Thus, 5-*O*-trimethylsilyl derivative **5** (mp 147–148 °C, $[\alpha]^{20}_D$ = −93.6°, *c* 1, $CHCl_3$), readily obtainable either from **3a** (90%, TMSCl, pyridine), or directly from the condensation reaction between **2a** and **1** where the citric acid/MeOH treatment was avoided (51%), was transformed into β-L-*ribo*-D-*gluco*-nonuronolactone **6** (65%, mp 185–186 °C, $[\alpha]^{20}_D$ = −13.8°, *c* 0.85, EtOH) via anti-selective cis-dihydroxylation of the α,β-double bond using the $KMnO_4$/dicyclohexyl-18-crown-6/CH_2Cl_2 protocol developed by Mukaiyama.[11,12] Subsequent treatment of the diol **6** with dimethoxypropane (solvent) in the presence of a catalytic amount of TsOH at room temperature resulted in lactone ring opening, desilylation, and isopropylidene blocking of the four contiguous 5,6:7,8 OH groups, to generate crystalline nonofuranuronic acid methyl ester **7** in 60% yield (mp 96–97 °C, $[\alpha]^{20}_D$ = −31.5°, *c* 1.9, $CHCl_3$). The reduction of the ester moiety in **7** was achieved by using DIBAL-H either at −60 °C (THF), or at 25 °C (toluene), providing β-L-*ribo*-D-*gluco*-nonodialdofuranose **8** (73%, an oil, $[\alpha]^{20}_D$ = −44.5°, *c* 0.27, $CHCl_3$), or β-L-*ribo*-D-*gluco*-nonofuranose **9** (75%, an oil, $[\alpha]^{20}_D$ = −22.3°, *c* 0.13, $CHCl_3$), respectively. Alternatively, furanose **9** was quantitatively generated from **8** by $NaBH_4$ reduction of the C-9 aldehydo group (MeOH, 20 °C). Compounds **5–9** were obtained as single diastereoisomers (^{1}H NMR, HPLC), suggesting that no epimerization occurred during the overall sequence.

We will continue to evaluate the synthetic scope of the reaction and reiterate the elongation procedure outlined herein en route to higher sugar derivatives.

Acknowledgment. We thank the Consiglio Nazionale delle Ricerche, Progetto Finalizzato Chimica Fine II for the generous support of our programs and Prof. G. Gasparri Fava and Prof. M. Ferrari Belicchi (University of Parma) for performing the X-ray analysis.

Supplementary Material Available: Experimental procedures and ^{1}H NMR data for all new compounds (6 pages). Ordering information is given on any current masthead page.

(11) Mukaiyama, T.; Tabusa, F.; Suzuki, K. *Chem. Lett.* **1983**, 173.
(12) The stereochemistry of the diol **6** was assigned from ^{1}H NMR experiments, and shown to be 6,7-trans:7,8 cis, in accordance with a completely *erythro*-selective cis-hydroxylation process (see ref 11). Conventional IUPAC numbering system was adopted for structures **6–9**.

New Synthesis of Macrocyclic Dialkynyl Imines

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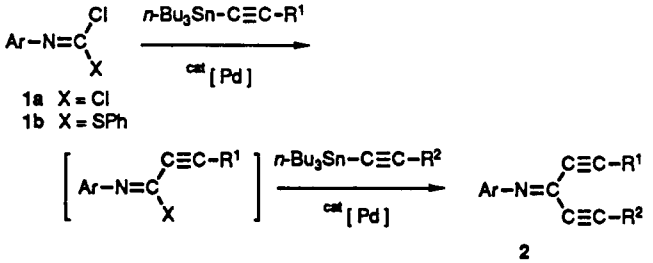
Summary: New macrocyclic N-substituted dialkynyl imines were successfully synthesized by the reaction of N-substituted isocyanide dichlorides with bifunctional alkynyltin compounds and were synthetically elaborated to novel bicyclic heteroatom-containing compounds.

During the last 2 decades, a variety of crown ethers have been prepared and attracted much attention from the view points of organic synthesis and bioorganic chemistry.[1] Various heteroatom analogues[2] of the crown ethers have also been designed and synthesized in efforts to develop new functional host molecules. Recently, we have reported palladium-catalyzed coupling reactions of N-substituted imidoyl chloride derivatives (**1**) with alkynyltins, giving symmetrical and unsymmetrical N-substituted dialkynyl imines (**2**).[3]



2

We now report that new macrocyclic N-substituted dialkynyl imines (**4**)[4] may be successfully synthesized by the reaction of N-substituted isocyanide dichlorides (**1a**) with bifunctional alkynyltin compounds (**3**) and may be further elaborated to novel bicyclic heteroatom-containing compounds.

The reaction of N-substituted isocyanide dichloride (**1**) with bis(alkynyltin) compounds (1.2 molar equiv)[5] was carried out in the presence of bis(triphenylphosphine)-palladium(II) dichloride (0.05 molar equiv) and lithium perchlorate (1 molar equiv) at 50 °C under high dilution conditions (0.01 M), giving macrocyclic N-substituted dialkynyl imines (**4**) in satisfactory yields after column chromatography. Synthesis of macrocyclic dialkynyl imines of 12–20-membered rings are summarized in Table I.

The presence of lithium perchlorate in the cyclization reaction was significant and improved the product yields, although the role of lithium perchlorate remains to be clarified. Indeed, the yields of the products (**4**) in the absence of lithium perchlorate decreased to about half of the yields described in Table I. The cyclization might be favored by complexation of lithium perchlorate with bis(alkynyltin) compounds containing ether linkages.

Typical experimental procedure for the preparation of **4** was exemplified by the synthesis of **4h**: A solution of *N*-phenyl isocyanide dichloride (0.25 mmol), 1,13-bis(tributylstannyl)-4,7,10-trioxa-1,12-tridecadiyne (0.30 mmol), lithium perchlorate (0.25 mmol), and bis(triphenylphosphine)palladium(II) dichloride (0.0125 mmol) in

(1) For reviews: Cram, D. J. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 1039. Lehn, J.-M. *Ibid.* **1988**, *27*, 89.
(2) Krakowiak, K. E.; Bradshaw, J. S.; Krakowiak, D. J. Z. *Chem. Rev.* **1989**, *89*, 929. Cooper, S. R. *Acc. Chem. Res.* **1988**, *21*, 141. Tsvetkov, E. N.; Borin, A. N.; Syundyukova, V. Kh. *Uspekhi Khimii* **1988**, *57*, 1353.
(3) Ito, Y.; Inouye, M.; Murakami, M. *Tetrahedron Lett.* **1988**, *29*, 5379; *Chem. Lett.* **1989**, 1261.
(4) Some macrocyclic dialkynyl ketones have been prepared: Sondheimer, F.; Pilling, G. M. *J. Am. Chem. Soc.* **1971**, *93*, 1977. Duckworth, V. F.; Hitchcock, P. B.; Mason, R. *J. Chem. Soc. D* **1971**, 963 and references cited therein.
(5) Bis(alkynyltin) compounds (**3**) were prepared by the following procedure: to a solution of diyne (3.0 mmol) in THF (6 mL) was added a hexane solution of butyllithium (6.0 mmol) dropwise at 0 °C. After 30 min, tributyltin chloride (6.0 mmol) was added, and then the reaction mixture was stirred at room temperature for 12 h. Extractive workup followed by evaporation of organic solvent afforded bis(alkynyltin) compound in >90% yield, which was used in the reaction with N-substituted isocyanide dichloride without further purification.

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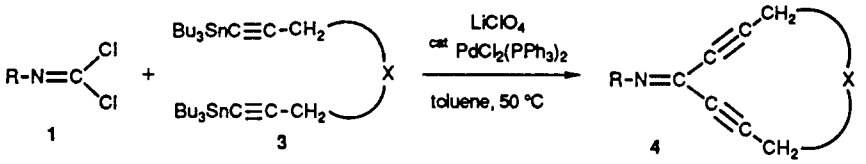
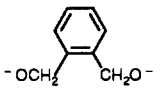
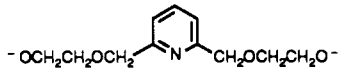
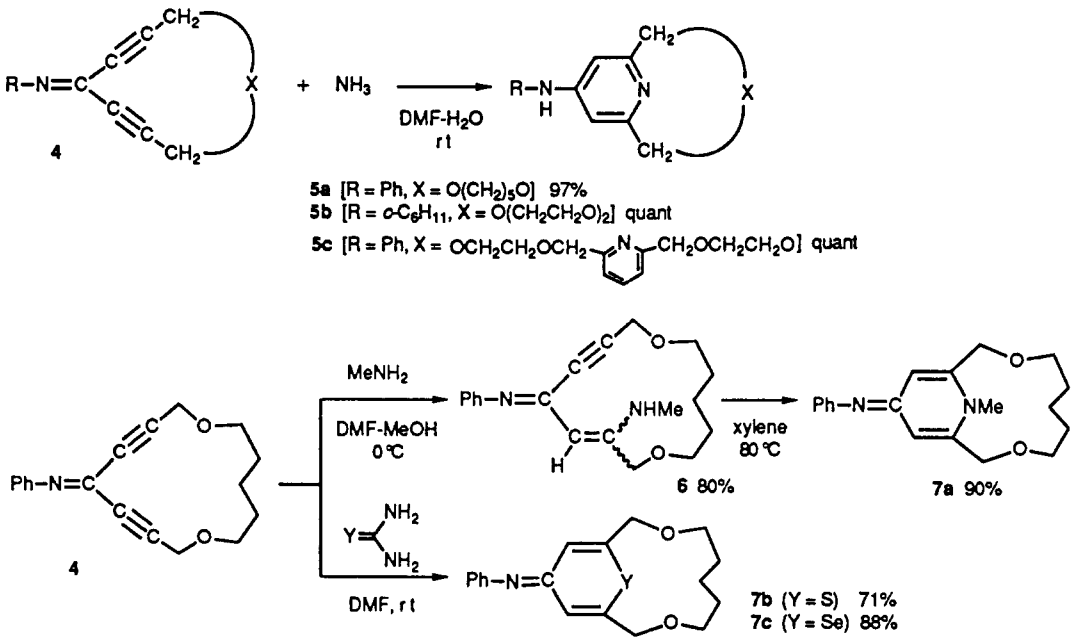
Table I. Syntheses of Macrocyclic Dialkynyl Imines (4)



entry	R	X	product[a]	ring size	yield, %
1	Ph	$-O(CH_2)_3O-$	**4a**	12	31
2	Ph	$-O(CH_2)_4O-$	**4b**	13	42
3	Ph	$-O(CH_2)_5O-$	**4c**	14	45
4	p-ClC_6H_4	$-O(CH_2)_5O-$	**4d**	14	52
5	Ph	$-O(CH_2)_6O-$	**4e**	15	42
6	Ph	$-O(CH_2)_8O-$	**4f**	17	28
7	Ph	$-O(CH_2)_{10}O-$	**4g**	19	24
8	Ph	$-O(CH_2CH_2O)_2-$	**4h**	14	52
9	c-C_6H_{11}	$-O(CH_2CH_2O)_2-$	**4i**	14	17
10	p-ClC_6H_4	$-O(CH_2CH_2O)_2-$	**4j**	14	55
11	Ph	$-O(CH_2CH_2O)_3-$	**4k**	17	32
12	Ph	$-(CH_2)_7-$	**4l**	14	34
13	Ph	$-N(i\text{-Pr})(CH_2)_5N(i\text{-Pr})-$	**4m**	14	41
14	Ph		**4n**	13	40
15	Ph		**4o**	20	23[b]

[a] Satisfactory ^1H NMR and IR spectra and combustion analyses or high-resolution mass spectra were obtained for all products (**4**). [b] Sodium perchlorate was used instead of lithium perchlorate.

Scheme I



toluene (25 mL) was stirred at 50 °C for 30 h. After evaporation of toluene in vacuo, the reaction mixture was subjected to column chromatography on silica gel (hexane–ether, 10:1–2:1) gave **4h**[6] in 52% yield.

Macrocyclic dialkynyl imines (**4**) thus prepared were converted into the novel bicyclic heteroatom-containing compounds by the reaction with some heteroatom nucleophiles[7] as shown in the Scheme I. For instance, **4** (0.01 mmol) reacted with aqueous ammonium hydroxide (0.3 mL) in DMF (0.5 mL) at room temperature to produce 4-aminopyridine derivative (**5**) in high yield. Of note is that **4d** was treated with methylamine in DMF/MeOH at 0 °C for 30 min to give primarily a Michael adduct (**6**) in 80% yield, which was converted to **7a** in 90% yield on heating at 80 °C for 2 h in xylene.

Further application directed to organic synthesis and enzyme modeling are in progress in our laboratory.

Supplementary Material Available: Spectral and analytical data for **4–7** (5 pages). Ordering information is given on any current masthead page.

(6) **4h**: 52%; mp 116–117 °C (hexane–CH_2Cl_2); IR (KBr) 2212, 1576 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 3.66–3.73 (m, 4 H), 3.81–3.92 (m, 4 H), 4.22 (s, 2 H), 4.38 (s, 2 H), 7.12–7.25 (m, 3 H), 7.27–7.38 (m, 2 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 58.92, 59.11, 69.80, 70.06, 70.19, 81.67, 85.57, 89.48, 94.68, 121.21, 126.29, 128.70, 132.31, 149.23; MS (EI, 20 eV) m/e 283 (M^+). Anal. Calcd for $C_{17}H_{17}NO_3$: C, 72.07; H, 6.05; N, 4.94. Found: C, 71.94; H, 6.04; N, 4.91.

(7) Migliorese, K. G.; Miller, S. I. *J. Org. Chem.* **1974**, *39*, 843.