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Novel Cyclization of Dimeric Dianions of Anils or Aldehydes with Triphosgene: A Safe and Efficient Synthesis of Substituted Imidazolidin-2-ones and 4,5-Diaryl-1,3-dioxolan-2-ones

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ABSTRACT: *The reaction of Schiff bases or aldehydes with samarium diiodide in dry THF, followed by addition of triphosgene, gives substituted imidazolidin-2-ones and 4,5-diaryl–1,3-dioxolan-2-ones, respectively, in moderate to good yields under mild conditions.* Heteroatom Chem 14:46–49, 2003; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.10065

INTRODUCTION

Recently, samarium metal, its salts, and organosamarium compounds have been widely employed as useful reagents in organic synthesis [1]. Subsequent to the pioneering work by Kagan and his coworkers [2] samarium diiodide has been extensively investigated as a mild, neutral, and versatile one-electron transfer reductant. The utilization of samarium diiodide in synthetic organic chemistry has been well documented, such as in radical cyclizations [3], Ketyl-olefin coupling reactions [4], Barbier-type reactions [5], Reformatsky reactions [6], and reductive coupling cyclizations [7]. Imamoto et al. [8] and Kagan [9] reported, respectively, reductive coupling of Schiff bases and aldehydes, mediated by samarium diiodide, with 1,2-diamines and pinacols being obtained. However, little attention has been paid to the dianionic intermediates derived from aniles and aldehydes by SmI_2 treatment, which, when trapped by electrophilic reagents, may lead to some reactions that are difficult to accomplished by other existing methodologies. Herein we report that triphosgene can be used to trap the anion radical formed in the reaction of anils or aldehydes with SmI_2 in dry THF. By applying this method substituted imidazolidin-2-ones and 4,5-diaryl-1,3-dioxolan-2-ones were obtained in moderate to good yields.

RESULTS AND DISCUSSION

The reaction of different Schiff bases (**1**) with triphosgene in the presence of SmI_2 led, after hydrolysis with 2 M aqueous K_2CO_3 solution, to the

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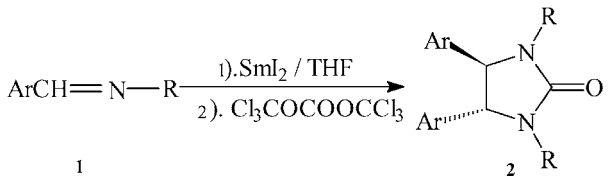
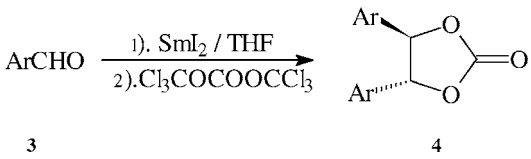


SCHEME 1 Formation of substituted imidazolidin-2-ones.



SCHEME 2 Formation of 4,5-diaryl-1,3-dioxolan-2-ones.

corresponding substituted imidazolidin-2-ones (**2**, Scheme 1).

All reactions were completed within 2–4 h, with moderate to good yields of imidazolidin-2-ones being isolated. The product formation was ascertained by TLC monitoring and the product isolation was achieved by quenching the reaction with 2 M aqueous K_2CO_3 followed by solvent extraction. The reactions were generally clean and only imidazolidin-2-ones could be detected by examination of ^{1}H NMR spectra of the crude products. However, purification, wherever necessary, was performed by flash chromatography. The results and the scope of these reactions are summarized in Table 1, which clearly indicates that the present strategy is a general method for the synthesis of substituted imidazolidin-2-ones.

Similar to the reaction of Schiff bases, when aromatic aldehydes (**3**) were treated with triphosgene in the presence of SmI_2 at room temperature, they reacted smoothly to give *dl*-4,5-diaryl-1,3-dioxolan-2-ones (**4**) in good yields (Scheme 2).

From Table 2 it can be seen that aromatic aldehydes (entry A–F) coupled with SmI_2 and were then trapped by triphosgene to form directly *dl*-4,5-diaryl-1,3-dioxolan-2-ones. However, when an aliphatic aldehyde (entry G) was treated under the same conditions only the coupling product (pinacol) was detected. The reactions are not influenced in any minor manner by the presence of the methoxy group (entry C) and of nitro group (entry F). Furthermore, the presence of a halo substitution did not alter remarkable selectively to give the product without any dehalogenation (entry E).

In conclusion, the present study describes a safe and efficient method for the synthesis of substituted imidazolidin-2-ones and 4,5-diaryl-1,3-dioxolan-2-ones, some of which have potential biological activities [10]. This method has a distinct superiority over the conventional method of condensing by use of diethyl carbonate, as the preparation of diamines alone involves several steps. This appears to be a very convenient and practical method in terms of mild reaction conditions, simple operation, and high yields.

EXPERIMENTAL

Tetrahydrofuran was distilled from sodium-benzophenone immediately prior to use. All reactions were conducted under a nitrogen atmosphere. Melting points are uncorrected. ^{1}H NMR spectra were recorded on a Bruker AC-400 instrument, using $CDCl_3$ solutions (TMS as an internal standard). Chemical shifts (δ) are reported as δ values and coupling constants J are given in Hz. IR spectra were recorded using KBr disks with a Bruker Vector-22 infrared spectrometer. Elemental analyses were performed on a EA-1110 instrument. Metallic samarium and all solvents were purchased from commercial sources and were used without further purification.

TABLE 1 Preparations of Substituted Imidazolidin-2-ones

Entry	*Ar*	*R*	*Molar Ratio of SmI_2/imine*	*Yield[a] (%)*	*dl/meso[b,c]*
A	C_6H_5	C_6H_5	2	80	95/5
B	C_6H_5	$4CH_3C_6H_4$	4	78	96/4
C	$4CH_3C_6H_4$	C_6H_5	2	76	90/10
D	$4CH_3C_6H_4$	$4CH_3C_6H_4$	4	68	96/4
E	$2CH_3C_6H_4$	C_6H_5	2	81	96/4
F	C_6H_5	$4ClC_6H_4$	2	83	98/2
G	$4CH_3OC_6H_4$	$4CH_3OC_6H_4$	4	75	98/2
H	C_6H_5	C_3H_7	8	62	98/2
I	$4ClC_6H_4$	C_3H_7	8	63	98/2
J	C_6H_5	C_7H_{15}	8	67	98/2
K	C_6H_5	*c*-C_6H_{11}	8	65	98/2
L	$4CH_3C_6H_4$	*c*-C_6H_{11}	8	63	98/2

[a]Isolated yields based on the starting imines utilized.
[b]Pure dl isomer was obtained by recrystallization.
[c]Ratio of dl and meso isomer was determined by ^{1}H NMR spectroscopy.

TABLE 2 Preparation of 4,5-Diaryl-1,3-dioxolan-2-ones

Entry	*Ar*	*Time (h)*	*Compounds*[a]	*Yields*[b] *(%)*	*dl/meso*[c]
A	C_6H_5	2	**4a**	83	85/15
B	p-$CH_3C_6H_4$	2.5	**4b**	75	80/20
C	p-$CH_3OC_6H_4$	2.5	**4c**	83	85/15
D	3,4-$(OCH_2O)C_6H_3$	2.5	**4d**	78	8515
E	p-ClC_6H_4	1.5	**4e**	85	80/20
F	p-$NO_2C_6H_4$	1.5	**4f**	60	80/20
G	$CH_3CH_2CH_2CHO$	2	**4g**	0[d]	

[a]Only pure dl isomer was isolated.
[b]Isolated yields based on the starting aromatic aldehydes utilized.
[c]Ratio of dl and meso isomer was determined by ^{1}H NMR spectroscopy.
[d]Only pinacol was isolated.

*General Procedure for the Synthesis of Imidazolidin-2-ones (**2**)*

A solution of the Schiff base (2 mmol) in dry THF (3 ml) was added to the solution of SmI_2 in THF (22 ml) at 60°C and under a nitrogen atmosphere. After being stirred for about 1 h (the reaction being monitored by TLC) triphosgene was added. The reaction mixture was stirred for an additional 2 h, treated with saturated K_2CO_3 solution (2 M, 5 ml), and extracted with ether (3 × 10ml). The combined organic extract was washed with brine (10 ml) and then dried over anhydrous $MgSO_4$ and concentrated. The residue was purified by silica-gel column, using ethyl acetate and cyclohexane (1:5) as eluent to give a pure product.

*General Procedure for the Synthesis of 4,5-Bisaryl-1,3-bisoxolan-2-ones (**4**)*

Each aromatic aldehyde (2 mmol), dissolved in 2 ml of THF, was added at room temperature, under nitrogen, to 20 ml of 0.1 M SmI_2 (2 mmol) in THF. The typical color of SmI_2 immediately changed to orange. After the mixture had been stirred for 10 min, triphosgene was added and the reaction mixture was stirred again for about 2 h. The mixture was hydrolyzed with 0.1 M HCl, extracted with ether, and washed with sodium thiosulfate and saturated NaCl solution; then dried over anhydrous $MgSO_4$ and concentrated. The residue was purified by silica-gel column, using ethyl acetate and cyclohexane (1:3) as eluent to give a pure product.

DATA OF PRODUCTS

*1,3,4,5-Tetrakisphenyl-imidazolidin-2-one (**2a**)*: Colorless crystals, m.p.: 209°C[10], ν_{max}(KBr)/cm^{-1}: 1694, δ_H: 6.98–7.45 (20H, m), 5.04 (2H, s), *m/z*(%): 390 (M^+, 100).

*1,3-Bis(4-methylphenyl)-4,5-bisphenyl-imidazolidin-2-one (**2b**)*: Colorless crystals, m.p.: 223–224°C [10], ν_{max}(KBr)/cm^{-1}: 1720, δ_H: 7.10–7.20 (18H, m), 5.66 (2H, s), 2.27 (6H, s), *m/z*(%): 418 (M^+, 100).

*1,3-Bisphenyl-4,5-bis(4-methylphenyl)-imidazolidin-2-one (**2c**)*: Colorless crystals, m.p.:135–136°C [10], ν_{max}(KBr)/cm^{-1}: 1695, δ_H: 7.58–7.80 (18H, m), 5.50 (2H, s), 2.23 (6H, s), *m/z*(%): 418 (M^+, 100).

*1,3,4,5-Tetrakis(4-methylphenyl)-imidazolidin-2-one (**2d**)*: Colorless crystals, m.p.: 171–173°C [10], ν_{max}(KBr)/cm^{-1}: 1700, δ_H: 7.18–7.25 (16H, m), 5.56 (2H, s), 2.26 (12H, m), *m/z*(%): 446 (M^+, 100).

*1,3-Bisphenyl-4,5-bis(2-methylphenyl)-imidazolidin-2-one (**2e**)*: Colorless crystals, m.p.: 189–191°C [10], ν_{max}(KBr)/cm^{-1}: 1700, δ_H: 7.05–7.20 (18H, m), 5.76 (2H, s), 2.25 (6H, s), *m/z*(%): 418 (M^+, 100).

*1,3-Bis(4-chlorophenyl)-4,5-bisphenyl-imidazolidin-2-one (**2f**)*: Colorless crystals, m.p.: 186–188°C [10], ν_{max}(KBr)/cm^{-1}: 1700, δ_H: 7.05–7.20 (18H, m), 5.55 (2H, s).

*1,3,4,5-Tetrakis(4-methoxyphenyl)-imidazolidin-2-one (**2g**)*: Colorless crystals, m.p.: 236–238°C, ν_{max}(KBr)/cm^{-1}: 1728, δ_H: 6.47–7.39 (16H, m), 6.20 (2H, s), 3.62 (12H, m), *m/z*(%): 510 (M^+, 2.09), Anal. $C_{31}H_{30}N_2O_5$. Calcd. C, 72.94; H, 5.88; N, 5.49. Found C, 72.91; H, 5.80; N, 5.50%.

*1,3-Dipropyl-4,5-bisphenyl-imidazolidin-2-one (**2h**)*: Colorless crystals, m.p.: 156–158°C, ν_{max}(KBr)/cm^{-1}: 1712, δ_H: 6.75–7.19 (10H, m), 6.22 (2H, s), 3.08–3.45 (4H, m), 0.57–1.56 (10H, m), *m/z*(%): 322 (M^+, 4,68), Anal. $C_{21}H_{26}N_2O$. Calcd. C, 78.26; H, 8.07; N, 8.69. Found C, 78.20; H, 8.12; N, 8.71%.

*1,3-Dipropyl-4,5-bis(4-chlorophenyl)-imidazolidin-2-one (**2i**)*: Colorless crystals, m.p.: 162–164°C, ν_{max}(KBr)/cm^{-1}: 1720, δ_H: 7.18–7.53 (8H, m), 6.24 (2H, s), 3.10–3.48 (4H, m), 0.57–1.55 (10H, m), *m/z*(%): 390 (M^+, 3.37), Anal. $C_{21}H_{24}Cl_2N_2O$. Calcd. C, 64.62; H, 6.15; N, 7.18. Found C, 64.70; H, 6.19; N, 7.20%.

*1,3-Diheptyl-4,5-bisphenyl-imidazolidin-2-one (**2j**)*: Colorless crystals, m.p.: 106–108°C, ν_{max}(KBr)/ cm^{-1}: 1715, δ_H: 6.79–8.04 (10H, m), 6.30 (2H, s), 3.50–3.68 (4H, m), 0.80–1.35 (26H, m), *m/z*(%): 434 (M^+, 1.99), Anal. $C_{29}H_{42}N_2O$. Calcd. C, 80.18; H, 9.67; N, 6.45. Found C, 80.16; H, 9.63; N, 6.47%.

*1,3-Dicyclohexyl-4,5-bisphetnyl-imidazolidin-2-one (**2k**)*: Colorless crystals, m.p.: 164–166°C, ν_{max}(KBr)/cm^{-1}: 1720, δ_H: 7.22–7.60 (10H, m), 6.26 (2H, s), 3.44 (2H, m), 0.51–1.85 (20H, m), *m/z*(%): 402 (M^+, 2.09), Anal. $C_{27}H_{34}N_2O$. Calcd. C, 80.59; H, 8.45; N, 6.96. Found C, 80.57; H, 8.43; N, 6.94%.

*1,3-Dicyclohexyl-4,5-bis (4-methylphenyl)-imidazolidin-2-one (**2l**)*: Colorless crystals, m.p.: 174–176°C, ν_{max}(KBr)/cm^{-1}: 1720, δ_H: 6.75–7.12 (8H, m), 6.26 (2H, s), 3.38 (2H, m), 2.19 (6H, s), 0.99–1.83 (20H, m), *m/z*(%): 430 (M^+, 2.09), Anal. $C_{29}H_{38}N_2O$. Calcd. C, 80.93; H, 8.84; N, 6.51. Found C, 80.9; H, 8.87; N, 6.53%.

*4,5-Bisphenyl-1,3-dioxolan-2-one (**4a**)*: Colorless crystals, m.p.: 120–122°C, ν_{max}(KBr)/cm^{-1}: 1785, 1498, 1450, 774, 748, 696, δ_H: 6.92–7.32 (10H, m), 5.98 (2H, s), *m/z*(%): 240 (M^+, 17.86), 212 (17.65), 195 (16.45), 178 (9.81), 105 (100), Anal. $C_{15}H_{12}O_3$. Calcd. C, 75.00; H, 5.00. Found C, 74.90; H, 5.04%.

*4,5-Bis(4-methylphenyl)-1,3-dioxolan-2-one (**4b**)*: Colorless crystals, m.p.: 118–121°C, ν_{max}(KBr)/ cm^{-1}: 1797, 1516, 1456, 1171, 1051, 882, δ_H: 6.82–6.84 (4H, d, $J = 8.0$ Hz), 6.94–6.96 (4H, d, $J = 8.0$ Hz), 5.91 (2H, s), 2.23 (6H, s), *m/z*(%): 268 (M^+, 39.46), 224 (25.89), 104 (100), Anal. $C_{17}H_{16}O_3$. Calcd. C, 76.12; H, 5.97. Found C, 76.08; H, 5.90%.

*4,5-Bis(4-methoxyphenyl)-1,3-dioxolan-2-one (**4c**)*: Colorless crystals, m.p.:170–171°C, ν_{max}(KBr)/ cm^{-1}: 1805, 1523, 1507, 1449, 832, 758, δ_H: 6.90–6.93 (4H, m), 7.45–7.49 (4H, m), 5.92 (2H, s), 3.84 (6H, s), *m/z*(%): 298 (M^+, 100), 226 (47.16), 211 (67.23), Anal. $C_{17}H_{16}O_5$. Calcd. C, 68.00; H, 5.33. Found C, 67.86; H, 5.30%.

*4,5-Bis(3,4-methylenedioxyphenyl)-1,3-dioxolan-2-one (**4d**)*: Colorless crystals, m.p.:154–156°C, ν_{max}(KBr)/cm^{-1}: 1789, 1499, 1450, 1403, 934, 858, 817, 771, δ_H: 6.43–6.65 (6H, m), 5.90 (4H, s), 5.83 (2H, s), *m/z*(%): 328 (M^+, 54.20), 284 (2.61), 268 (1.86), 134 (100), Anal. $C_{17}H_{12}O_7$. Calcd. C, 62.19; H, 3.66. Found C, 62.10; H, 3.64%.

*4,5-Bis(4-chlorophenyl)-1,3-dioxolan-2-one (**4e**)*: light green crystals, m.p.:122–124°C, ν_{max}(KBr)/ cm^{-1}: 1797, 1494, 1417, 1345, 821, 799, δ_H: 6.88–6.90 (4H, d, $J = 8.0$ Hz), 7.16–7.18 (4H, d, $J = 8.0$ Hz), 5.95 (2H, s), *m/z*(%): 308 (M^+, 21.26), 248 (2.23), 89 (100), Anal. $C_{15}H_{10}ClO_3$. Calcd. C, 58.25; H, 3.24. Found C, 58.20; H, 3.25%.

*4,5-Bis(4-nitrophenyl)-1,3-dioxolan-2-one (**4f**)*: light green crystals, m.p.: 162–164°C, ν_{max}(KBr)/ cm^{-1}: 1745, 1608, 1523, 1388, 1347, 944, 849, δ_H: 7.54–7.56 (4H, d, $J = 8.0$ Hz), 8.23–8.25 (4H, d, $J = 8.0$ Hz), 5.28 (2H, s), *m/z*(%): 330(M^+, 2.03), 137 (100), Anal. $C_{15}H_{10}N_2O_3$. Calcd. C, 54.55; H, 3.03; N, 8.48. Found C, 54.50; H, 3.06; N, 8.45%.

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