) are colorless mobile liquids with a characteristic odor of esters, resistant to long-term storage. The composition and structures of the compounds were established based on the IR and NMR spectra and elemental analysis data.

Conclusions

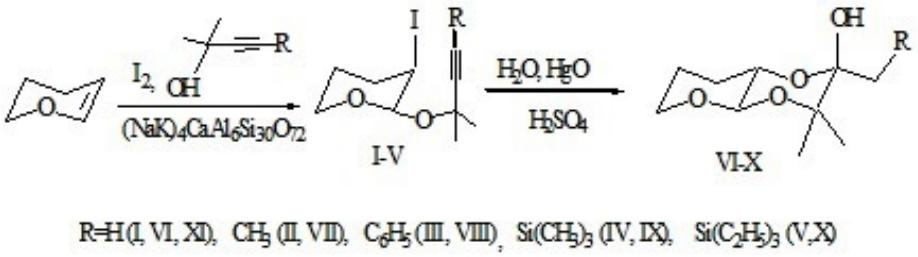
Iodoalkoxylation of 3,4-dihydro-2H-pyran with dimethylacetilenkarbinol (DAC) (also with its C_{sp}-substituted derivatives) of clinoptilolite in the presence of $(NaK)_4CaAl_6Si_{30}O_{72}$ and crystalline iodine leads to 3-iodine-2-[(2-methyl-4-organyl-but-3-in-2-il)oxy]oksanewith a high yield. The latter, under the conditions of the Kucherov reaction, turn into heterocyclic compounds. The formation of heterocyclic compounds is explained by the intramolecular cyclization of the resulting intermediate-ketohydroxyester, i.e. tandem hydrolysis of C–I and hydration of C≡C bonds of the reaction products.

Experimental part

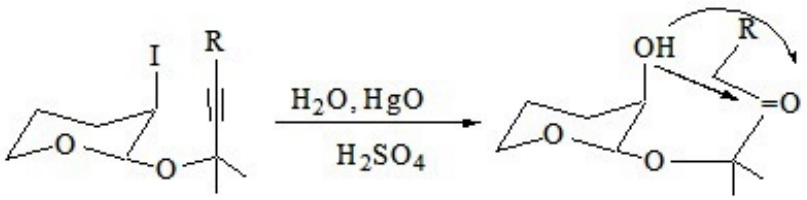
The IR spectra of the compounds were taken on the Specord 75 IR device in a thin layer and in tablets with KBr. NMR spectra of substances in $CDCl_3$ solution were recorded on the Bruker SF-300 (300.134 MHz) device, the internal standard being GMDS. The purity of the synthesized compounds was 95–98%, according to the ^{1}H NMR and TLC spectra (developer –iodine).

3-Iodine-2-[(2-methylbutyl-3-in-2-il)oxy]oxane (I)

0.05 g of clinoptilolite $(NaK)_4CaAl_6Si_{30}O_{72}\cdot 24H_2O$ was added to the cooled (–5...0^{0}C) and intensively stirred mixture of 14 g (0.25 mol) dimethylacetylenecarbinol and 21 g (0.25 mol) 3,4-dihydro-2H-piran, then in portions (1 g) 31.5 g (0.12 mol) finely ground crystalline iodine. Mixing was continued at room temperature for another 3–4 hours, then the mixture was filtered, the filtrate was washed with a solution of $Na_2S_2O_3$ and extracted with ether. The extract was dried through $CaCl_2$, the ether was removed in a rotary evaporator, and the remainder was recrystallized. 45.2 g (68.2%) of substance (I) was obtained with bp 108–110^{0}C (1 mm Hg). IR spectrum, ν, cm^{-1}: 3330, 2952, 2858, 2100, 1439, 1375, 1174, and 565. NMR spectrum



Scheme 1



Scheme 2

^{1}H, δ, ppm, MHz: 1.07 s (6H, $(CH_3)_2$), 1.54−1.58 m (1H, CH), 1.83−1.79 m (1H, CH), 1.98−2.03 m (1H, CH), 2.32−2.36 m (1H, CH), 2.5 t (1H, J=2.5 Hz, ≡CH), 3.59−3.63 m (1H, CH), 3.93−3.95 m (1H, CH), 4.12−4.20 m (1H, J=4.6 Hz, ICH), 4.87 d (1H, J=4.6 Hz, OCHO). ^{13}C NMR spectrum ($CDCl_3$, 67.8 Hz): 3.6, 28.7, 31.7, 55.4, 62.9, 74.2, 83.1, and 100.2. Found, %: C 40.81; H 5.18; I 43.21. $C_{10}H_{15}IO_2$. Calculated, %: C 40.83; H 5.14; I 43.15.

3-Iodine-2-[(2-methylpent-3-in-2-yl)oxy]oxane (II)

Obtained with a yield of 60%, bp 128−130°C (1 mm Hg). IR spectrum, ν, cm^{-1}: 2952, 2858, 2110, 1439, 1375, and 1172. NMR spectrum ^{1}H, δ, ppm, MHz: 1.07 s (6H, $(CH_3)_2$), 1.54−1.57 m (1H, CH), 1.83−1.88 m (1H, CH), 1.86 s (3H, CH_3), 1.98−2.03 m (1H, CH), 2.32−2.36 m (1H, CH), 3.59−3.63 m (1H, CH), 3.93−3.95 m (1H, CH), 4.12−4.20 m (1H, J=4.6 Hz, ICH), 4.87 d (1H, J=4.6 Hz, OCHO). ^{13}C NMR spectrum ($CDCl_3$, 67.8 Hz): 3.7, 28.7, 31.7, 55.4, 62.9, 74.2, 83.1, and 100.2. Found, %: C 42.84; H 5.54; I 41.45. $C_{11}H_{17}IO_2$. Calculated, %: C 42.87; H 5.56; I 41.18.

3-Iodine-2-[(2-methyl-4-phenylbutyl-3-in-2-yl)oxy]oxane (III)

Received 65.6% of the substance (III) with a volume of 78−80^{0}C (from ethanol). IR spectrum, ν, cm^{-1}: 3100, 3080, 2233, 3040, 1620, 1515, 1175, 1175, 1070, 1026, 776, 738, and 560. NMR spectrum ^{1}H, δ, ppm, MHz: 1.07 s (6H, $(CH_3)_2$), 1.57−1.60 m (1H), 1.85−1.86 m (1H), 2.02−2.07 m (1H), 2.36−2.39 m (1H), 3.63−3.66 m (1H), 4.50 d (2H, CH_2, J=6.4 Hz), 4.96 d (1H, J=4.6 Hz), 7.31−7.35 m (3H), 7.45−7.48 m (2H). ^{13}C NMR spectrum ($CDCl_3$, 67.8 Hz): 24.9, 28.5, 31.9, 55.5, 63.2, 84.2, 86.6, 100.4, 122.5, 128.3, 128.5, and 131.8. Found, %: C 52.12; H 5.14; I 34.56. $C_{16}H_{19}IO_2$. Calculated, %: C 51.91; H 5.17; I 34.28.

3-Iodine-2-[(2-methyl-4-trimethylsilyl-3-in-2-yl)oxy]oxane (IV)

Obtained with a yield of 68%, bp 112−114^{0}C (1 mm Hg.). IR spectrum, ν, cm^{-1}: 2952, 2858, 1439, 1375, 1250, and 1174. NMR spectrum-^{1}H, δ, ppm, MHz: 0.03 s (9H, $(CH_3)_3$), 1.07 s (6H, $(CH_3)_2$), 1.54−1.58 m (1H, CH), 1.83−1.83 m (1H, CH), 1.98−2.03 m (1H, CH), 3.59−3.63 m (1H, CH), 3.93−3.95 m (1H, CH), 4.01−4.05 m (1H, CH), 4.12−4.20 m (1H, J=4.6 Hz, ICH), 4.87 d (1H, J=4.6 Hz, OCHO). ^{13}C NMR spectrum ($CDCl_3$, 67.8 Hz): 3.8, 28.7, 31.7, 55.4, 62.9, 74.2, 83.1, and 100.2. Found, %: C 42.33; H 6.28; I 34.77; Si, 7.51. $C_{13}H_{23}IO_2Si$. Calculated, %: C 42.62; H 6.33; I 34.64; Si 7.67.

3-Iodo-2-(3-trielsilylprop-2-iniloxy)-tetrahydropyran (V)

The yield is 68%, bp 118−120^{0}C (1 mm Hg). IR spectrum, ν, cm^{-1}: 2952, 2858, 1439, 1375, 1255, and 1172. NMR spectrum ^{1}H, δ, ppm, MHz: 0.75 d.k (6H, $(CH_2)_3$, J=7.5, 14.2 Hz), 1.08 s (6H, $(CH_3)_2$), 1.15 t (9H, $(CH_3)_3$, J=7.5 Hz), 1.52-1.55 m (1H, CH), 1.83−1.83 m (1H, CH), 1.98−2.03 m (1H, CH), 2.32−2.36 m (1H, CH), 3.59−3.63 m (1H, CH), 3.93−3.95 m (1H, CH), 4.02−4.06 m (1H, CH), 4.87 d (1H, J=4.6 Hz, OCHO). ^{13}C NMR spectrum ($CDCl_3$, 67.8 Hz). 3.7, 28.7, 31.7, 55.4, 62.9, 74.2, 83.1, and 100.2. Found, %: C 46.96; H 7.12; I 31.11; Si 6.42. $C_{16}H_{29}IO_2Si$. Calculated, %: C 47.06; H 7.16; I 31.07; O 7.84; Si 6.88.

2,3,3-Trimethylhexahydro-4aH-piran[2,3-b][1,4]dioxin-2-ol (VI)

13.3 g (0.05 mol) of compound (I) was gradually added to the heated to 60^{0}C and stirred mixture of 0.65 g of red mercury oxide, 1 ml of concentrated sulfuric acid and 23.5 ml of water. The mixture was boiled for 6 hours at 60−65^{0}C, extracted with ether, the water layer was saturated with table salt and extracted with ether again. The combined organic phases were dried with Na_2SO_4, the solvent was removed, and the remainder was distilled in vacuum. 7.7 g (57%) of the substance (6) was isolated with a temperature of 94−96^{0}C (1 mm Hg). IR spectrum, ν, cm^{-1}: 3600, 1174, and 1120. NMR spectrum-^{1}H, δ, ppm, MHz: 1.04 s (3H, (CH_3)), 1.09 s (3H, (CH_3)), 1.18 s (3H, CH_3), 1.89 m (2H, CH_2), 1.98 br.s (1H, OH), 3.45 m (2H, CH_2), 3.89 m (2H, CH_2), 4.81 d (1H, J=4.7 Hz, OCH), 5.27 d (1H, J=3.0, OCHO). ^{13}C NMR spectrum ($CDCl_3$, 67.8 Hz): 26.3 (CH_3), 37.8 (CH_2), 39.1 (CH_2), 63.2 (CH_2), 66.2 (CH_2), 69.1 (CHO), 94.2 (CHO), and 99.5 (OCHO). Found, %: C 64.52; H 9.33. $C_{10}H_{18}O_3$. Calculated, %: C 64.49; H 9.74.

2-Ethyl-3,3-dimethylhexahydro-4aH-piran[2,3-b][1,4] dioxin-2-ol (VII)

The yield is 65.8%, bp 97−99^{0}C (1 mm Hg). IR spectrum, ν, cm^{-1}: 3600, 1176, and 1110. NMR spectrum ^{1}H, δ, ppm, MHz: 0.98 t (3H, CH_3, J=7.1), 1.04 s (6H, $(CH_3)_2$), 1.24 s (2H, CH_2), 1.89−1.92 m (2H, CH_2), 1.98 br.s (1H, OH), 3.45 m (2H, CH_2), 3.89 m (2H, CH_2), 4.02 d.d.d (1H, J=4.7, 7.3, 7.8 Hz, CH), 4.81 d (1H, J= 4.7 Hz, OCHO). ^{13}C NMR spectrum ($CDCl_3$, 67.8 Hz): 26.3 (CH_3), 37.8 (CH_2), 39.1 (CH_2), 63.2 (OCH_2), 66.2 (OCH_2), 69.1 (CHO), 94.2 (OCHO), and 99.5 (OCHO). Found, %: C 63.84; H 10.64. $C_{10}H_{20}O_3$. Calculated, %: C 63.80; H 10.71.

2-Benzyl-3,3-dimethylhexahydro-4aH-piran[2,3-b][1,4] dioxin-2-ol (VIII)

The yield is 67.8%, bp 112–114°C (1 mm Hg). IR spectrum, ν, cm^{-1}: 3600, 1173, and 1110. NMR spectrum ^1H, δ, ppm, MHz: 1.04 s (3H, (CH_3)), 1.09 s (3H, (CH_3)), 1.24 s (2H, CH_2), 1.89 m (2H, CH_2), 1.98 br.s (1H, OH), 3.45 m (2H, CH_2), 3.89 m (2H, CH_2), 4.02 d.d.d (1H, J=4.7, 7.3, 7.8 Hz, CHO), 4.81 m (1H, OCHO), 7.30–7.36 m (3H), 7.43–7.48 m (2H). ^{13}C NMR spectrum ($CDCl_3$, 67.8 Hz): 26.3 (CH_3), 37.8 (CH_2), 39.1 (CH_2), 63.2 (OCH_2), 66.2 (OCH_2), 68.2 (OCH_2), 69.1 (CHO), 94.2 (OCHO), and 99.5 (OCHO). Found, %: C 73.21; H 8.42. $C_{16}H_{22}O_3$. Calculated, %: C 73.25; H 8.45.

2-Trimethylsilylmethyl-3,3-dimethylhexahydro-4aH-piran[2,3-b][1,4]dioxin-2-ol (IX)

Yield 62.8%, bp 98–99°C (1 mm Hg). IR spectrum, ν, cm^{-1}: 3600, 1255, 1173, and 1110. NMR spectrum ^1H, δ, ppm, MHz: 0.45 s (9H, $(CH_3)_3$), 1.04 s (3H, (CH_3)), 1.09 s (3H, (CH_3)), 1.89 m (2H, CH_2), 1.98 br.s (1H, OH), 2.69 m (2H, CH_2), 3.45 m (2H, CH_2), 3.89 m (2H, CH_2), 4.02 d.d.d (1H, J=4.7, 7.3, 7.8 Hz, CHO), 4.81 m (1H, OCHO). ^{13}C NMR spectrum ($CDCl_3$, 67.8 Hz): −0.6 ($Si(CH_3)_3$), 26.3 (CH_3), 37.8 (CH_2), 39.1 (CH_2), 63.2 (OCH_2), 66.2 (OCH_2), 69.1 (CHO), 94.2 (OCHO), and 99.5 (OCHO). Found, %: C 60.56; H 10,12; Si 10,84. $C_{13}H_{26}O_3Si$. Calculated, %: C 60.42; H 10.14; Si 10.87.

2-Triethylsilylmethyl-3,3-dimethylhexahydro-4aH-piran [2,3-b][1,4]dioxin-2-ol(X)

The yield is 66.8%, bp 104–106°C (1 mm Hg). IR spectrum, ν, cm^{-1}: 3620 (us.s), 1250, 1172, and 1110. NMR spectrum ^1H, δ, ppm, MHz: 0.73 k (6H, $(CH_2)_3$, J=7.5 Hz), 1.04 s (3H, (CH_3)), 1.09 s (3H, (CH_3)), 1.18 t (9H, $((CH_3)_3$, J=7.5 Hz), 1.89 m (2H, CH_2), 1.98 br.s (1H, OH), 2.45 m (2H, CH_2), 3.45 m (2H, CH_2), 3.89 m (2H, CH_2), 4.02 d.d.d (1H, J=4.7, 7.3, 7.8 Hz, CHO), and 4.81 m (1H, OCHO). ^{13}C NMR spectrum ($CDCl_3$, 67.8 Hz): −0.6 ($Si(CH_3)_3$), 6.7 (Seach2), 26.3 (CH_3), 37.8 (CH_2), 39.1 (CH_2), 63.2 (OCH_2), 66.2 (OCH_2), 69.1 (CHO), 94.2 (OCHO), and 99.5 (OCHO). Found, %: C 63.45; H 10.66; Si 9.31. $C_{16}H_{32}O_3Si$. Calculated, %: C 63.95; H 10.73; Si 9.35.

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ВНУТРІШНЬОМОЛЕКУЛЯРНА ЦИКЛІЗАЦІЯ ПРОДУКТУ ЙОД-АЛКОКСИЛЮВАННЯ 3,4-ДИГІДРО-2Н-ПІРАНОДИМЕТИЛАЦЕТИЛЕНКАРБІНОЛОМ ТА ЙОГО C_{SP}-ЗАМІЩЕНИМИ ПОХІДНИМИ

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У результаті дослідження реакції йод-алкілування 3,4-дигідро-2Н-пірано-диметилацетиленкарбінолу (також з його C_{sp}-заміщеними похідними) на кліноптилоліті в присутності $(NaK)_4CaAl_6Si_{30}O_{72}$ та кристалічного йоду, одержали 3-йод-2-[(2-метил-4-органіл-бут-3-ін-2-іл)окси]оксан. Цей спосіб одержання гетероциклічних сполук дозволяє проводити реакцію за відсутності розчинників, що зменшує кількість реагентів і дозволяє одержувати продукт високої чистоти з високим виходом (67,5%). Встановлено, що останні в умовах реакції Кучерова перетворюються на гетероциклічні сполуки. Таким чином, розроблено ефективні регіоселективні методи синтезу похідних діоксину. Цей факт, ймовірно, пов'язаний і, очевидно, пояснюється внутрішньомолекулярною циклізацією утвореного проміжного кетогідроксіефіру, тобто тандемним гідролізом C–I та гідратацією зв'язків C≡C продуктів реакції. Вихід 2-бензил-3,3-диметилгексагідро-4аН-піран[2,3-b][1,4]діоксин-2-олу вищий, ніж у структурних аналогів. Слід також зазначити, що синтезовані сполуки мають підвищену реакційну здатність, багаті нуклеофільними центрами. На основі експериментальних даних встановлено, що одержані таким чином сполуки стабільні і не піддаються гідролізу. Наведено деякі фізико-хімічні властивості синтезованих сполук, їх склад і будову підтверджено даними елементного аналізу, усі синтезовані сполуки ідентифіковано за допомогою ІЧ- та ЯМР-спектроскопії.

Ключові слова: 3,4-дигідро-2Н-піран, кліноптилоліт, внутрішньомолекулярна циклізація, кристалічний йод, диметилацетиленкарбінол.

INTRAMOLECULAR CYCLIZATION OF THE PRODUCT OF IODO-ALKOXYLATION WITH 3,4-DIHYDRO-2H-PYRANO DIMETHYLACETYLENE CARBINOL AND WITH ITS C_{SP}-SUBSTITUTED DERIVATIVES

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As a result of the research of the reaction of 3,4-dihydro-2H-pyrano-dimethylacetylene carbinol (also with its C_{sp}-substituted derivatives) of iodo-alkylation on clinoptilolite in the presence of $(NaK)_4CaAl_6Si_{30}O_{72}$ and crystalline iodine, 3-iodine-2-[(2-methyl-4-organyl-but-3-in-2-yl)oxy]oxane was prepared. This method of preparation of heterocyclic compounds allows the reaction to be carried out in the absence of solvents, which reduces the amount of reagents and allows obtaining a product with high purity and high yield (67.5%). It was established that the latter under the conditions of the Kucherov reaction turn into heterocyclic compounds. Thus, effective regioselective methods for the synthesis of dioxin derivatives have been developed. This fact is probably related and is obviously explained by the intramolecular cyclization of the resulting intermediate-ketohydroxyester, i.e. tandem hydrolysis of C–I and hydration of C≡C bonds of the reaction products. The yield of 2-benzyl-3,3-dimethylhexahydro-4aH-piran[2,3-b][1,4]dioxin-2-ol is higher than that of structural analogues. It should also be noted that the synthesized compounds have an increased reactivity, and are rich in nucleophilic centers. Based on experimental data, it was established that the compounds obtained in this way are stable and do not undergo hydrolysis. Some physicochemical properties of the synthesized compounds were given, their composition and structure were confirmed by elemental analysis data, and all synthesized compounds were identified by IR and NMR spectroscopy.

Keywords: 3,4-dihydro-2H-pyran; clinoptilolite; intramolecular cyclization; crystalline iodine; dimethylacetylene carbinol.

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