Research Article

Ultrasonic-Assisted Synthesis of Two *t*-Butoxycarbonylamino Cephalosporin Intermediates on SiO₂

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Herein, we describe a facile and high efficient strategy for the synthesis of two forms of the 7β-*t*-butoxycarbonylamino-3-chloromethyl-3-cephem-4-carboxylates using ultrasonic irradiation. By SiO₂ as weak Lewis acid catalyst, 4-methoxybenzyl 7β-*t*-butoxycarbonylamino-3-chloromethyl-3-cephem-carboxylate (Boc-ACLE) and benzhydryl 7β-*t*-butoxycarbonylamino-3-chloromethyl-3-cephem-4-carboxylate (Boc-ACLH) were successfully synthesized through the efficient protection of the *N*-*t*-butoxycarbonyl (*N*-Boc), and the reactions occurred at low temperature requiring short reaction times and exhibiting excellent isolated yields (96% and 96.2%, resp.). The advantages of this reaction route including the usage of economical reagents and mild reaction conditions and high isolated yield make the two significant *t*-butoxycarbonylamino cephalosporin intermediates possible in large-scale production.

1. Introduction

7β-*t*-Butoxycarbonylamino-3-chloromethyl-3-cephem-4-carboxylates serving as the extremely important intermediates are employed to synthesize the commonly used antibiotics, cephalosporin. As shown in Figure 1, the chemical structure of cephalosporin intermediate contains a chemically active 3-chloromethyl-group at 3-side chain, which can be easily coupled with drug-active functional groups forming cephalosporin derivatives, especially the fourth-generation cephalosporins Cefoselis sulfate [1, 2]. However, owing to their presence in various biological environments, the amine functionality at 7 positions needs to be protected which is one of the most challenging issues in this synthetic chemistry. Among the current amine protection methods, the *t*-butoxycarbonyl (Boc) protection has been considered as the useful one because of its excellent stability regarding catalytic hydrogenation and extreme resistance to underlying basic or nucleophilic reactions [3].

In the past decade, multiple processes have been available to introduce the Boc protecting group using Boc₂O (di-*t*-butyl dicarbonate) to synthesize 4-methoxybenzyl

7β-*t*-butoxycarbonylamino-3-chloromethyl-3-cephem-carboxylate (Boc-ACLE). The synthesis of Boc-ACLE has been reported by Lee et al. [4] that they dissolved 4-methoxybenzyl 7β-amino-3-chloromethyl-3-cephem-carboxylate (ACLE·HCl) into CH₂Cl₂ solvent first. Next, the mixture was reacted with di-*t*-butyldicarbonate (Boc₂O) in the presence of a catalyst of *N*-(trimethylsilyl) acetamide (NSA). However, the catalyst of NSA has numerous drawbacks for the practical reaction such as its high costs, sensitivity to moisture, the low yield (51%), and other further troubles from processing (number 1, Table 1). Recently, Du [5] used tetrabutylammonium bromide (TEBA) as phase transfer catalyst to synthesize Boc-ACLE compound, where ACLE·HCl was reacted with Boc₂O in weak basic aqueous solution at room temperature. However, Boc₂O was easily decomposed under basic aqueous solution environment in which Boc₂O was largely lost, and the reaction required long reaction times (10 h) giving a yield of 80% (number 2, Table 1). In 2010, Lin [6] reported that the Boc-ACLE could be synthesized via a catalyst-free method starting from the reaction of ACLE·HCl and Boc₂O in tetrahydrofuran (THF). Using triethylamine as acid binding agent, they finally got a high yield of 87.21%. Unfortunately,

SCHEME 1: Synthetic route of Boc-ACLH.

TABLE 1: Comparison of three methods for the synthesis of Boc-ACLE.

Number	Catalyst	Reaction time	Solvent	Yield%
1	NSA	12 h	CH ₂ Cl ₂	51 [4]
2	TEBA	10 h	Dioxane/H ₂ O	80 [5]
3*	Catalyst-free	8 h	THF	15 [6]

*The HPLC assay indicated the yield was 15% according to the reported methods.

FIGURE 1: General structure of 3-chloromethyl cephalosporin.

the reproducibility seems not good and we determined that the yield was only 15% (number 3, Table 1).

Another *t*-butoxycarbonylamino cephalosporin intermediate, benzhydryl 7β-*t*-butoxycarbonylamino-3-chloromethyl-3-cephem-4-carboxylate (Boc-ACLH), was typically synthesized by Dai's group using 7-aminocephalosporanic acid (7-ACA) as starting material following the approach outlined in Scheme 1 [7]. Key intermediate **1** was obtained when 7-ACA was hydrolyzed in basic solution at -30°C . Sequentially, compound **1** reacted with Boc_2O to protect amine group catalyzed by TEBA in $\text{NaCO}_3\text{-H}_2\text{O}$ -acetone solution to produce compound **2**, which was then treated with diphenyl-diazomethane in *n*-hexane forming compound **3**. In the last step, the hydroxyl group of compound **3** was substituted by chlorine in presence of phosphorus pentachloride and pyridine in dichloromethane at -45°C to get the desired product **4b** (Boc-ACLH). It is apparent that this synthetic route includes tedious steps, complex experimental operations, and harsh conditions. Alternative synthetic strategies

with advantages such as short steps, mild conditions, and high efficiency are keen to be developed.

It can be deduced from the above-mentioned cases that the choice of raw materials, catalyst, solvent, and the reaction conditions play significant roles in synthesizing the two *t*-butoxycarbonylamino cephalosporin intermediates. Generally, in terms of producing these *N*-Boc derivatives, there are two kinds of catalytic methods (i.e., using base catalyst and Lewis acid catalyst). There have been plenty of base-catalyzed Boc-protection studies reported by using Boc_2O /DMAP system; however, the high toxicity of DMAP was not neglectable [8]. What is worse, the base-catalyzed reactions reported often resulted in the generation of byproducts like isocyanate, urea, and *N,N*-di-Boc derivatives [9, 10]. Other catalytic approaches involving Lewis acids, such as $\text{La}(\text{NO}_3)_3\cdot 6\text{H}_2\text{O}$, ZrCl_4 , LiClO_4 , $\text{Cu}(\text{BF}_4)_2\cdot 9\text{H}_2\text{O}$, $\text{Zn}(\text{ClO}_4)_2\cdot 6\text{H}_2\text{O}$, Yttria-Zirconia, $\text{HClO}_4/\text{SiO}_2$, montmorillonite K-10, amberlyst-15, $\text{H}_3\text{PW}_{12}\text{O}_{40}$, sulfamic acid, I_2 , and hexafluoroisopropanol (HFIP), have been attempted [11–15]. As the increasing demand of mild reaction conditions encourages the development of greener route to achieve these significant synthetic works in recent years, the sonochemistry has offered a solution that a large variety of organic/medical transformations succeeded using this more efficient and facile method [16]. For instance, Amira et al. [17] have applied ultrasonic irradiation technology for the *N*-Boc protection which not only eliminated the harsh reaction conditions but also assisted in impressive yield. Dighe and Jadhav [18] found microwave assisted chemoselective method could shorten the reaction time for the generation of *N*-Boc products with excellent isolated yield. It is worth mentioning that solvent-free synthetic strategies using ionic liquid catalyst have emerged which show great potential for *N*-Boc formation [19, 20].

In this paper, we aim at proposing an optimum route for the synthesis of the two *t*-butoxycarbonylamino cephalosporin intermediates based upon the synergetic effect of ultrasonic assistance and SiO_2 catalyst. The efficiency of our route for *N*-Boc formation of our targeted product was analyzed and the mechanism of the proposed ultrasonic-assisted strategy for *N*-Boc protection of amines was investigated.

TABLE 2: The effect of SiO₂ and ultrasound on the yields of the Boc-ACLE.

Number	SiO ₂	Ultrasound	Reaction time	Yield%
1	×	×	6 h	15
2	✓	×	6 h	35
3	×	✓	6 h	40
4	✓	✓	30 min	96

Note: ×: no; ✓: yes.

In addition, the products were confirmed by spectrometric methods. In comparison to conventional methods, our route may offer a highly efficient and methodologically simple catalytic process to introduce *N*-Boc protecting group into our desired products.

2. Experimental Section

2.1. General Information. ACLE-HCl and ACLH-HCl were purchased from Shanghai Arbor Chemical Co., Ltd. The other reagents and solvents were obtained from Sigma-Aldrich and used as received without any further purification. All reactions were monitored by thin-layer chromatography (TLC) using commercial silica gel plates. JL-120DTH ultrasonic bath was purchased from Shanghai Jnsh Testmart Co., Ltd. The purity was measured by high performance liquid chromatography (HPLC) on Agilent 1,100 series. The liquid chromatographic system was equipped with an ODS-3 C18 column (GL Science Co. Ltd., 180 × 4.6 mm i.d., 5.0 μm). Melting points were observed on YRT-3 Melting Point Tester and were uncorrected. NMR spectra were determined on Bruker AV300 in DMSO-*d*₆ with TMS as internal standard for ¹H NMR (300 MHz) and ¹³C NMR (75 MHz), respectively. HRMS were carried out on an Agilent 6230-LC/TOF MS mass spectrometer.

2.2. General Procedure for *t*-Butoxycarbonylamino Cephalosporin Intermediates. ACLE-HCl (**5a**) or ACLH-HCl (**5b**) as starting reagent was added to CH₂Cl₂ (200 mL) firstly; triethylamine was then introduced into the mixture to neutralize the pH at 7–8 at 0–5°C. Then, appropriate amounts of SiO₂ and Boc₂O were added to the mixture for the appropriate time of bath ultrasonication at 0–5°C (Table 2). After completion of the reaction indicated by thin-layer chromatography (TLC), the mixture was poured into water and the organic phase was separated followed by washing with brine water and drying with anhydrous sodium sulfate under vacuum evaporation. The crude product was purified by column chromatography over silica gel to yield the desired compounds.

4-Methoxyphenyl 7β-*t*-Butyl-carbonylamino-3-chloromethyl-3-cephem-4-carboxylate (4a**).** **4a**: Solid, m.p. 63–65°C. The yield was 96.0%. HPLC assay confirmed the purity of **4a** was 98.5%. The column oven temperature was set at 295 K. The mobile phase consisted of methanol and deionized water (75:25, v/v) and flowed through the column in 15 min with the flow rate of 1.0 mL/min. Photodiode array detection was used to detect the Boc-ACLE at the wavelength of 254 nm. ¹H

TABLE 3: Comparison of ¹H NMR data (**4a**).

Lee et al. reported (500 MHz, CDCl ₃) ^a	Synthetic 4a (300 MHz, DMSO- <i>d</i> ₆) ^b
1.45 (s, 9H)	1.37 (s, 9H)
3.47 (d, 1H, <i>J</i> = 18.2 Hz),	3.48 (d, 1H, <i>J</i> = 17.91 Hz)
3.66 (d, 1H, <i>J</i> = 18.2 Hz)	3.64 (d, 1H, <i>J</i> = 9.65 Hz)
	3.73 (s, 3H)
4.55 (d, 1H, <i>J</i> = 12.1 Hz)	4.41 (d, 1H, <i>J</i> = 11.31 Hz)
	4.49 (d, 1H, <i>J</i> = 11.07 Hz)
4.95 (d, 1H, <i>J</i> = 4.6 Hz)	5.07 (d, 1H, <i>J</i> = 3.93 Hz)
5.23 (s, 2H)	5.12 (d, 1H, <i>J</i> = 12.09 Hz)
	5.19 (d, 1H, <i>J</i> = 11.73 Hz)
5.61 (dd, 1H, <i>J</i> = 5.0, 9.5 Hz)	5.48 (s, 2H)
6.88–6.91 (dt _{app} , 2H)	6.89–6.92 (dt _{app} , 2H)
7.33–7.36 (dt _{app} , 2H)	7.32–7.34 (dt _{app} , 2H)

^aData taken from [4]; ^bthis work.

and ¹³C NMR refer to Tables 3 and 4. ESI-HRMS: calcd. for C₂₁H₂₄ClN₂O₆S ([M–H][–]) 467.1049, found 467.1045.

Benzhydryl 7β-*t*-Butoxycarbonylamino-3-chloromethyl-3-cephem-4-carboxylate (4b**).** (**4b**): Solid, m.p. 140–142°C (decomposed). The yield was 96.2%. (HPLC assay of **4b** was 98.1%). The HPLC method of **4b** was similar to the **4a**. ¹H NMR refer to Table 5. ¹³C NMR (75 MHz, DMSO-*d*₆): δ 170.86, 165.01, 161.06, 159.34, 135.70, 130.25, 28.93, 128.16, 126.84, 126.43, 125.29, 124.83, 113.77, 67.28, 59.18, 57.96, 57.86, 55.06, 43.72, 41.55, 40.33, 26.09. ESI-HRMS: calcd. for C₂₆H₂₇ClN₂O₅NaS ([M+Na]⁺) 537.1221, found 537.1243.

3. Results and Discussion

In present work, as described in Scheme 2, we selected inexpensive ACLE-HCl (**5a**) or benzhydryl 7β-amino-3-chloromethyl-3-cephem-carboxylate (ACLH-HCl, **5b**) as starting materials. They were neutralized by triethylamine in CH₂Cl₂ solvent at 0–5°C for 30 min, and then the free base (ACLE or ACLH) was reacted with Boc₂O by *N*-acylation reaction at presence of SiO₂ under ultrasonic irradiation for 30 min to form 7β-*t*-butoxycarbonylamino-3-chloromethyl-3-cephem-4-carboxylates (**4a**, Boc-ACLE, or **4b**, Boc-ACLH).

To overcome the exothermicity of the reaction while carrying out the reaction on a large-scale operation, the reaction temperature should be controlled and determining an appropriate solvent which depends on substrate reactivity and solubility seems very important [14]. As the exothermic phenomenon was found in our *N*-acylation reaction, therefore, to maintain the stability of thermos-sensitive cephalosporin compounds, we chose dichloromethane as solvent and kept the reaction temperature below 10°C.

SCHEME 2: Ultrasonic synthesis of Boc-ACLE and Boc-ACLH.

TABLE 4: Comparison of ^{13}C NMR data (**4a**).

Lee et al. reported (125 MHz, CDCl_3) ^a	Synthetic 4a (75 MHz, $\text{DMSO}-d_6$) ^b
—	170.86
165.6	165.01
161.4	161.06
160.2	159.34
154.7	135.70
149.6	130.25
131.0	128.16
126.8	126.84, 126.43
125.9	125.29, 124.83
114.2	113.77
81.5	—
68.5	67.28
61.2	59.18
58.3	57.96, 57.86
55.5	55.06
43.6	43.72, 40.33
28.4	28.93
27.4	26.09

^aData taken from [4]; ^bthis work.

The effect of SiO_2 and ultrasound on the yields of the formation of Boc-ACLE was recorded in Table 2. The proposed route without both catalyst and ultrasonic irradiation took 6 hours to achieve the reaction but the resulting isolated yield was only 15%. When Lewis acid catalyst SiO_2 was added to the route, the yield of the reaction was improved up to 35%. To find the synergic effect of ultrasound and SiO_2 , another control reaction using ultrasound alone was performed under the same reaction time without SiO_2 that a low yield of 40% was found. Notably, when the Lewis acid catalyst of SiO_2 and ultrasonic power were utilized together, an overwhelming yield of 96% was discovered after 30 mins. The similar impressive result also happened to synthesize Boc-ACLH (the yield is 96.2%) using both ultrasound and SiO_2 which implied these results were attributed to the synergy effect of ultrasonic irradiation and SiO_2 .

TABLE 5: Comparison of ^1H NMR data (**4b**).

Dai et al. reported (500 MHz, CDCl_3) ^a	Synthetic 4b (300 MHz, $\text{DMSO}-d_6$) ^b
1.49 (s, 9H)	1.38 (s, 9H)
3.49, 3.57 (d, 2H, $J = 14$ Hz)	3.52 (d, 1H, $J = 1.38$ Hz)
	3.66 (d, 1H, $J = 17.97$ Hz)
4.98 (d, 1H, $J = 4$ Hz)	5.12 (d, 1H, $J = 4.14$ Hz)
5.21 (d, 1H, $J = 8$ Hz)	—
5.65 (dd, 1H, $J = 4, 8$ Hz)	5.56 (s, 1H)
6.98 (s, 1H)	6.93 (s, 1H)
	7.27–7.49 (dt _{app} , 10H)
7.3–7.5 (m, 10H)	7.38 (s, 1H)
	8.01–8.04 (d, 1H, $J = 8.49$)

^aData taken from [7]; ^bthis work.

To explain this mechanism, we believe that, as a result of the electronic and steric molecular structure of 7β-amino-3-chloromethyl-3-cephem-4-carboxylates, the amine group is low nucleophilic which could be activated by the weak Lewis acid support body of SiO_2 under ultrasonic irradiation. Figure 2 describes the structure of SiO_2 surface. Tran et al. [21] believed that the adjacent hydroxyl and double hydroxyl groups of SiO_2 surface showing weak acidity could activate the carbonyl compounds. We hypothesize that the surface of SiO_2 support body formed the polyhydroxyl matrix and the $(\text{Boc})_2\text{O}$ was attacked by the free base (ACLE or ACLH) on the matrix which was consistent with the conclusion of Sunseri et al. [22]. Ultrasonic vibrations enable the formation of intermolecular extrusions and confusions which has a significant influence on carbon dioxide generated from mono-*t*-butyl carbonate (compound **6**). We believe there are two reasonable mechanisms of facilitating the nucleophilic attack of amine group on the carbonyl group involved during the process; the former is that with the bubble formation and breakdown; the cavitation contributes to the efficient generation of the *N*-Boc amide (Boc-ACLE or BOC-ACLH); the latter is based on the reaction equilibrium that the continuous escape of CO_2 results in the reaction preferring a forward tendency (Scheme 3).

SCHEME 3: The proposed ultrasonic-assisted synthetic mechanism of *N*-Boc protection for amines.

FIGURE 2: The structure of silicon dioxide surface (note: 1: silicon oxygen group; 2: isolated hydroxyl group; 3: adjacent hydroxyl group; 4: double hydroxyl group).

4. Conclusions

In summary, the ultrasonic-assisted approach catalyzed by SiO_2 for the synthesis of two *t*-butoxycarbonylamino compounds at low temperature was investigated. By means of the synergetic effect of the ultrasound and SiO_2 , the designed reaction system showed a high efficiency on the desired products without any harsh conditions. Additionally, compared with existing production processing of the two *t*-butoxycarbonylamino cephalosporin intermediates, the work described in this study allows for stabilization of the real-time reaction temperature and low cost for the reaction. Importantly, this study greatly advances not only the practical cephalosporin production field but also the field of other synthetic drugs and their derivatives requiring Boc protection of amines.

Competing Interests

The authors declare that there are no competing interests regarding the publication of this paper.

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References

- [1] H. Ohki, K. Kawabata, S. Okuda, T. Kamimura, and K. Sakane, "FK037, a new parenteral cephalosporin with a broad antibacterial spectrum: synthesis and antibacterial activity," *Journal of Antibiotics*, vol. 46, no. 2, pp. 359–361, 1993.
- [2] K. Sakane, K. Kawabata, and H. Ohki, "Process for the preparation of cephalosporin compound," JP 92173792, 1992.
- [3] C. Agami and F. Couty, "The reactivity of the *N*-Boc protecting group: an underrated feature," *Tetrahedron*, vol. 58, no. 14, pp. 2701–2724, 2002.
- [4] M. Lee, D. Heseck, M. Suvorov, W. Lee, S. Vakulenko, and S. Mobashery, "A Mechanism-based inhibitor targeting the DD-transpeptidase activity of bacterial penicillin-binding proteins," *Journal of the American Chemical Society*, vol. 125, no. 52, pp. 16322–16326, 2003.
- [5] Z. Y. Du, "Cefoselis sulfate intermediate and preparation method," CN 102827190A, 2012.
- [6] K. C. Lin, "Improved method for synthesizing cefoselis sulfate," CN 1993450B, 2010.
- [7] X. Y. Dai, L. W. Li, P. Guo, and C. H. Sun, "Synthesis of diphenylmethyl 7 β -*t*-butoxycarbonylamino-3-chloromethyl-3-cephem-4-carboxylate," *Chinese Journal of Pharmaceuticals*, vol. 40, pp. 16–18, 2009.
- [8] D. V. Sweet, *Registry of Toxic Effects of Chemical Substances 1985–86*, US Government Printing Office, Washington, DC, USA, 1988.
- [9] Y. Basel and A. Hassner, "Di-*tert*-butyl dicarbonate and 4-(dimethylamino)pyridine revisited. Their reactions with amines and alcohols," *Journal of Organic Chemistry*, vol. 65, no. 20, pp. 6368–6380, 2000.
- [10] S. V. Chankeshwara and A. K. Chakraborti, "Catalyst-free chemoselective *N*-*tert*-butyloxycarbonylation of amines in water," *Organic Letters*, vol. 8, no. 15, pp. 3259–3262, 2006.
- [11] A. K. Chakraborti and S. V. Chankeshwara, " HClO_4 - SiO_2 as a new, highly efficient, inexpensive and reusable catalyst for *N*-*tert*-butoxycarbonylation of amines," *Organic & Biomolecular Chemistry*, vol. 4, no. 14, pp. 2769–2771, 2006.
- [12] S. V. Chankeshwara and A. K. Chakraborti, "Montmorillonite K 10 and montmorillonite KSF as new and reusable catalysts for conversion of amines to *N*-*tert*-butylcarbamates," *Journal of Molecular Catalysis A: Chemical*, vol. 253, no. 1-2, pp. 198–202, 2006.
- [13] F. Jahani, M. Tajbakhsh, S. Khaksar, and M. R. Azizi, "An efficient and highly chemoselective *N*-Boc protection of amines, amino acids, and peptides under heterogeneous conditions," *Monatshefte für Chemie*, vol. 142, no. 10, pp. 1035–1043, 2011.
- [14] R. Varala, S. Nuvula, and S. R. Adapa, "Molecular iodine-catalyzed facile procedure for *N*-Boc protection of amines," *Journal of Organic Chemistry*, vol. 71, no. 21, pp. 8283–8286, 2006.
- [15] A. Heydari, S. Khaksar, and M. Tajbakhsh, "1,1,1,3,3,3-Hexafluoroisopropanol: a recyclable organocatalyst for *N*-Boc protection of amines," *Synthesis*, vol. 19, Article ID Z11408SS, pp. 3126–3130, 2008.

- [16] G. A. Dilbeck, L. Field, A. A. Gallo, and R. J. Gargiulo, "Biologically oriented organic sulfur chemistry. 19. Synthesis and properties of 2-amino-5-mercapto-5-methylhexanoic acid, a bishomologue of penicillamine. Use of boron trifluoride etherate for catalyzing Markownikoff addition of a thiol to an olefin," *Journal of Organic Chemistry*, vol. 43, no. 24, pp. 4593–4596, 1978.
- [17] A. Amira, H. K'tir, M. Berredjem, and N.-E. Aouf, "A simple, rapid, and efficient N-Boc protection of amines under ultrasound irradiation and catalyst-free conditions," *Monatshefte für Chemie*, vol. 145, no. 3, pp. 509–515, 2014.
- [18] S. N. Dighe and H. R. Jadhav, "Microwave assisted mild, rapid, solvent-less, and catalyst-free chemoselective *N*-tert-butyloxycarbonylation of amines," *Tetrahedron Letters*, vol. 53, no. 43, pp. 5803–5806, 2012.
- [19] S. Majumdar, J. De, A. Chakraborty, and D. K. Maiti, "General solvent-free highly selective *N*-tert-butyloxycarbonylation strategy using protic ionic liquid as an efficient catalyst," *RSC Advances*, vol. 4, no. 47, pp. 24544–24550, 2014.
- [20] A. Sarkar, S. R. Roy, N. Parikh, and A. K. Chakraborti, "Non-solvent application of ionic liquids: organo-catalysis by 1-alkyl-3-methylimidazolium cation based room-temperature ionic liquids for chemoselective *N*-tert-butyloxycarbonylation of amines and the influence of the C-2 hydrogen on catalytic efficiency," *The Journal of Organic Chemistry*, vol. 76, no. 17, pp. 7132–7140, 2011.
- [21] N. T. Tran, T. Min, and A. K. Franz, "Silanediol hydrogen bonding activation of carbonyl compounds," *Chemistry—A European Journal*, vol. 17, no. 36, pp. 9897–9900, 2011.
- [22] J. D. Sunseri, W. T. Cooper, and J. G. Dorsey, "Reducing residual silanol interactions in reversed-phase liquid chromatography: thermal treatment of silica before derivatization," *Journal of Chromatography A*, vol. 1011, no. 1-2, pp. 23–29, 2003.