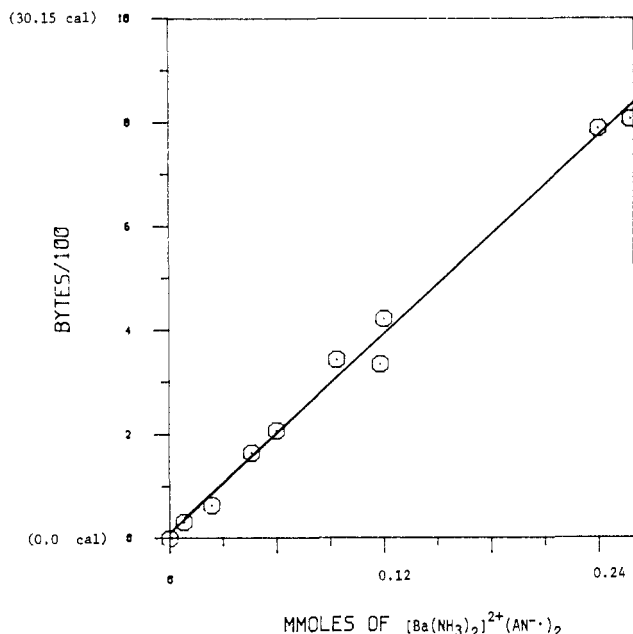


Table I. Heats of Reaction at 25 °C in Kilocalories per Mole

reaction	$\Delta H^\circ$ <sup>a</sup>	ref
$\text{ANH}_2(\text{s}) + \text{AN}(\text{s}) + 2\text{NH}_3(\text{aq}) + \text{Ba}(\text{OH})(\text{aq}) \rightarrow \text{Ba}(\text{NH}_3)_2(\text{AN})_2(\text{s}) + 2\text{H}_2\text{O}(\text{l})$	$+95.9 \pm 2.9$	this work
$\text{Ba}(\text{s}) + 2\text{H}_2\text{O}(\text{l}) \rightarrow \text{Ba}(\text{OH})(\text{aq}) + \text{H}_2(\text{g})$	-101.94	6
$\text{AN}(\text{s}) + \text{H}_2(\text{g}) \rightarrow \text{ANH}_2(\text{s})$	-17.0	7
$2\text{NH}_3(\text{g}) \rightarrow 2\text{NH}_3(\text{aq})$	-17.1	8
$\text{Ba}(\text{s}) + 2\text{NH}_3(\text{g}) + 2\text{AN}(\text{s}) \rightarrow \text{Ba}(\text{NH}_3)_2(\text{AN})_2(\text{s})$	$-40.1 \pm 3.2$	

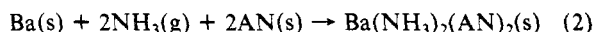
<sup>a</sup> The standard deviations were obtained from the standard deviation in the slope of the line in Figure 1, and the errors reported in ref 6-8.



**Figure 1.** Plot of the change in the temperature of the calorimeter (in computer bytes) vs. the millimoles of the barium complex in the glass bulbs. Multiplying the slope of this line ( $3.181 \pm 0.097$  bytes/millimol) by the capacity of the calorimeter (0.03015 cal/byte) yields the enthalpy of reaction 1. When the contents of the calorimeter are titrated, a millimole of HCl is used for each millimole of ammonia and each half millimole of barium hydroxide.

the calorimeter vs. the millimoles of salt in the glass bulbs is linear, Figure 1, and it yields an enthalpy for reaction 1 of  $95.9 \pm 2.9$  kcal/mol (Table I).

The data obtained from Figure 1 can be placed into a thermochemical cycle, Table I, to obtain the heat of formation of the compound from barium metal, ammonia, and anthracene in their standard states, reaction 2. The heat of reaction of barium with



ammonia and anthracene is about 40% as exothermic as the reaction of barium with water, Table I.

The solid barium complex as well as similar complexes of strontium and calcium are paramagnetic. On the basis of their ESR signals (a single line at  $g = 2.0$ ), the two anthracene molecules exist in the form of the anion radicals. All three of these alkaline earth metal complexes have the same composition relative to anthracene and ammonia, but they differ widely in color ranging from bright yellow for the calcium complex to red brown for the strontium complex. Similar salts can be formed with other organic anion radicals, which are still to be explored. In general there

appears to be a myriad of thermodynamically stable alkaline earth metal complexes with the structure  $[\text{M}(\text{NH}_3)_2]^{2+}(\text{anion radical})_2$ .

**Acknowledgment.** We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this work.

**Registry No.**  $\text{Ba}(\text{NH}_3)_2(\text{AN}^-)_2$ , 85681-26-1;  $\text{Sr}(\text{NH}_3)_2(\text{AN}^-)_2$ , 85681-27-2;  $\text{Ca}(\text{NH}_3)_2(\text{AN}^-)_2$ , 85681-28-3.

## 2-Oxoazetidine-1-phosphonic Acids: Synthesis and Transesterification

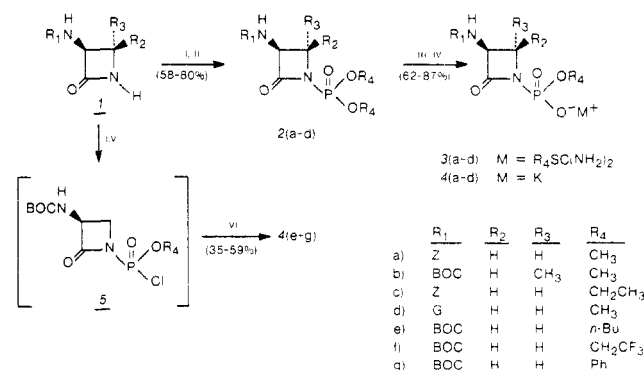
W. H. Koster,\* R. Zahler,\* H. W. Chang, C. M. Cimarusti, G. A. Jacobs, and M. Perri

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Received November 22, 1982

Aztreonam is the first example of a monocyclic  $\beta$ -lactam antibiotic having clinically useful activity.<sup>1</sup> The N-1 sulfonate moiety, characteristic of monobactams provides both activation for the  $\beta$ -lactam ring and the anionic site necessary for enzyme-substrate interaction. Although hexavalent sulfur and pentavalent phosphorus are sterically similar, an N-1 phosphonate moiety should exert less of an inductive effect on the ring compared to sulfonate. However, unlike the sulfur case, tetracoordinate phosphorus provides an extra valence for functionalization. Therefore, the synthesis and chemistry of 2-oxoazetidine-1-phosphonic acids were examined.

### Scheme 1<sup>a</sup>



Z = PhCH<sub>2</sub>OCO-, BOC = t-BuOCO-, G = PhCH<sub>2</sub>CO-

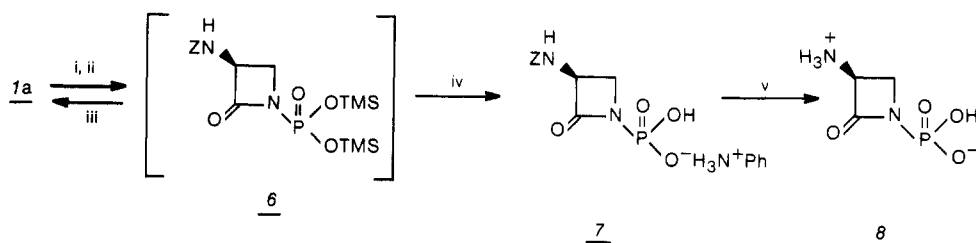
<sup>a</sup> Key: (i) *n*-BuLi, THF, -78 °C. (ii) ClPO(OR<sub>4</sub>)<sub>2</sub>, -78 °C. (iii) H<sub>2</sub>NCSNH<sub>2</sub>, CH<sub>3</sub>CN, reflux. (iv) Dowex 50 (K<sup>+</sup> form). (v) R<sub>4</sub>OP(O)Cl<sub>2</sub>, -78 °C. (vi) pH 6 phosphate buffer, dioxane, 0-5 °C.

(6) Keller, R. A. "Basic Tables in Chemistry"; McGraw-Hill: New York, 1967.

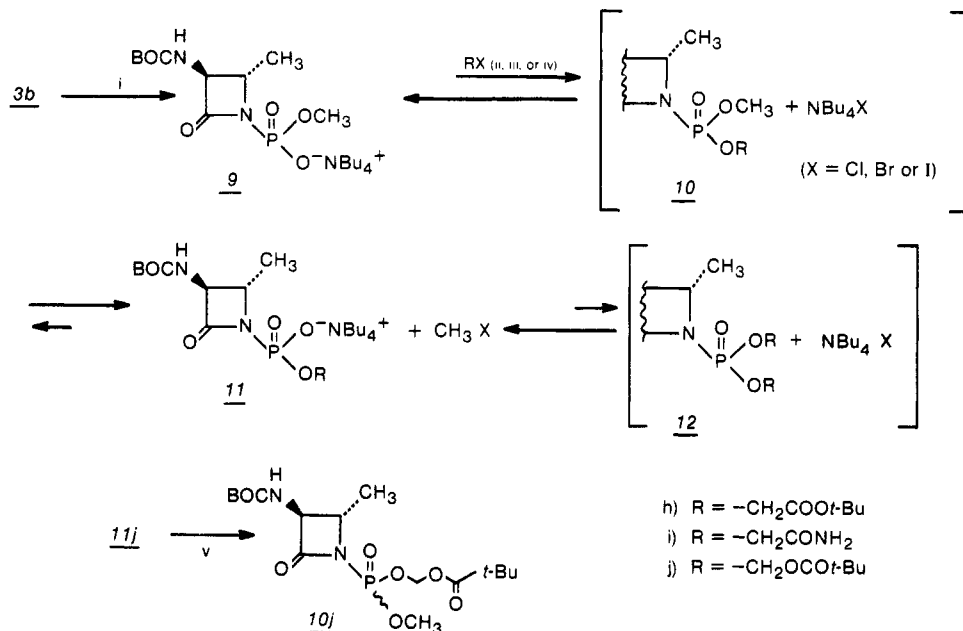
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(1) Sykes, R. B.; Bonner, D. P.; Bush, K.; Georgopapadakou, N. H. *Antimicrob. Agents Chemother.* **1982**, *21*, 85.

Scheme II<sup>a</sup>

<sup>a</sup> Key: (i) *n*-BuLi, THF, -78 °C, then ClPO(OMe)<sub>2</sub>. (ii) TMSBr, BSA. (iii) pH 4 phosphate buffer, reflux. (iv) PhNH<sub>2</sub>-EtOH. (v) H<sub>2</sub>, Pd-C, then HP-20 resin.

Scheme III<sup>a</sup>

<sup>a</sup> Key: (i) Ion-pair extraction, CH<sub>2</sub>Cl<sub>2</sub>. (ii) BrCH<sub>2</sub>COO-*t*-Bu, CH<sub>3</sub>CCl<sub>3</sub>, reflux. (iii) ICH<sub>2</sub>CONH<sub>2</sub>, CH<sub>3</sub>CCl<sub>3</sub>, reflux. (iv) ClCH<sub>2</sub>OCO-*t*-Bu, CH<sub>3</sub>CCl<sub>3</sub>, reflux. (v) Me<sub>2</sub>SO<sub>4</sub>.

The accessibility of chiral, monocyclic azetidinones **12**<sup>3</sup> suggested a general approach involving direct phosphorylation of the azetidinone nitrogen. Phosphorylation of an azetidinone N-1 anion generated from **1** was appealing; however, it has been reported that strong bases polymerize or racemize 3-(acylamino)azetidinones such as **1**.<sup>3</sup> In addition, the side-chain and azetidinone N-H's should have similar p*K*<sub>a</sub>'s, thereby making chemoselective phosphorylation questionable. Nevertheless, generation of lithioazetidinones from **1** at -78 °C (*n*-BuLi, THF) followed by treatment with a phosphorochloridate provided 60–80% yields of N-phosphorylated β-lactams **2a–d**.<sup>4</sup> These conditions were compatible with either a urethane or amide side chain at C-3 (Scheme I).

Racemization does not occur under the phosphorylation conditions as evidenced by cleavage of dimethyl ester **2a** (TMSBr, BSA) and subsequent hydrolysis (pH 4.2, reflux, 3 h).<sup>5</sup> The optical rotation of **1a** ([α]<sub>D</sub><sup>20</sup> -17.2°) recovered from this sequence was identical with that of the precursor **1a** ([α]<sub>D</sub><sup>20</sup> -17.4°, Scheme II). By quenching bis(silyl ester) **6** in the presence of aniline, the monoanilinium salt of 2-oxoazetidine-1-phosphonic acid **7** was obtained in 94% yield. Zwitterion **8**, the phosphonate analogue

of 3-aminomonobactamic acid (3-AMA),<sup>2a</sup> was prepared by hydrogenolysis of **7**.

Selective cleavage of the neutral diesters **2a–d** to form monoalkyl phosphonates was crucial for evaluating antimicrobial activity. Although a number of methods for selective cleavage were available,<sup>6</sup> mild conditions were needed to avoid destruction of the activated β-lactam ring. By refluxing the dialkyl esters **2a–d** with thiourea<sup>7</sup> in acetonitrile, cleavage to the corresponding thiuronium salts **3a–d** could be achieved under neutral conditions. Ion-exchange chromatography converted **3a–d** to the potassium salts **4a–d** (Scheme I).

A complementary, one-pot synthesis of 2-oxoazetidine-1-phosphonic acid monoesters involved lithiation of azetidinone **1** and then treatment with an alkyl phosphorodichloridate. The resulting 2-oxoazetidine-1-phosphonyl chlorides **5e–g** were hydrolyzed in situ to the desired acids **4e–g** (Scheme I). These results are noteworthy, since hydrolysis of 2-oxoazetidine-1-sulfonyl chlorides results in formation of N-1 unsubstituted β-lactams.<sup>8</sup>

The versatility of these phosphorylation methods is limited by the accessibility of the phosphorylating agents and their compatibility with the reaction conditions. Transesterification of the alkyl residue on the phosphonate moiety was developed to overcome these limitations. Taking advantage of the nucleophilicity of tetraalkylammonium phosphonate salts,<sup>9</sup> ester interchange with

(2) (a) Cimarusti, C. M.; Applegate, H. E.; Chang, H. W.; Floyd, D. M.; Koster, W. H.; Slusarchyk, W. A.; Young, M. G. *J. Org. Chem.* **1982**, *47*, 179. (b) Floyd, D. M.; Fritz, A. W.; Cimarusti, C. M. *Ibid.* **1982**, *47*, 176. (c) Floyd, D. M.; Fritz, A. W.; Pluscec, J.; Weaver, E. R. *Ibid.* **1982**, *47*, 5160. (3) Mattingly, P. G.; Miller, M. J. *J. Org. Chem.* **1981**, *46*, 1557 and references therein.

(4) Satisfactory IR, NMR, MS, and/or elemental analyses were obtained for all new compounds.

(5) Humber, D. C.; Laing, S. B.; Weingarten, G. G. *Spec. Publ.* **1981**, No. 38, 38–45.

(6) (a) Sasse, K. *Methoden Org. Chem. (Houben-Weyl)*, 4th Ed. **1964**, 12, part 2, 252–269. (b) Takeuchi, Y.; Demachi, Y.; Yoshii, E. *Tetrahedron Lett.* **1979**, 20, 1231. (c) Gray, M. D. M.; Smith, D. J. H. *Ibid.* **1980**, 21, 859.

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(8) Mukerjee, A. K. *Synthesis* **1975**, 547 and references therein.

more complex alkyl residues was effected by manipulating the equilibrium in Scheme III.<sup>10</sup> This equilibrium was influenced by the quantity of alkylating agent, RX, and by the volatility of the leaving methyl halide. Dialkyl phosphonates **10** and **12** are not favored, apparently because of the greater thermodynamic stability of tetrabutylammonium phosphonate vs. tetrabutylammonium halide under the reaction conditions.<sup>11</sup>

The utility of the transesterification technique was demonstrated by synthesis of phosphonate monoesters unobtainable by direct phosphorylation. Carboxymethyl and carbamylmethyl phosphonate esters **11h** and **11i** were prepared using this method. The labile prodrug ester<sup>12</sup> **10j** was synthesized in a one-pot procedure. Transesterification of **9** with (pivaloyloxy)methyl chloride, followed by methylation with dimethyl sulfate, afforded mixed diesters **10j** in 84% yield from **9** (Scheme III).

In summary, 3-(acylamino)azetidinones were selectively phosphorylated at the N-1 position without loss of chirality at the C-3 position. Biologically active N-1 phosphonate monoesters were obtained by selective cleavage of phosphonate diesters or by hydrolysis of N-1 phosphonyl chlorides.<sup>13</sup> The utility of the

monoalkyl 2-oxoazetidine-1-phosphonates was expanded by transesterification of the tetrabutylammonium salts of the simple methyl esters. Ester interchange by this method should be applicable to the synthesis of a variety of sensitive substrates containing phosphoric esters.

**Acknowledgment.** We are grateful to Dr. M. A. Porubcan and The Squibb Institute Analytical Department for assistance during the course of this work.

**Registry No.** **1a**, 80082-81-1; **1b**, 80582-03-2; **1d**, 80543-45-9; **1e**, 72229-74-4; **2a**, 84486-00-0; **2b**, 84486-58-8; **2c**, 84486-32-8; **2d**, 84486-03-3; **3a**, 85719-53-5; **3b**, 85760-77-6; **3c**, 85710-24-3; **3d**, 85710-25-4; **4a**, 84486-06-6; **4b**, 84520-10-5; **4c**, 84486-33-9; **4d**, 84486-07-7; **4e**, 84486-48-6; **4f**, 84486-41-9; **4g**, 84486-54-4; **5e**, 85710-26-5; **5f**, 85710-27-6; **5g**, 85710-28-7; **6**, 85710-29-8; **7**, 85710-31-2; **8**, 85710-32-3; **9**, 84520-20-7; **10j**, 85710-37-8; **11h**, 85760-79-8; **11i**, 85710-34-5; **11j**, 85710-36-7; ClPO(OCH<sub>3</sub>)<sub>2</sub>, 813-77-4; ClPO(OCH<sub>2</sub>C-H<sub>3</sub>)<sub>2</sub>, 814-49-3; H<sub>2</sub>NCSNH<sub>2</sub>, 62-56-6; *n*-BuOP(O)Cl<sub>2</sub>, 1498-52-8; F<sub>3</sub>C-CH<sub>2</sub>OP(O)Cl<sub>2</sub>, 462-56-6; PhOP(O)Cl<sub>2</sub>, 770-12-7; TMSBr, 2857-97-8; BrCH<sub>2</sub>COOBu-*t*, 5292-43-3; ICH<sub>2</sub>CONH<sub>2</sub>, 144-48-9; ClCH<sub>2</sub>OCOBu-*t*, 18997-19-8.

**Supplementary Material Available:** Listing of physical and spectral data for representative compounds (2 pages). Ordering information is given on any current masthead page.

(13) Koster, W. H.; Zahler, R.; Bonner, D. P.; Chang, H. W.; Cimarusti, C. M.; Jacobs, G. A.; Perri, M. 22nd Interscience Conference on Antimicrobial Agents and Chemotherapy, Miami, 1982.

(9) (a) Carayon-Gentil, A.; Thank, T. N.; Gonzy, G.; Chabrier, P. *Bull. Soc. Chim. Fr.* **1967**, 1616. (b) Cheymol, J.; Chabrier, P.; Selim, M.; Leduc, P. *C. R. Hebd. Seances Acad. Sci.* **1959**, 249, 2573.

(10) Clark, V. M.; Todd, A. R. *J. Chem. Soc.* **1950**, 2031.

(11) In a typical procedure only a 1–4-fold excess of alkylating agent was required. Significant dialkylation is not observed even in the presence of a 10-fold excess of alkylating agent.

(12) Ferres, H. *Chem. Ind. (London)* **1980**, 435.

## Additions and Corrections

**Effect of Particle Size on the Activity of Supported Palladium Catalysts** [*J. Am. Chem. Soc.* **1982**, *104*, 5249–5250]. YOSHIO TAKASU,\* TSUTOMU AKIMARU, KENJI KASAHARA, YOSHIHARU MATSUDA, HIROYUKI MIURA, and ISAMU TOYOSHIMA.

Page 5249, second paragraph, last sentence: The sentence should be read as follows—These workers found a dramatic *increase* in the rate of carbon formation, as the average particle size decreased.

**Effect of Electron Correlation on Theoretical Equilibrium Geometries. 2. Comparison of Third-Order Perturbation and Configuration Interaction Results with Experiment** [*J. Am. Chem. Soc.* **1982**, *104*, 5576–5580]. DOUGLAS J. DEFREES, KRISHNAN RAGHAVACHARI, H. BERNHARD SCHLEGEL, and JOHN A. POPLE.\*

Page 5578: In Table I the MP3/6-31G\* bond length for N<sub>2</sub> should be 1.106 Å. The values in Table II are not affected while the MP3/6-31G\* number for N≡N in Table III should be +8.

**Micellar Effects upon Spontaneous Hydrolyses and Their Relation to Mechanism** [*J. Am. Chem. Soc.* **1982**, *104*, 6654–6660]. H. AL-LOHEDAN, C. A. BUNTON,\* and M. MHALA.

Page 6655, Table I: The value of 10<sup>3</sup>k<sub>w</sub>' for PhCOCl should be 860 s<sup>-1</sup>.

**A Systematic Investigation on the Structure and Stability of the Lowest Singlet and Triplet States of Si<sub>2</sub>H<sub>4</sub> and SiH<sub>3</sub>SiH and the Analogous Carbon Compounds SiH<sub>2</sub>CH<sub>2</sub>, SiH<sub>3</sub>CH, CH<sub>3</sub>SiH, C<sub>2</sub>H<sub>4</sub>, and CH<sub>3</sub>CH** [*J. Am. Chem. Soc.* **1982**, *104*, 5884–5889]. HANS JOACHIM KÖHLER and HANS LISCHKA.\*

Pages 5886 and 5887: Due to an error in processing off diagonal elements of the force constant matrix the harmonic vibrational frequencies for the structures containing SiH<sub>3</sub> and CH<sub>3</sub> groups in Table V (p 5886) and in Table VIII (p 5887) are incorrect. The correct values are given below. These modifications affect

to a very small extent zero-point energy corrections but have no influence on our conclusions concerning relative stabilities.

Table A. Harmonic Vibrational Frequencies (cm<sup>-1</sup>) and Zero-Point Energy ε<sub>0</sub> (kcal/mol)

symmetry	methylmethlene		methylsilylene		silylmethylene	
	<sup>1</sup> A'	<sup>3</sup> A''	<sup>1</sup> A'	<sup>3</sup> A''	<sup>1</sup> A'	<sup>3</sup> A''
a'	3280	3368	3275	3278	3209	3410
	3146	3251	3170	3204	2295	2285
	3119	3183	2083	2249	2245	2266
	1625	1642	1548	1616	1005	1028
	1502	1572	1419	1431	985	1015
	1374	1261	1018	955	893	799
	1120	1131	679	688	672	738
a''	965	876	644	599	542	543
	3178	3222	3221	3275	2249	2259
	1632	1627	1633	1602	1128	1010
	986	1093	651	856	960	691
ε <sub>0</sub>	134	334	518	209	506	476
	31.5	32.2	28.4	28.5	23.8	20.0

**Selective Coupling of [(Alkylthio)allyl]titanium Reagent with Carbonyl Compounds. Facile Entry to Alkenyl Oxiranes and 2-(Arylthio)-1,3-butadienes** [*J. Am. Chem. Soc.* **1982**, *104*, 7663]. YOSHIHIKO IKEDA, KYOJI FURUTA, NORIYUKI MEGURIYA, NOBUO IKEDA, and HISASHI YAMAMOTO.\*

NMR values of **6** and **7** given in the text and in the supplementary material should be exchanged.

**6:** <sup>1</sup>H NMR (CCl<sub>4</sub>) 1.76 (s, 3 H), 4.76–5.37 (m, 3 H), 6.65 (dd, 1 H, 10.4 and 17.6 Hz); IR (CCl<sub>4</sub>) 2920, 1800, 1645, 1595, 1440, 990, 900 cm<sup>-1</sup>.

**7:** <sup>1</sup>H NMR (CCl<sub>4</sub>) 1.71 (d, 3 H, 1.5 Hz), 4.72–5.39 (m, 3 H), 6.24 (dd, 1 H, 10.8 and 17.6 Hz); IR (CCl<sub>4</sub>) 2920, 1780, 1640, 1610, 1440, 990, 890 cm<sup>-1</sup>.