Poly[styrene(iodosodiacetate)]-Promoted Ring Expansion Reaction of 1-Alkynylcycloalkanols: A Novel Synthesis of (*Z*)-2-(1-Iodo-1-organyl)methylenecycloalkanones

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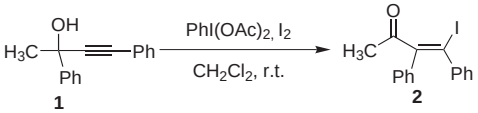
Abstract: The ring expansion reaction of 1-alkynylcycloalkanols with poly[styrene(iodosodiacetate)] and iodine affords (*Z*)-2-(1-iodo-1-organyl)methylenecycloalkanones in moderate to good yields.

Key words, poly[styrene(iodosodiacetate)], ring expansion, 1-alkynyl substituted tertiary alcohols, 2-(1-iodo-1-organyl)methylenecycloalkanones

During the last decades, polymer supported hypervalent iodine reagents have gained an increasing popularity in organic synthesis on account of their versatile reactivity.[1] Among them, poly[styrene(iodosodiacetate)] was widely used as a mild and clean oxidant. 2-Disubstituted methylenecycloalkanones are very important intermediates in the synthesis of biologically active natural products,[2] but reports concerning transformations from 1-alkynylcycloalkanols to 2-disubstituted methylenecycloalkanones are rare.[3] To the best of our knowledge, there are no reports on the ring expansion reaction promoted by poly[styrene(iodosodiacetate)]. Herein, we wish to report the ring expansion reaction of 1-alkynylcycloalkanols promoted by poly[styrene(iodosodiacetate)] to give (*Z*)-2-(1-iodo-1-organyl)methylenecycloalkanones with the advantages such as mild reaction conditions, and convenient manipulation. Moreover, the polymer reagent could be regenerated and reused.

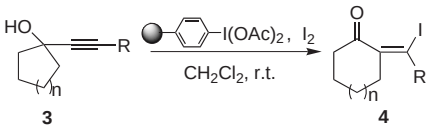
First we tried our experiments with 2,4-diphenyl-3-butyn-2-ol (**1**), which was treated with iodine and (diacetoxyiodo)benzene in dichloromethane at room temperature overnight. This afforded (*Z*)-4-iodo-2,4-diphenylbut-3-en-2-one (**2**)[4] in 77% yield (Scheme 1).



1 **2**

Scheme 1

With this result in hand, we supposed that ring expansion products may be obtained from the substrates, 1-alkynylcycloalkanols, which were prepared from the corresponding cycloalkanones. Poly[styrene(iodosodiacetate)] has the similar reactivity to (diacetoxyiodo)benzene,[1b] and the most important is that the byproduct, poly(4-iodostyrene) can be recycled, which provide an environment benign system. Considering that five- and six-membered rings are stable, we carried out the ring expansion reaction (Scheme 2) with 1-(2-phenylethynyl)cyclopentanol (**3a)** in the presence of poly[styrene(iodosodiacetate)] and iodine. Luckily, the expected product **4a** was obtained in 80% yield (Table 1, entry 1).

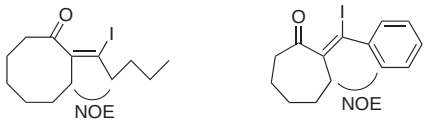


3 **4**

n = 1, 2, 3

Scheme 2

As a solvent for this reaction, CH_2Cl_2 was found to be more efficient than MeCN, $CHCl_3$, and $ClCH_2CH_2Cl$. Various 1-alkynylcycloalkanols **3** were reacted with iodine and poly[styrene(iodosodiacetate)] in CH_2Cl_2 at room temperature overnight to give (*Z*)-2-(1-iodo-1-organyl)methylenecycloalkanones. The stereochemistry of the products **4d** and **4h** has been established on the basis of ^1H-^1H COSY as well as from ^1H-^1H NOESY experiments (Figure 1). The results are summarized in Table 1.



4h **4d**

Figure 1 NOESY correlations of **4h** and **4d**

(*Z*)-2-(1-Iodo-1-phenyl)methylenecycloalkanones, which may react with various reagents owing to a vinyl iodine atom, can obviously be applied as useful building blocks in organic synthesis. We examined a Sonogashira cross-coupling reaction of (*Z*)-2-(1-iodo-1-phenyl)methylenecy-

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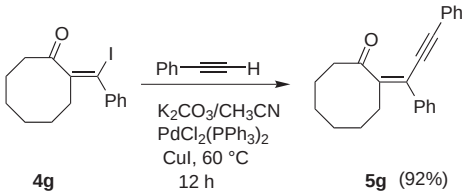
Table 1 Ring Expansion Reaction of 1-(2-Substituted-ethynyl)cycloalkanols

Entry	n	R	Time (h)	Product (Yield, %)[a]
1	1	C_6H_5	11	**4a** (80)
2	1	*n*-C_4H_9	14	**4b** (64)
3	1	*p*-$CH_3C_6H_4OCH_2$	13	**4c** (72)
4	2	C_6H_5	11	**4d** (70)
5	2	$C_6H_5CH_2OCH_2$	12	**4e** (61)
6	2	*p*-$CH_3C_6H_4OCH_2$	13	**4f** (60)
7	3	C_6H_5	11	**4g** (67)
8	3	*n*-C_4H_9	12	**4h** (58)
9	3	*p*-$CH_3C_6H_4OCH_2$	12	**4i** (55)
10	3	$C_6H_5CH_2OCH_2$	12	**4j** (58)
11	3	C_6H_5	11	**4g** (66)[b]

[a] Isolated yields.
[b] Using the regenerated resin.

clooctanone with phenylacetylene. This gave (*Z*)-2-(1-phenyl-1-phenylethynyl)methylenecyclooctanone (**5g**) in high yield (Scheme 3).



Scheme 3

In conclusion, we have developed a convenient and efficient method for the synthesis of 2-(1-iodo-1-organyl)-methylenecycloalkanones in moderate to good yields by the ring expansion reaction of 1-alkynylcycloalkanols with poly[styrene(iodosodiacetate)] and iodine in dichloromethane. The polymer reagent could be regenerated and reused.

Melting points are uncorrected. ^{1}H NMR spectra were recorded on a Bruker Avance 400 spectrometer in $CDCl_3$ with TMS as the internal standard. ^{13}C NMR spectra were recorded on a Bruker AC-400 (100 MHz) spectrometer in $CDCl_3$. IR spectra were recorded on a Shimadzu IR-408 spectrometer. EIMS were run on a HP 5989B mass spectrometer. Elemental analyses were performed on an EA-1110 instrument. Poly[styrene(iodosodiacetate)] was prepared as described in the literature[5] and its loading in terms of the functional group is 2.50 mmol/g by iodometry.

1-(2-Phenylethynyl)cycloheptanol (3g); Typical Procedure

To a suspension of Mg (319 mg, 13.3 mmol) and catalytic quantities of I_2 in THF (15 mL) was added dropwise a solution of EtBr (1.45 g, 13.3 mmol) in THF (10 mL) under N_2. After the disappearance of Mg, phenylacetylene (1.36 g, 13.3 mmol) in THF (15 mL) was added dropwise and the solution was stirred at r.t. for 1 h. Then the solution was cooled to 0 °C and the corresponding cycloheptanone (1.12 g, 10 mmol) in THF (10 mL) was added dropwise. The mixture was stirred at the same temperature for 2 h, quenched with sat. aq NH_4Cl and extracted with EtOAc (3 × 5 mL). The organic phases were combined, washed with brine and dried ($MgSO_4$). After evaporation of the solvent, the residues were purified via chromatography on silica gel with *n*-hexane–EtOAc (10:1) as the eluent to afford the tertiary alkynol **3g**.

IR (neat): 3416, 2932, 2858, 1598, 1489, 1216, 1024, 756 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.44–7.41 (m, 2 H), 7.29–7.25 (m, 3 H), 2.32 (br, 1 H), 2.15–2.09 (m, 2 H), 1.95–1.88 (m, 2 H), 1.71–1.59 (m, 8 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 131.6, 128.2, 128.1, 123.0, 93.9, 83.6, 72.2, 43.2, 27.9, 22.3.

MS (EI): *m*/*z* (%) = 214 (M^+, 19), 197 (39), 157 (100), 129 (84), 115 (55).

Anal. Calcd for $C_{15}H_{18}O$: C, 84.07; H, 8.47. Found: C, 83.89; H, 8.53.

Oxidative Rearrangement Reaction of Tertiary Alkynol 1 Promoted by (Diacetoxyiodo)benzene; (*Z*)-4-Iodo-2,4-diphenylbut-3-ene-2-one (2)

A suspension of tertiary alkynol **1** (1.0 mmol), (diacetoxyiodo)benzene (322 mg, 1.0 mmol) and I_2 (0.6 mmol) in CH_2Cl_2 (10 mL) was stirred at r.t. for 12 h. The mixture was then washed with aq 5% Na_2SO_3 (15 mL) and extracted with CH_2Cl_2 (3 ×). The organic phases were combined and dried ($MgSO_4$). After evaporation of the solvent, the residue was purified via chromatography on silica gel with *n*-hexane–EtOAc (20:1) as the eluent to afford **2**[4] (77%).

IR (neat): 1666 cm^{-1} (C=O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32–7.11 (m, 10 H), 2.41 (s, 3 H).

MS (EI): *m*/*z* (%) = 348 (M^+).

Ring Expansion Reaction of 1-(2-Substituted Ethynyl)cycloalkanols 3; (*Z*)-2-(1-Iodo-1-phenyl)methylenecyclooctanone (4g); General Procedure

A suspension of tertiary alkynol **3g** (1.0 mmol), poly[styrene(iodosodiacetate)] (0.4 g, 1.0 mmol) and I_2 (0.6 mmol) in CH_2Cl_2 (10 mL) was stirred at r.t. for 11 h. The mixture was then washed with aq 5% $Na_2S_2O_3$ (15 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The organic phases were combined and dried ($MgSO_4$). After evaporation of the solvent, Et_2O was added to cause precipitation, the precipitate was collected by filtration for reusing, and the filtrate was evaporated the solvent and the residue was purified via chromatography on silica gel with *n*-hexane–EtOAc (20:1) as the eluent to afford 228 mg (67%) of **4g**.

IR (neat): 2927, 2855, 1664, 1596, 1579, 1449, 1239, 734, 693 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99 (d, 2 H, *J* = 8.4 Hz), 7.62–7.58 (m, 1 H), 7.51–7.47 (t, 2 H, *J* = 7.6 Hz), 2.64–2.61 (t, 2 H, *J* = 6.0 Hz), 2.38–2.36 (m, 2 H), 1.79–1.54 (m, 8 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.0, 151.6, 134.4, 134.0, 130.5 129.1, 91.6, 40.9, 33.9, 29.9, 29.0, 27.9, 26.0.

MS (EI): *m*/*z* (%) = 341 [$(M + 1)^+$, 35], 340 (M^+, 21), 213 (22), 157 (21), 105 (100).

Anal. Calcd for $C_{15}H_{17}IO$: C, 52.96; H, 5.04. Found: C, 52.81; H, 5.11.

4a

IR (neat): 2938, 1666, 1489, 1090, 908, 733, 688 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.60–7.56 (m, 2 H), 7.50–7.46 (m, 1 H), 7.42–7.38 (m, 2 H), 3.22 (t, 2 H, *J* = 5.6 Hz), 2.72 (t, 2 H, *J* = 6.4 Hz), 1.95–1.84 (m, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 187.5, 133.5, 131.2, 129.1, 120.3, 91.5, 88.1, 44.6, 32.9, 25.4, 6.3.

MS (EI): *m*/*z* (%) = 313 [(M + 1)$^+$, 26.0], 231 (15.8), 185 (49.9), 129 (100).

Anal. Calcd for $C_{13}H_{13}IO$: C, 50.02; H, 4.20. Found: C, 50.10; H, 4.12.

4b

IR (neat): 2957, 2929, 2870, 1703, 1672, 1401, 1207, 1102 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.24 (t, 2 H, *J* = 6.8 Hz), 2.84–2.80 (m, 2 H), 2.71–2.67 (m, 2 H), 1.96–1.91 (m, 2 H), 1.88–1.83 (m, 2 H), 1.81–1.79 (m, 2 H), 1.52–1.45 (m, 2 H), 1.00–0.95 (m, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 201.1, 100.9, 97.3, 47.8, 37.9, 32.1, 30.6, 24.7, 21.1, 14.3, 6.3.

MS (EI): *m*/*z* (%) = 293 [(M + 1)$^+$, 34.8], 292 (M$^+$, 21.1), 271 (21.4), 211 (23.9), 183 (31.7), 65 (63.9), 109 (100), 41 (71.0).

Anal. Calcd for $C_{11}H_{17}IO$: C, 45.22; H, 5.86. Found: C, 45.29; H, 5.92.

4c

IR (neat): 2922, 1704, 1611, 1509, 1398, 1212, 1175, 817 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.11 (d, 2 H, *J* = 8.4 Hz), 6.83 (d, 2 H, *J* = 8.8 Hz), 4.74 (s, 2 H), 3.21 (t, 2 H, *J* = 6.8 Hz), 2.81 (t, 2 H, *J* = 6.4 Hz), 2.30 (s, 3 H), 1.93–1.90 (m, 2 H), 1.83–1.80 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.2, 155.3, 131.4, 130.1, 115.4, 96.2, 95.1, 37.3, 32.5, 29.3, 24.1, 20.5, 5.8.

MS (EI): *m*/*z* (%) = 356 (M$^+$, 30.9), 244 (12.9), 187 (30.7), 135 (54.1), 107 (88.7), 77 (100), 55 (93.9), 41 (54.1).

Anal. Calcd for $C_{15}H_{17}IO_2$: C, 50.58; H, 4.81. Found: C, 50.64; H, 4.88.

4d

IR (neat): 3060, 2931, 2855, 1663, 1597, 1446, 1265, 1220, 700 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00–7.96 (m, 2 H), 7.62–7.56 (m, 1 H), 7.54–7.47 (m, 2 H), 2.57 (t, 2 H, *J* = 6.0 Hz), 2.24 (t, 2 H, *J* = 6.0 Hz), 1.76–1.72 (m, 2 H), 1.61–1.44 (m, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.5, 150.0, 134.4, 134.1, 130.4, 129.1, 88.2, 39.3, 33.6, 27.9, 27.8, 26.2.

MS (EI): *m*/*z* (%) = 327 [(M + 1)$^+$, 50.3], 326 (M$^+$, 29.6), 199 (75.9), 157 (22.5), 129 (21.2), 105 (100), 77 (31.1).

Anal. Calcd for $C_{14}H_{15}IO$: C, 51.55; H, 4.64. Found: C, 51.48; H, 4.70.

4e

IR (neat): 3029, 2929, 2857, 1703, 1453, 1398, 1105, 738, 698 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.43–7.31 (m, 5 H), 4.55 (s, 2 H), 4.31 (s, 2 H), 3.21 (t, 2 H, *J* = 6.8 Hz), 2.79 (t, 2 H, *J* = 6.4 Hz), 1.89–1.86 (m, 2 H), 1.76–1.72 (m, 2 H), 1.51–1.47 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.6, 137.1, 128.5, 128.1, 128.0, 97.7, 95.3, 78.5, 72.1, 38.4, 33.2, 29.9, 22.2, 6.5.

MS (EI): *m*/*z* (%) = 370 (M$^+$, 1.0), 254 (24.5), 127 (16.7), 91 (100), 55 (13.8), 41 (16.8).

Anal. Calcd for $C_{16}H_{19}IO_2$: C, 51.91; H, 5.17. Found: C, 51.81; H, 5.20.

4f

IR (neat): 2929, 1698, 1601, 1508, 1398, 1212, 1177, 818 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.07 (d, 2 H, *J* = 8.0 Hz), 6.84 (d, 2 H, *J* = 8.4 Hz), 4.74 (s, 2 H), 3.22–3.18 (m, 2 H), 2.81–2.77 (m, 2 H), 2.31 (s, 3 H), 1.89–1.71 (m, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.2, 138.3, 131.4, 130.1, 115.4, 96.2, 95.2, 36.3, 33.5, 29.3, 27.4, 23.1, 20.6, 6.8.

MS (EI): *m*/*z* (%) = 370 (M$^+$, 3.8), 254 (28.1), 127 (15.2), 91 (100), 55 (19.2), 41 (11.1).

Anal. Calcd for $C_{16}H_{19}IO_2$: C, 51.91; H, 5.17. Found: C, 52.01; H, 5.23.

4h

IR (neat): 2931, 2858, 1703, 909, 732 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.20 (t, 2 H, *J* = 6.8 Hz), 2.78 (t, 2 H, *J* = 6.8 Hz), 2.68 (t, 2 H, *J* = 7.6 Hz), 1.89–1.81 (m, 2 H), 1.74–1.67 (m, 2 H), 1.61–1.53 (m, 2 H), 1.48–1.36 (m, 6 H), 0.96 (m, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 201.2, 100.4, 93.4, 47.5, 38.8, 33.2, 30.2, 27.9, 23.1, 21.5, 14.0, 7.1.

MS (EI): *m*/*z* (%) = 321 [(M + 1)$^+$, 11.2], 320 (M$^+$, 4.8), 239 (16.7), 193 (10.7), 109 (61.1), 81 (38.3), 55 (59.4), 41 (100).

Anal. Calcd for $C_{13}H_{21}IO$: C, 48.76; H, 6.61. Found: C, 48.69; H, 6.68.

4i

IR (neat): 2930, 2858, 1704, 1611, 1509, 1213, 1176, 908, 733 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.11 (d, 2 H, *J* = 8.0 Hz), 6.83 (d, 2 H, *J* = 8.0 Hz), 4.74 (s, 2 H), 3.19 (t, 2 H, *J* = 6.8 Hz), 2.78 (t, 2 H, *J* = 7.2 Hz), 2.30 (s, 3 H), 1.87–1.80 (m, 2 H), 1.73–1.69 (m, 2 H), 1.46–1.39 (m, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.7, 140.3, 131.3, 130.1, 115.3, 96.9, 96.6, 36.5, 33.2, 31.1, 30.1, 27.8, 23.0, 20.5, 6.9.

MS (EI): *m*/*z* (%) = 384 (M$^+$, 26.7), 239 (9.4), 187 (18.4), 173 (33.5), 159 (21.8), 145 (44.3), 108 (100), 77 (68.8), 41 (73.3).

Anal. Calcd for $C_{17}H_{21}IO_2$: C, 53.14; H, 5.51. Found: C, 53.19; H, 5.58.

4j

IR (neat): 3062, 3029, 2930, 2856, 1703, 1496, 1454, 1396, 1206, 1099, 739, 698 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49–7.38 (m, 5 H), 4.61 (s, 2 H), 4.38 (s, 2 H), 3.26 (t, 2 H, *J* = 7.2 Hz), 2.84 (t, 2 H, *J* = 7.6 Hz), 1.91 (t, 2 H, *J* = 6.8 Hz), 1.79 (t, 2 H, *J* = 6.8 Hz), 1.52 (m, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.8, 137.1, 128.5, 128.1, 128.0, 97.7, 95.6, 78.5, 72.1, 38.5, 33.2, 30.2, 27.9, 23.0, 7.1.

MS (EI): *m*/*z* (%) = 385 [(M + 1)$^+$, 2.1], 384 (M$^+$, 0.6), 239 (4.1), 181 (6.0), 91 (100), 65 (9.1), 41 (16.6).

Anal. Calcd for $C_{17}H_{21}IO_2$: C, 53.14; H, 5.51. Found: C, 53.08; H, 5.55.

(*Z*)-2-(1-Phenyl-1-phenylethynyl)methylenecyclooctanone (5g)

Under N_2, a slurry of the **4g** (170 mg, 0.5 mmol), phenylacetylene (61 mg, 0.6 mmol), $PdCl_2(PPh_3)_2$ (17 mg, 5 mol%), CuI (9.5 mg, 10 mol%), K_2CO_3 (207 mg, 1.5 mmol) in MeCN (15 mL) was stirred at 60 °C for 12 h. The reaction mixture was filtered through a short pad of silica gel to remove precipitated inorganic salts. The silica gel pad was washed three times with a small amount of EtOAc and the combined solution was evaporated to dryness under reduced pressure. The residue was chromatographed on silica gel using *n*-hexane–EtOAc (20:1) as eluent to give 144 mg (92%) of **5g**.

IR (neat): 3059, 2925, 2853, 2193, 1669, 1596, 1489, 1448, 1237, 755, 690 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.06–7.96 (m, 2 H), 7.68–7.25 (m, 8 H), 2.83–2.16 (m, 4 H), 1.82–1.62 (m, 8 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.2, 160.3, 136.7, 133.3, 131.2, 129.9, 128.4, 128.2, 128.1, 123.4, 119.1, 97.5, 86.0, 36.1, 33.0, 29.6, 29.0, 27.4, 26.9.

MS (EI): *m*/*z* (%) = 314 (M^+, 13.1), 257 (10.3), 105 (100), 91 (14.5), 77 (58.2).

Anal. Calcd for $C_{23}H_{22}O$: C, 87.86; H, 7.05. Found: C, 87.69; H, 7.12.

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