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Syntheses of aza-analogues of macrosphelides via RCM strategy and their biological evaluation

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ABSTRACT

Syntheses of 16-membered macrolactams, which were aza-analogues of macrosphelides, could be established effectively by a ring-closing metathesis (RCM) strategy. Novel 19 analogues and six aza-macrosphelide–epothilone hybrids were furnished according to simple operations. Biological assay of these artificial aza-macrosphelides revealed that some of them showed stronger apoptosis-inducing activity against human lymphoma cells than the parent compound.

1. Introduction

In the field of drug discovery, syntheses of 'non-natural' natural products[1] have received much attention because natural products possess highly promising frameworks for biological activities. Their importance was proved as diversity-oriented synthesis proposed by Schreiber and Burke.[2] and also known for natural products-based libraries practiced by Waldmann et al.[3] Similarly, natural product hybrids were recognized as another promising approach for novel lead compounds, and numerous artificial hybrids were introduced in the review summarized by Tietze et al.[1a] Furthermore, as a fact, more than a half of recent drugs on market have been developed via some modifications of naturally occurring resources.[4] Considering such significant potential of 'non-natural' natural product, our research was progressed to afford several artificial biologically active molecules derived from natural sources, such as OSW-1 derivatives,[5] denosomin,[6] and macrosphelide analogues.[7] During our research program aiming at development of potential anti-tumor agents under RCM-based divergent synthesis of macrosphelides, we could fortunately find a notable macrosphelide–epothilone hybrid having higher potency than the parent natural macrosphelide.[7g] Encouraged by our successful RCM-based derivatization of macrosphelides and the impressive work on the structural arrangement of ester (epothilone) to amide (ixabeplone),[8] which has been believed as one of the hopeful solutions to metabolic instability in vivo, we next designed aza-analogues (azaMSs) of bioactive macrosphelides A, B, and oxidized **3** by replacement of the one ester oxygen in the macrolactone scaffold by nitrogen as shown in Fig. 1. We will describe herein an effective synthesis of artificial aza-macrosphelides, **4-azaMSs**, **10-azaMSs**, and **16-azaMSs**, and their hybrids with epothilones utilizing our RCM strategy practically and also report a biological evaluation of those derivatives as an apoptosis inducer on human lymphoma cells.

2. Result and discussion

Our synthesis commenced with common enantiopure secondary alcohol **4** as a C7–O10 fragment, which was prepared from commercially available methyl L-lactate according to our preceding total syntheses of macrosphelides (Scheme 1).[7l] Alcohol **4** was condensed with **5**, which was readily prepared by the asymmetric dihydroxylation[9] of ethyl sorbate, under Yamaguchi condition to afford ester **6**. Selective desilylation of the TBS group followed by condensation with *N*-protected β-amino acid **8**[10] afforded the N4–O16–O10–C7 segment **9**. The N-terminus of **9** was transformed into acryloyl amide via deprotection–condensation steps then removal of the TBDPS group with TBAF–AcOH furnished the

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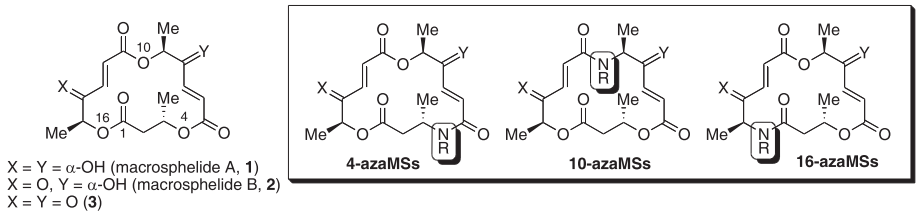
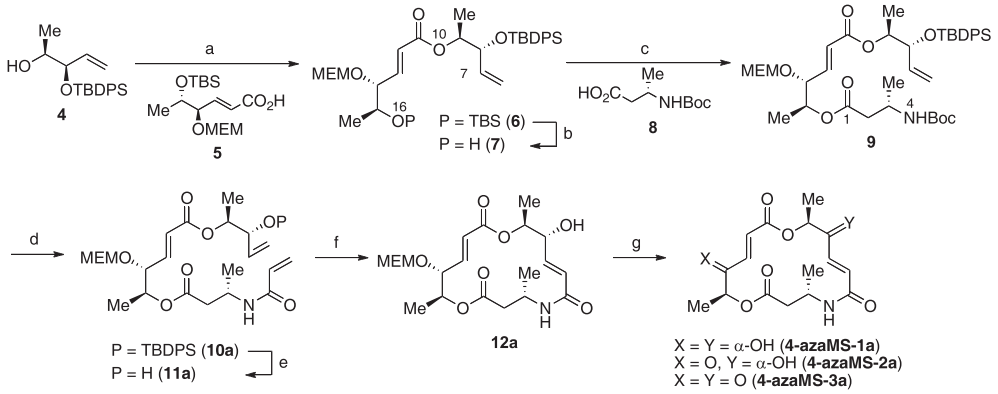


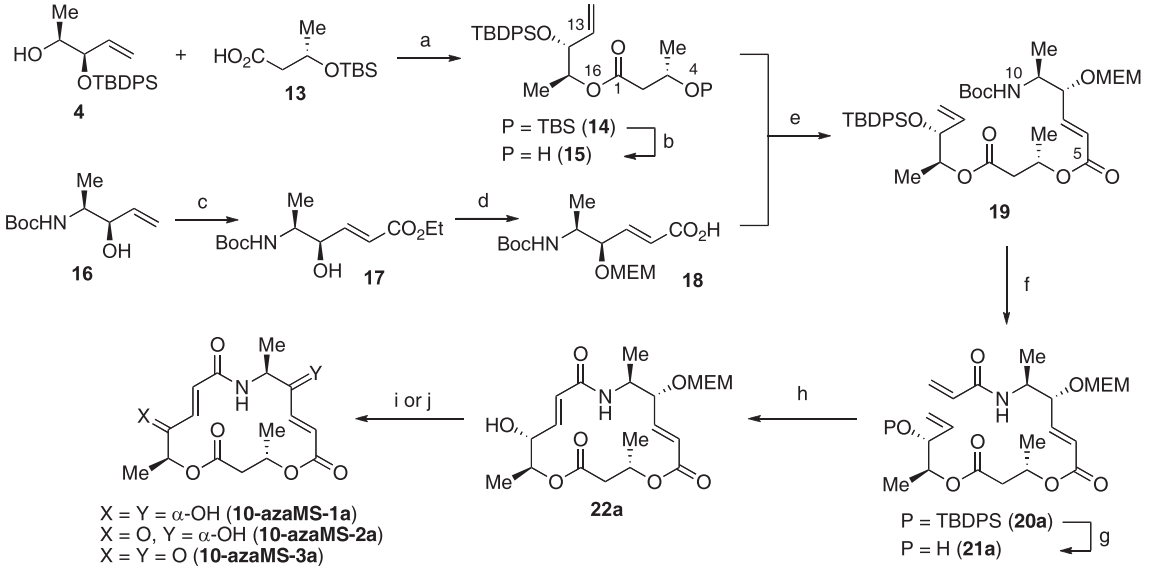
Fig. 1. Macrosphelides and their aza-analogues.



Scheme 1. Reagents and conditions: (a) **5**, 2,4,6-trichlorobenzoyl chloride, Et_3N, toluene; then **4**, DMAP, 84%; (b) AcOH, THF, H_2O, 70%; (c) EDCI, DMAP, CH_2Cl_2, quant.; (d) (1) TFA, CH_2Cl_2; (2) acryloyl chloride, DIPEA, CH_2Cl_2, 77% (two steps); (e) TBAF, AcOH, THF, 66%; (f) Grubbs' cat. second, CH_2Cl_2, 78%; (g) (1) TFA, CH_2Cl_2, 65% (**4-azaMS**–**1a**); (2) DMP, CH_2Cl_2, 50% (**4-azaMS**–**2a**), and 47% (**4-azaMS**–**3a**).

RCM precursor **11a**. RCM was conducted with Grubbs' catalyst second generation to give the corresponding macrolactam **12a** in satisfactory yield. Cleavage of the MEM group by TFA afforded the desired azamacrosphelide **4-azaMS**–**1a**. Dess–Martin oxidation gave the partially oxidized hydroxyketone **4-azaMS**–**2a** and the fully oxidized diketone **4-azaMS**–**3a** in 50% and 47% yield, respectively.

10-Aza-macrosphelides were also prepared from **4** as a C13–O16 fragment by the alteration of the ring-closure position (Scheme 2). Carboxylic acid **13**, which was obtained by a silylation–saponification sequence from commercially available methyl (*R*)-hydroxybutyrate, was lead to the requisite C13–O16–O4 fragment **15** via Yamaguchi esterification with **4** followed by selective desilylation. In parallel with that, the known allyl alcohol **16**[11] was subjected to cross metathesis with ethyl acrylate and subsequent hydrolysis provided the C5–N10 fragment **18**. After condensation of alcohol **15** with amino acid **18**, resultant **19** was transformed into the RCM precursor **21a** through a removal of the Boc group, introduction of the acryloyl group, and selective desilylation. RCM of **21a** uneventfully established the desired



Scheme 2. Reagents and conditions: (a) **13**, 2,4,6-trichlorobenzoyl chloride, Et_3N, toluene; then **4**, DMAP, 95%; (b) AcOH, THF, H_2O, 84%; (c) ethyl acrylate, Grubbs' cat. second, CH_2Cl_2, 92%; (d) (1) MEMCl, DIPEA, TBAI, $CHCl_3$, 99%; (2) NaOH, MeOH, THF, H_2O, quant.; (e) **18**, 2,4,6-trichlorobenzoyl chloride, Et_3N, toluene; then **15**, DMAP, 91%; (f) (1) TFA, CH_2Cl_2; (2) acryloyl chloride, DIPEA, CH_2Cl_2, 74% (two steps); (g) TBAF, AcOH, DMF, 67%; (h) Grubbs' cat. second, CH_2Cl_2, 76%; (i) (1) DMP, CH_2Cl_2; (2) TFA, CH_2Cl_2, 80% (two steps, **10-azaMS**–**2a**); (j) (1) TFA, CH_2Cl_2, 71% (**10-azaMS**–**1a**); (2) DMP, CH_2Cl_2, 88% (**10-azaMS**–**3a**).

macrolactam **22a**. Deacetalization afforded the diol **10-azaMS–1a** and Dess–Martin oxidation gave the diketone **10-azaMS–3a**. On the other hand, the hydroxyketone **10-azaMS–2a** was provided in 80% via an oxidation–deprotection sequence.

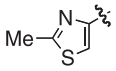
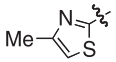
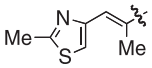
Starting from the common fragment **4** as a C7–O10 unit, we could prepare **16-azaMS**s in a similar fashion (Scheme 3). The C7–O10–N16 chain was assembled by dehydrative condensation between alcohol **4** and α,β-unsaturated carboxylic acid **18**. Further skeletal elongation was accomplished upon treatment with TFA and condensation with **13**. Deprotection and acryloylation of the O4-terminus followed by removal of the TBDPS group set up the RCM precursor **27**. Exposure of **27** to Grubbs' catalyst second generation gave the desired macrolactam in good yield. Finally, the combination of Dess–Martin oxidation and acidic deacetalization provided **16-azaMS–1a**, **16-azaMS–2a**, and **16-azaMS–3a**.

Next, we examined syntheses of *N*-substituted 10-aza analogues, including aza-macrosphelide–epothilone hybrids containing a thiazole side chain, utilizing the RCM protocol (Scheme 4 and chemical yields in each step are summarized in Table 1). Removal of the Boc group on **19**, subsequent reductive amination with 2-picoline-borane and acryloylation of the N-terminus afforded secondary acrylamides **20b–f**. Desilylation of the TBDPS ethers followed by treatment with Grubbs' catalyst second generation successfully gave *N*-substituted macrolactam **22b–f** in good yields. Compounds **10-azaMS–1b–f** were furnished by acidic cleavage of the MEM group and they were finally oxidized to **10-azaMS–3b–f** with Dess–Martin periodinane or PDC.

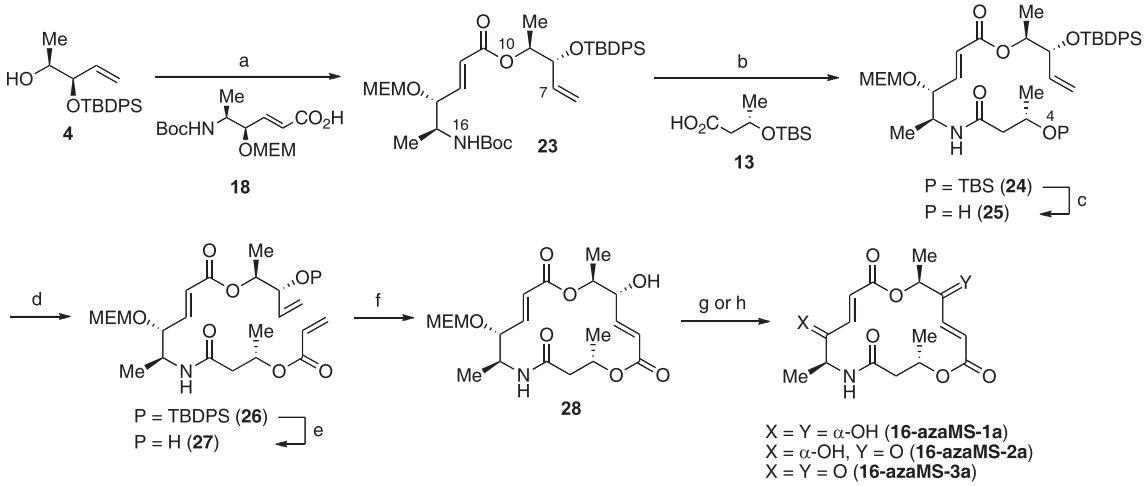
As depicted in Scheme 5, *N*-benzyl derivatives of **4-azaMS**s were prepared from the formerly synthesized N4–O16–O10–C7 fragment **9**. After deprotection on nitrogen, reductive amination with benzaldehyde, followed by condensation led to acryl amide **10b**. Desilylated **11b** was allowed to react with Grubbs' catalyst to afford macrolactam **12b** and the further deacetalization–oxidation protocol established **4-azaMS–1b** and **4-azaMS–3b**, respectively.

Including a reductive amination step, the C13–N16 fragment **16** was uneventfully transformed into *N*-benzyl **16-azaMS**s according to Scheme 6. Allyl alcohol **16** was protected by a TBDPS group to give silyl ether **29**. Then removal of the Boc group, reductive amination with benzaldehyde, followed by condensation with carboxylic acid **13** furnished the O4–N16–C13 fragment **30**. After desilylation, installation of the corresponding C5–O10 fragment was achieved by esterification with α,β-unsaturated carboxylic acid **5**. Selective removal of the TBS group and acryloylation set up the

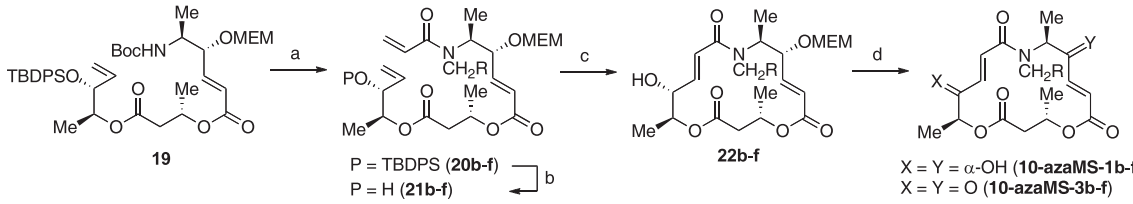
Table 1
Chemical yields for the transformations described in Scheme 4

Compound	R	Yield (%)				
		a (three steps)	b	c	d—(1)	d—(2)
b	Ph	66	61	79	50	73
c	$PhCH_2$	72	62	61	94	71
d		64	68	54[a]	83	56
e		55	74	31[a,b]	83	32[c]
f		36	72	31	59	53

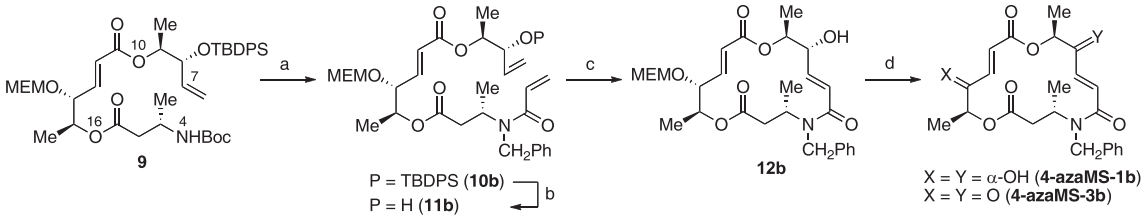
[a] The reactions were performed in refluxing benzene using modified Hoveyda–Grubbs' cat. second as an RCM catalyst. The other RCM reactions were in CH_2Cl_2 using Grubbs' cat. second. See, Supplementary data.
[b] The reaction was repeated two times using recovered substrate.
[c] PDC was used as an oxidant.



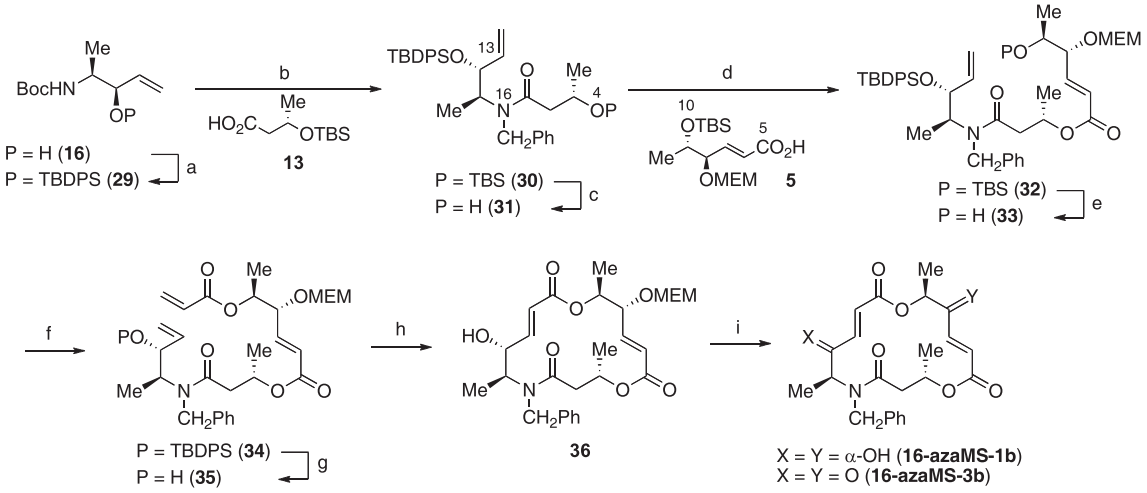
Scheme 3. Reagents and conditions: (a) **18**, 2,4,6-trichlorobenzoyl chloride, Et_3N, toluene; then **4**, DMAP, 94%; (b) (1) TFA, CH_2Cl_2; (2) **13**, EDCI, DMAP, CH_2Cl_2, 91% (two steps); (c) AcOH, THF, H_2O, 92%; (d) acryloyl chloride, DIPEA, CH_2Cl_2, 77%; (e) TBAF, AcOH, DMF, 59%; (f) Grubbs' cat. second, CH_2Cl_2, 82%; (g) (1) DMP, CH_2Cl_2; (2) TFA, CH_2Cl_2, 21% (two steps, **16-azaMS–2a**); (h) (1) TFA, CH_2Cl_2, 71% (**16-azaMS–1a**); (2) DMP, CH_2Cl_2, 48% (**16-azaMS–3a**).



Scheme 4. Reagents and conditions: (a) (1) TFA, CH_2Cl_2; (2) RCHO, 2-picoline·BH_3, AcOH, MeOH; (3) acryloyl chloride, DIPEA, CH_2Cl_2; (b) TBAF, AcOH, DMF; (c) RCM (see, Table 1); (d) (1) TFA, CH_2Cl_2 (**10-azaMS–1b–f**); (2) DMP or PDC, CH_2Cl_2 (**10-azaMS–3b–f**).



Scheme 5. Reagents and conditions: (a) (1) TFA, CH_2Cl_2; (2) PhCHO, 2-picoline·BH_3, AcOH, MeOH; (3) acryloyl chloride, DIPEA, CH_2Cl_2, 59% (two steps); (b) TBAF, AcOH, THF, quant.; (c) Grubbs' cat. second, CH_2Cl_2, 63%; (d) (1) TFA, CH_2Cl_2, 58% (**4-azaMS–1b**); (2) DMP, CH_2Cl_2, 53% (**4-azaMS–3b**).

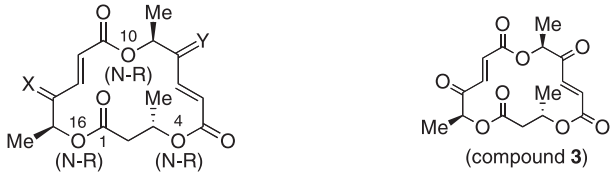


Scheme 6. Reagents and conditions: (a) TBDPSCl, imidazole, DMAP, DMF, 76%; (b) (1) TFA, CH_2Cl_2; (2) PhCHO, 2-picoline·BH_3, AcOH, MeOH; (3) **13**, EDCI, DMAP, CH_2Cl_2, 87% (three steps); (c) AcOH, THF, H_2O, 76%; (d) **5**, EDCI, DMAP, CH_2Cl_2, 37% (81% br s, m); (e) AcOH, THF, H_2O, 93%; (f) acryloyl chloride, DIPEA, CH_2Cl_2, 90%; (g) TBAF, AcOH, THF, 73%; (h) Grubbs' cat. second, CH_2Cl_2, quant.; (i) (1) TFA, CH_2Cl_2, 49% (90% br s, m) (**16-azaMS–1b**); (2) DMP, CH_2Cl_2, 63% (**16-azaMS–3b**).

triene **34**. After desilylation of **34**, metathesis in the presence of Grubbs' catalyst produced the desired 16-membered lactam **36**. Finally, cleavage of the MEM ether afforded **16-azaMS–1b** and Dess–Martin oxidation provided **16-azaMS–3b**.

Having prepared kinds of aza-analogues of macrosphelides, we performed examinations of apoptosis-inducing activities on human lymphoma cell line (U937) after exposure of 10 μM of each azaMS (Table 2).[7] The assay, which was evaluated by percentage of early apoptotic and secondary necrotic cells, revealed that the N–H analogues have no activities on cancer cell possibly due to their low lipophilicity (data not shown in Table 2). On the other hand, the *N*-substituted aza-derivatives were suggested to be a potent candidate for anti-tumor agent. Compared with the diol series (**azaMS-1**), the diketo-derivatives (**azaMS-3**) were proved to cause apoptosis more efficiently with low level of undesired necrosis. Among them, the epothilone–azaMS hybrid **10-azaMS–3f** exhibits a larger influence on lymphoma cells and the *N*-benzyl derivative **16-azaMS–3b** showed comparable potency with **3**, which was previously reported by us as the most potent apoptosis inducer among the natural-type macrosphelides. Finally we could fortunately find that the *N*-phenethyl derivative **10-azaMS–3c** serves as a specific apoptosis inducer with largest 43.0% early apoptosis and slight 3.53% secondary necrosis.

Table 2
Evaluation of apoptosis-inducing activity of synthesized azaMS compounds



Compound (X=Y=α-OH)	Early apoptosis[a] (secondary necrosis)	Compound (X=Y=O)	Early apoptosis[a] (secondary necrosis)
10-azaMS–1b	1.29 (0.26)	**10-azaMS–3b**	2.72 (0.58)
10-azaMS–1c	0.52 (0.32)	**10-azaMS–3c**	**43.0** (3.53)
10-azaMS–1d	2.05 (2.23)	**10-azaMS–3d**	7.26 (2.63)
10-azaMS–1e	1.62 (1.58)	**10-azaMS–3e**	6.12 (2.99)
10-azaMS–1f	2.34 (1.87)	**10-azaMS–3f**	**16.5** (1.33)
4-azaMS–1b	0.99 (1.08)	**4-azaMS–3b**	2.51 (0.99)
16-azaMS–1b	0.63 (0.42)	**16-azaMS–3b**	**22.5** (1.97)
Control	0.78 (0.84)	**Compound (3)**	**27.3** (19.6)

The results showing higher potency than the others are expressed as bold value.
[a] Represented as fraction of cells (%). Human lymphoma cells (U937) were treated with 10 μM concentrations of each azaMS compound for 12–14 h. Percentage of early apoptotic and secondary necrotic cells were measured by means of flow cytometry. Results are presented as an average of three experiments.

3. Conclusion

In conclusion, we could exhibit a potential of our RCM strategy for the construction of the fundamental macrolactam framework of aza-macrosphelides by delivering a large number of its analogues in the highly convergent, operationally simple manner. Additionally, this work let us reconfirm that the design of aza-analogue of natural products could be one of the promising derivatizations for practical drug discovery. Further syntheses and biological evaluations of azaMSs are now proceeding in our laboratory.

4. Experimental

4.1. General

Materials were obtained from commercial suppliers and used without further purification unless otherwise noted. Anhydrous THF

was purchased from Kanto Chemical Co., Inc. Anhydrous Et_2O, CH_2Cl_2, dioxane, DMF, DMSO, toluene, and MeCN were purchased from Wako Pure Chemical Industries. Anhydrous MeOH, EtOH, ^{i}PrOH, and NEt_3 were dried and distilled according to the standard protocols. Otherwise noted, all reactions were performed using oven-dried glassware, sealed with a rubber septum under a slight positive pressure of argon. Flash column chromatography was carried out using Kanto silica gel 60 N (spherical, neutral, 40–50 μm). Analytical TLC was performed on Merck 60 F_{254} glass plates precoated with a 0.25 mm thickness of silica gel. Optical rotations were measured on a JASCO DIP-1000 digital polarimeter. All melting points were determined on Yanagimoto micro melting point apparatus and uncorrected. IR spectra were measured on a JNM FT/IR-660 spectrometer. NMR spectra were measured on a VARIAN FX 270 spectrometer, VARIAN Gemini 300 spectrometer, JNM-ECX400P spectrometer, or a VARIAN UNITYplus 500 spectrometer.

Detailed experimental procedures (including biological assay) and compound characterization data were shown in Supplementary data.

Acknowledgements

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Supplementary data

Experimental procedures and characterization data for all new compounds are available in Supplementary data. Supplementary data related to this article can be found online. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2011.08.014.

References and notes

1. (a) Tietze, L. F.; Bell, H. P.; Chandrasekhar, S. *Angew. Chem., Int. Ed.* **2003**, *42*, 3996–4028; (b) Feyen, F.; Cachoux, F.; Gertsch, J.; Wartmann, M.; Altmann, K.-H. *Acc. Chem. Res.* **2008**, *41*, 21–31; (c) Avramova, S. I.; Galletti, E.; Renzulli, M. L.; Giorgi, G.; Sgaragli, G.; Alderighi, D.; Ghiron, C.; Corelli, F.; Radi, M.; Botta, M. *ChemMedChem* **2008**, *3*, 745–748.
2. Burke, M. D.; Schreiber, S. L. *Angew. Chem., Int. Ed.* **2004**, *43*, 46–58.
3. (a) Koch, M. A.; Wittenberg, L.-O.; Basu, S.; Jeyaraj, D. A.; Gourzoulidou, E.; Reinecke, K.; Odermatt, A.; Waldmann, H. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 16721–16726; (b) Koch, M. A.; Schuffenhauer, A.; Scheck, M.; Wetzel, S.; Casaulta, M.; Odermatt, A.; Ertl, P.; Waldmann, H. *Proc. Natl. Acad. Sci. U.S.A.* **2005**, *102*, 17272–17277.
4. Cragg, G. M.; Newman, D. J. *Pure Appl. Chem.* **2005**, *77*, 7–24.
5. (a) Matsuya, Y.; Ito, T.; Nemoto, H. *Eur. J. Org. Chem.* **2003**, 2221–2224; (b) Matsuya, Y.; Masuda, S.; Ohsawa, N.; Adam, S.; Tschamber, T.; Eustache, J.; Kamoshita, K.; Sukenaga, Y.; Nemoto, H. *Eur. J. Org. Chem.* **2005**, 803–808; (c) Tschamber, T.; Adam, S.; Matsuya, Y.; Masuda, S.; Ohsawa, N.; Maruyama, S.; Kamoshita, K.; Nemoto, H.; Eustache, J. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 5101–5106.
6. Matsuya, Y.; Yamakawa, Y.; Tohda, C.; Teshigawara, K.; Yamada, M.; Nemoto, H. *Org. Lett.* **2009**, *11*, 3970–3973.
7. (a) Matsuya, Y.; Kawaguchi, T.; Nemoto, H.; Nozaki, H.; Hamada, H. *Heterocycles* **2003**, *59*, 481–484; (b) Matsuya, Y.; Kawaguchi, T.; Nemoto, H. *Heterocycles* **2003**, *61*, 39–43; (c) Matsuya, Y.; Kawaguchi, T.; Nemoto, H. *Org. Lett.* **2003**, *5*, 2939–2941; (d) Matsuya, Y.; Ishihara, K.; Funamori, N.; Kawaguchi, T.; Nemoto, H. *Heterocycles* **2003**, *61*, 59–63; (e) Kawaguchi, T.; Funamori, N.; Matsuya, Y.; Nemoto, H. *J. Org. Chem.* **2004**, *69*, 505–509; (f) Ishihara, K.; Kawaguchi, T.; Matsuya, Y.; Sakurai, H.; Saiki, I.; Nemoto, H. *Eur. J. Org. Chem.* **2004**, 3973–3978; (g) Matsuya, Y.; Kawaguchi, T.; Ishihara, K.; Ahmed, K.; Zhao, Q.-L.; Kondo, T.; Nemoto, H. *Org. Lett.* **2006**, *8*, 4609–4612; (h) Ahmed, K.; Zhao, Q.-L.; Matsuya, Y.; Yu, D.-Y.; Feril, L. B., Jr.; Nemoto, H.; Kondo, T. *Int. J. Hyperthermia* **2007**, *23*, 353–361; (i) Ahmed, K.; Zhao, Q.-L.; Matsuya, Y.; Yu, D.-Y.; Feril, L. B., Jr.; Nemoto, H.; Kondo, T. *Chem. Biol. Interact.* **2007**, *170*, 86–99; (j) Matsuya, Y.; Matsushita, T.; Sakamoto, K.; Nemoto, H. *Heterocycles* **2009**, *77*, 483–492; (k) Ahmed, K.; Matsuya, Y.; Nemoto, H.; Zaidi, S. F. H.; Sugiyama, T.; Yoshihisa, Y.; Shimizu, T.; Kondo, T. *Chem. Biol. Interact.* **2009**, *177*, 218–226; (l) Matsuya, Y.; Kobayashi, Y.; Kawaguchi, T.; Hori, A.; Watanabe, Y.; Ishihara, K.; Ahmed, K.; Wei, Z.-L.; Yu, D.-Y.; Zhao, Q.-L.; Kondo, T.; Nemoto, H. *Chem.—Eur. J.* **2009**, *15*, 5799–5813; (m) Matsuya, Y.; Hori, A.; Kawamura, T.; Emam, H. F.; Ahmed, K.; Yu, D.-Y.; Kondo, T.; Toyooka, N.; Nemoto, H. *Heterocycles* **2010**, *80*, 579–591.
8. (a) Borzilleri, R. M.; Zheng, X.; Schmidt, R. J.; Johnson, J. A.; Kim, S.-H.; DiMarco, J. D.; Fairchild, C. R.; Gougoutas, J. Z.; Lee, F. Y. F.; Long, B. H.; Vite, G. D. *J. Am. Chem. Soc.* **2000**, *122*, 8890–8897; (b) Lee, F. Y. Y.; Borzilleri, R.; Fairchild, C. R.; Kim, S.-H.; Long, B. H.; Reventos-Suarez, C.; Vite, G. D.; Rose, W. C.; Kramer, R. A. *Clin. Cancer Res.* **2001**, *7*, 1429–1437; (c) Lee, F. Y. F.; Borzilleri, R.; Fairchild, C. R.; Kamath, A.; Smykla, R.; Kramer, R.; Vite, G. *Cancer Chemother. Pharmacol.* **2008**, *63*, 157–166; (d) Hunt, J. T. *Mol. Cancer Ther.* **2009**, *8*, 275–281.
9. Sharpless, K. B.; Amberg, W.; Bennani, Y.; Crispino, G. A.; Hartung, J.; Jeong, K. S.; Kwong, H. L.; Morikawa, K.; Wang, Z. M. *J. Org. Chem.* **1992**, *57*, 2768–2771.
10. Rae, A.; Aliev, A. E.; Anderson, J. E.; Castro, J. L.; Ker, J.; Parsons, S.; Stchedroff, M.; Thomas, S.; Tabor, A. B. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1933–1941.
11. Ibuka, T.; Habashita, H.; Otaka, A.; Fujii, N.; Oguchi, Y.; Uyehara, T.; Yamamoto, Y. *J. Org. Chem.* **1991**, *56*, 4370–4382.