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Variable-Sized bis(4-spiro-fused-β-lactam)-Based Unsaturated Macrocycles: Synthesis and Characterization

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Cite This: *ACS Omega* 2022, 7, 36795−36803

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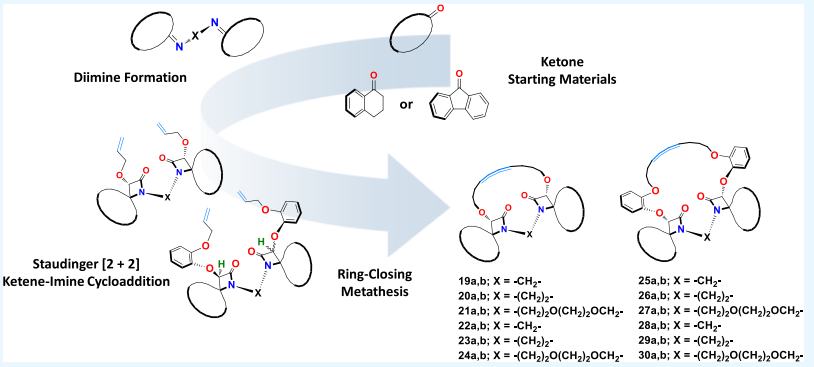

ABSTRACT: The synthesis with structural identifications including NMR and HRMS spectral data along with single-crystal X-ray diffraction analysis (for **20b**, **23b**, **25b−27b**) of a family of 14 new *syn*/*anti* bis-4-spiro-β-lactam-based unsaturated macrocycles (**19a,b−27a,b**), obtained by multistep synthesis including (i) diimine formation, (ii) Staudinger [2 + 2] ketene−imine cycloaddition, and (iii) ring-closing metathesis (RCM), is reported.

INTRODUCTION

Among azaheterocyclic ring systems, C3 and C4 spiro-fused β-lactams (azetidin-2-one) (Figure 1)[1−4] are uniquely important

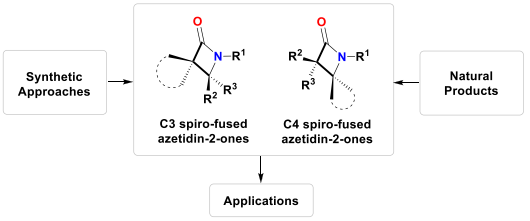

Figure 1. General representation of C3 and C4 spiro-fused azetidin-2-ones.

for their presence in a family of marine natural products, e.g., chartellines and chartelamides,[5] for their prominence in synthetic chemistry as versatile building blocks in the synthesis of α/β-amino acids,[6] alkaloids,[7] heterocycles,[8] toxoids, and other relevant molecular structures[9] and for their medicinal chemistry in synthesis of many biologically vital materials that behave as β-turn mimetics,[10] enzyme inhibitors,[11] and precursors of α,α-disubstituted β-amino acids,[12] as well as their biological activities including antibacterial agents,[13] active against HIV-1 and plasmodium,[14] along with cholesterol absorption inhibitors.[15]

In the light of their remarkable structural, chemical, and biological properties and applications, much attention has been devoted by our research group for demonstrating more complexed materials,[16] that is, bis-4-spiro-β-lactams containing unsaturated macrocycles (Figure 2).

During our recent interest in the construction of new types of azacrown ethers,[17−19] a wide spectrum of macrocycles composed of two β-lactam sites, which are covalently linked with various organic and organometallic linkers through their

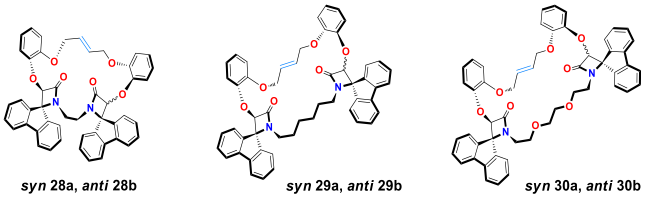

Figure 2. Chemical structures of bis(4-spiro-fused-β-lactam)-based unsaturated macrocycles.

Received: August 14, 2022
Accepted: September 19, 2022
Published: October 4, 2022

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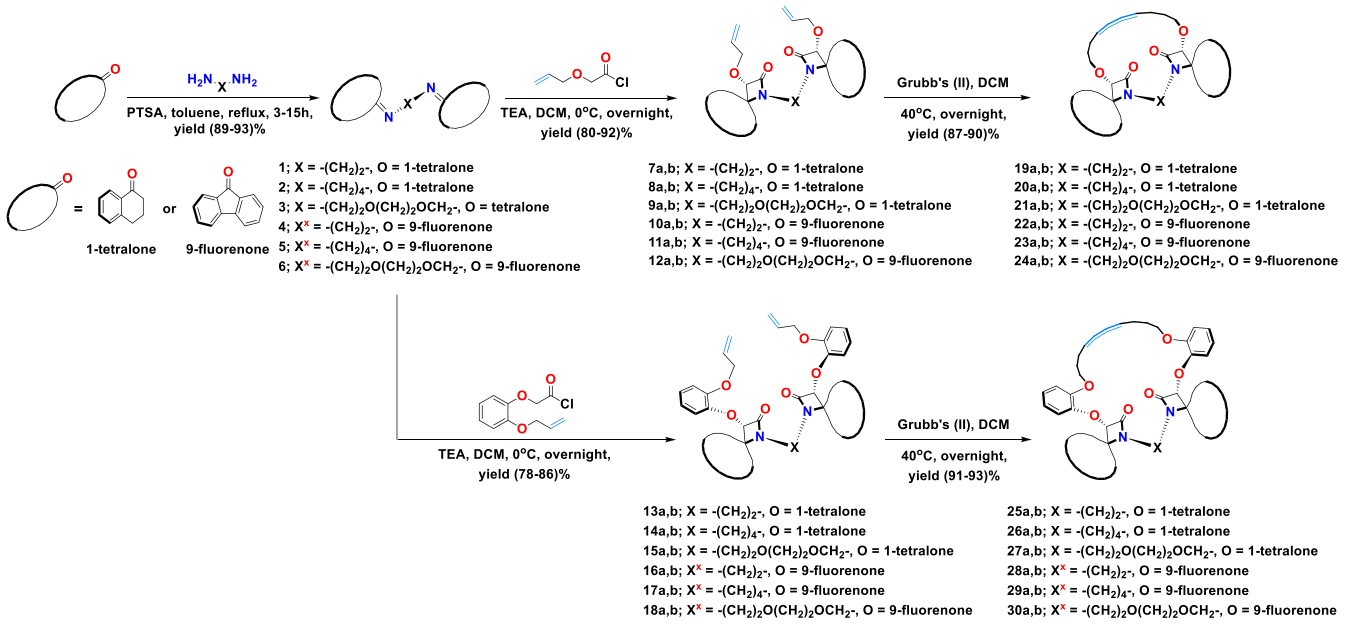
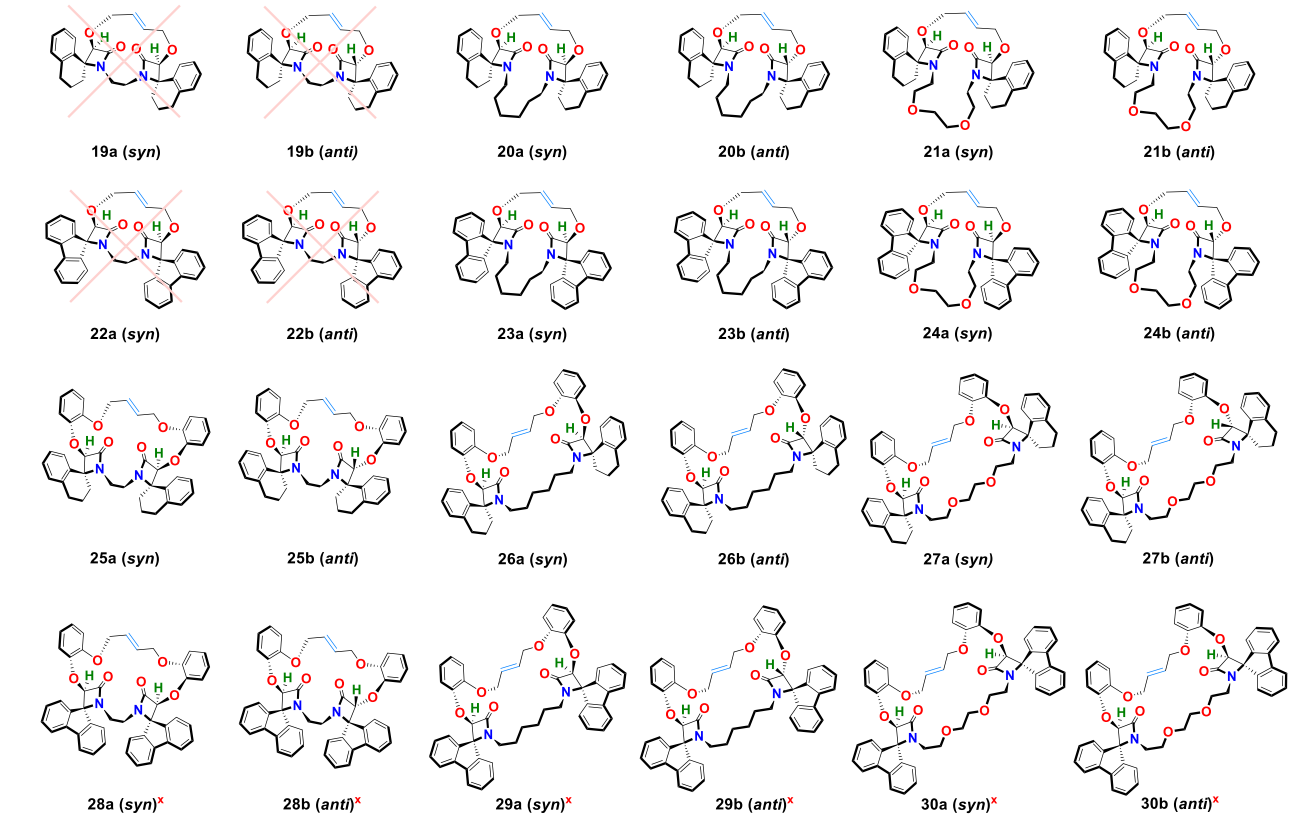
Scheme 1. Synthesis of bis(4-Spiro-fused-β-lactam)-based Unsaturated Macrocycles (19−30)





1,3-,1,4-, 3,4-, and 1,3,4-positions, have been achieved and reported in literature.[20] However, examples of macrocycles incorporating bis-4-spiro-β-lactams moieties in their backbone core structures are still limited. Recently, however, six bis-4-spiro-β-lactam-based macrocycles (Figure 2) have been successfully synthesized and utilized by our group following the classical sequential diimination, Staudinger [2 + 2] ketene−imine cycloaddition, and ring-closing metathesis (RCM) synthetic approach.

Continuing our work in architecting innovative (bis-4-spiro-β-lactam)-based azacrowns, a family of 14 new unsaturated macrocycles (seven *syn*/*anti* **20**, **21**, **23**−**27**configurational isomers) are described (Scheme 1). Azacrowns **28**−**30** were previously reported, and they are used for comparison with those newly prepared compounds. The structures of all macrocycles were established from their respective NMR and HRMS spectroscopic data along with their single-crystal X-ray diffraction analysis (for **20b**, **23b**, **25b**, **26b**, and **27b**).

https://doi.org/10.1021/acsomega.2c05212
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Complete data are presented in the Supporting Information (SI) section.

RESULTS AND DISCUSSION

Scheme 1 illustrates the synthetic procedure for the synthesis of the target *syn*/*anti* isomeric macrocycles. At first, the reaction of 1-tetralone or 9-fluorenone with 1,2-diaminoethane, 1,4-diaminobutane, and 2,2′-(ethylenedioxy)-bis-(ethylamine) in the presence of *para*-toluene sulfonic acid (PTSA) in refluxing ethanol afforded the diamine derivatives (**1**−**6**). The complimentary diimines were then treated with 2-allyloxyacetyl chloride or (2-allyloxy)phenoxyacetyl chloride with triethylamine (TEA) in dichloromethane (DCM) at room temperature to result in the *syn*/*anti* acyclic diene isomers (**7a**,**b**−**18a**,**b**), which upon RCM in the presence of a Grubbs (II) catalyst in refluxing DCM resulted in the formation of the desired *syn*/*anti* isomeric bis-4-spiranic macrocycles (**20**, **21**, and **23**−**30**). Diimines **1**−**3**, acyclic dienes **7**−**15**, and macrocycles **20**, **21**, and **23**−**27** are reported for the first time (SI).

Regarding the acyclic structures, dienes **7b**, **10a**, and **10b** were isolated in their pure isomeric forms by the fractional crystallization method. Their single-crystal X-ray diffraction (**10a** was obtained as a precipitate, and no appreciable crystals have been demonstrated), molecular packing, and ^{1}H-NMR spectra are presented in Figures 3−5, respectively, while the remaining dienes (**8**, **9**, **11**, **12**, **14**, **15**, and **16**) were attained as a mixture of both *syn*/*anti* isomers. The thermal ellipsoid representation (50% probability) of the crystal samples **7b** and **10b** along with their various crystallographic parameters are provided in the Supporting Information.

The ratio between the *syn*/*anti* configurations has been established from their spiro-fused 2-azitadinone protons (H_a) (Figure 6: full ^{1}H-NMR spectra of the allyloxy containing acyclic dienes **8**, **9**, **11**, and **12**, Table 1) which were allocated

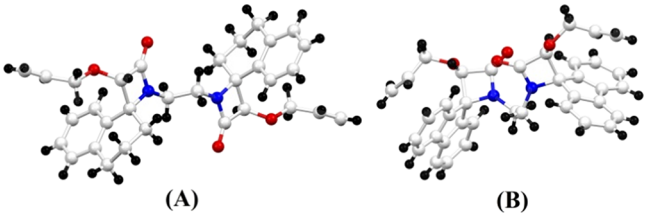

Figure 3. Crystal structures of (A) **7b** and (B) **10b**. Color code: blue—nitrogen; gray—carbon; red—oxygen; black—hydrogen.

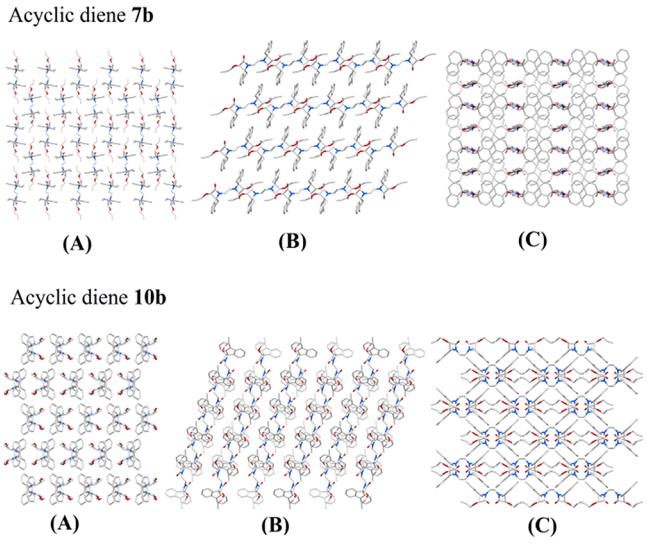

Figure 4. Packing pattern of *anti* **7b** and *anti* **10b** in their crystal network; view along the (A) a, (B) b, and (C) c directions. Color code: red—oxygen; blue—nitrogen; gray—carbon (hydrogens are hidden for clarity).

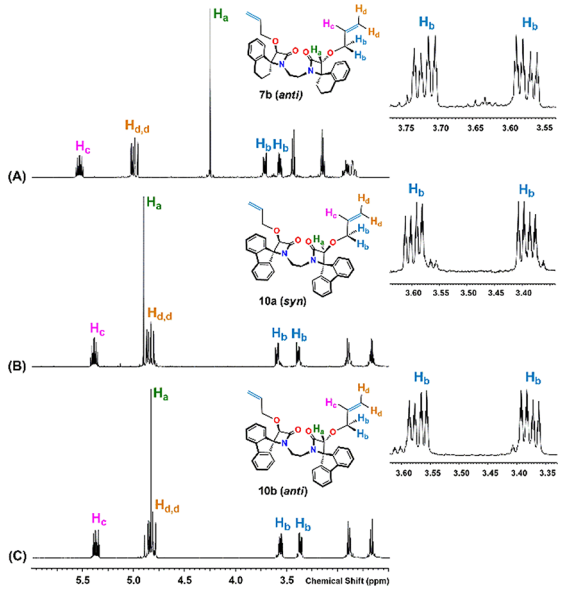

Figure 5. Partial ^{1}H NMR spectra of acyclic dienes (A) *anti* **7b**, (B) *syn* **10b**, and (C) *anti* **10b**.

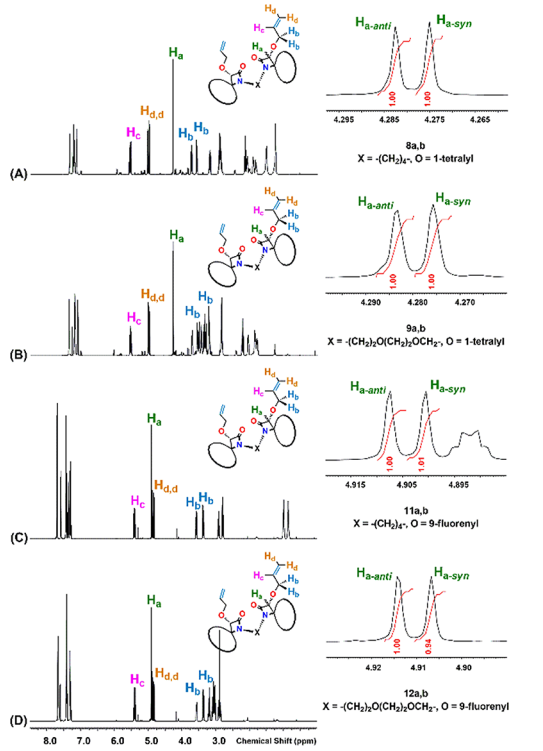

Figure 6. 1H NMR spectra of acyclic dienes (A) *syn*/*anti* **8**, (B) *syn*/*anti* **9**, (C) *syn*/*anti* **11**; and (D) *syn*/*anti* **12**.

https://doi.org/10.1021/acsomega.2c05212
ACS Omega 2022, 7, 36795−36803

based on the crystal structures of the isolated *anti* isomers **7b** and **10b**.

Table 1. Yield and H_a Chemical Shifts of *Syn*/*Anti* Acyclic Dienes 7−15 and Macrocycles 20, 21, and 23−27

compound	isomer	yield (%)	δH_a (ppm)
7a	*syn*	29 (**7a,b**, 92)	4.33 (s)
7b	*anti*	63 (**7a,b**, 92)	4.25 (s)
8a	*syn*	45 (**8a,b**, 90)	4.28 (s)
8b	*anti*	45 (**8a,b**, 90)	4.27 (s)
9a	*syn*	46 (**9a,b**, 92)	4.28 (s)
9b	*anti*	46 (**9a,b**, 92)	4.27 (s)
10a	*syn*	45 (**10a,b**, 90)	4.90 (s)
10b	*anti*	45 (**10a,b**, 90)	4.83 (s)
11a	*syn*	41 (**11a,b**, 82)	4.907 (s)
11b	*anti*	41 (**11a,b**, 82)	4.90 (s)
12a	*syn*	40 (**12a,b**, 80)	4.91 (s)
12b	*anti*	40 (**12a,b**, 80)	4.90 (s)
13a	*syn*	39 (**13a,b**, 78)	5.10 (s)
13b	*anti*	39 (**13a,b**, 78)	5.02 (s)
14a	*syn*	44 (**14a,b**, 88)	4.28 (s)
14b	*anti*	44 (**14a,b**, 88)	4.27 (s)
15a	*syn*	43 (**15a,b**, 86)	5.02 (s)
15b	*anti*	43 (**15a,b**, 86)	5.01 (s)
20a,b	*syn*/*anti*	(90)	4.90 (s)
21a,b	*syn*/*anti*	(88)	4.70 (s)
23a,b	*syn*/*anti*	(90)	5.70 (s)
24a,b	*syn*/*anti*	(87)	5.49 (s)
25a	*syn*	50 (**25a,b**, 93)	5.31 (s)
25b	*anti*	43 (**25a,b**, 93)	5.26 (s)
26a	*syn*	23 (**26a,b**, 93)	5.28 (s)
26b	*anti*	68 (**26a,b**, 91)	5.26 (s)
27a	*syn*	22 (**27a,b**, 92)	5.18 (s)
27b	*anti*	70 (**27a,b**, 92)	5.25 (s)

For the macrocyclic structures, no RCM formation took place for dienes **7a,b** and **10a,b**, and their corresponding macrocycles **19a,b** and **22a,b** were not formed. This can be explained from the crystal structures along with the ^{1}H-NMR spectra of both acyclic dienes **7b** (*anti*) and **10b** (*anti*) (Figures 3 and 5). Clearly, from the crystal structures (Figure 3), it can be observed that the short ethylene linker joining the two lactams together through their N atoms has a major role in rigidifying the diene structures, thus forcing the allyl groups to point away from each other. Moreover, the rigidity of the acyclic diene's backbones can be further supported from their ^{1}H-NMR spectra (Figure 5), by means of their multiplicity: two sets of triplets of triplets, of the allyloxy protons ($\mathbf{H_b}$, $-OC\underline{\boldsymbol{H}_2}CH{=}CH_2$). Owing to the lack of flexibility of the diene overall structures and the resulting outward facing of the allyloxy active sites, no metathesis reaction took place and no appreciable product formation has been attained.

Such limitation can be simply resolved by elongating the covalent spacers between the N atom conjugating the two lactam units together and/or by flexing the ethylene substituents based on the lactam centers. As expected, replacing the short alkyl likers $-(CH_2)_2-$ with $-(CH_2)_4$ or $-(CH_2)_2O(CH_2)_2O(CH_2)_2-$ spacers and/or substituting the allyloxy groups with phenoxy-containing allyloxy substituents afforded the macrocyclic structures **20a,b**−**27a,b** (Scheme 1). All compounds were achieved as a mixture of *syn*/*anti*, though macrocycles **20**,**23**, and **25**−**27** were further isolated in their pure isomeric structures by fractional crystallization. Single-crystal X-ray diffraction (Figure 7) of the *anti*-isomers **20b**, **23b**, and **25b**−**27b** was effectively gained, and their molecular packing is presented in Figure 8.

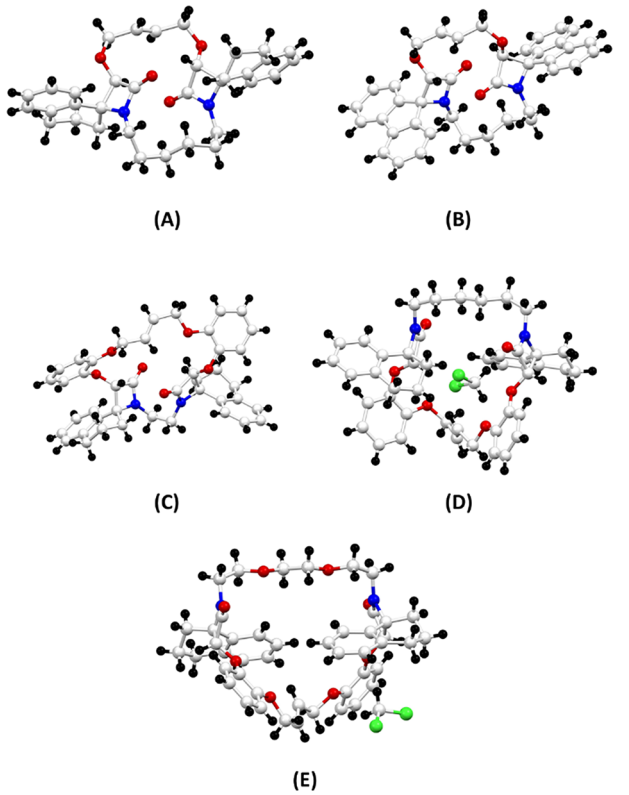

Figure 7. Crystal structures of (A) **20b**; (B) **23b**; (C) **25b**; (D) **26b**; and (E) **27b**. Color code: blue—nitrogen; gray—carbon; red—oxygen; black—hydrogen; green—chlorine.

In conclusion, a family of 14 (seven *syn* and seven *anti* configurational isomers) unsaturated macrocycles (**20**, **21**, **23**−**27**) bearing two 4-spiro-fused-*β*-lactam sites in their backbone structures has been successfully obtained following the traditional sequential organic transformations, that is, diimine formation, Staudinger [2 + 2] ketene−imine cycloaddition, and RCM reactions. All compounds have been characterized and utilized from their respective NMR and HRMS spectral data along with single X-ray diffraction analysis (for *anti* **20b**, *anti* **23b**, *anti* **25b**, *anti* **26b**, and *anti* **27b**).

EXPERIMENTAL SECTION

General. All reactions were carried out under nitrogen atmosphere unless otherwise noted, and all analyses were determined in the Research Sector Projects Unit (RSPU) at the Faculty of Science, Kuwait University. Thin layer chromatography (TLC) was performed using Polygram SIL G UV254 TLC plates, and visualization was carried out by ultraviolet lights at 254 and 350 nm. Column chromatography was performed using Merck silica gel 60 of mesh sizes 0.040−0.063 mm. H and C NMR spectra were recorded using Bruker DPX 600 at 600 MHz. Single-crystal data collection was made on a Bruker X8 Prospector diffractometer. Melting points were determined via differential scanning calorimetry (DSC) analyses on Shimadzu DSC-50.

https://doi.org/10.1021/acsomega.2c05212
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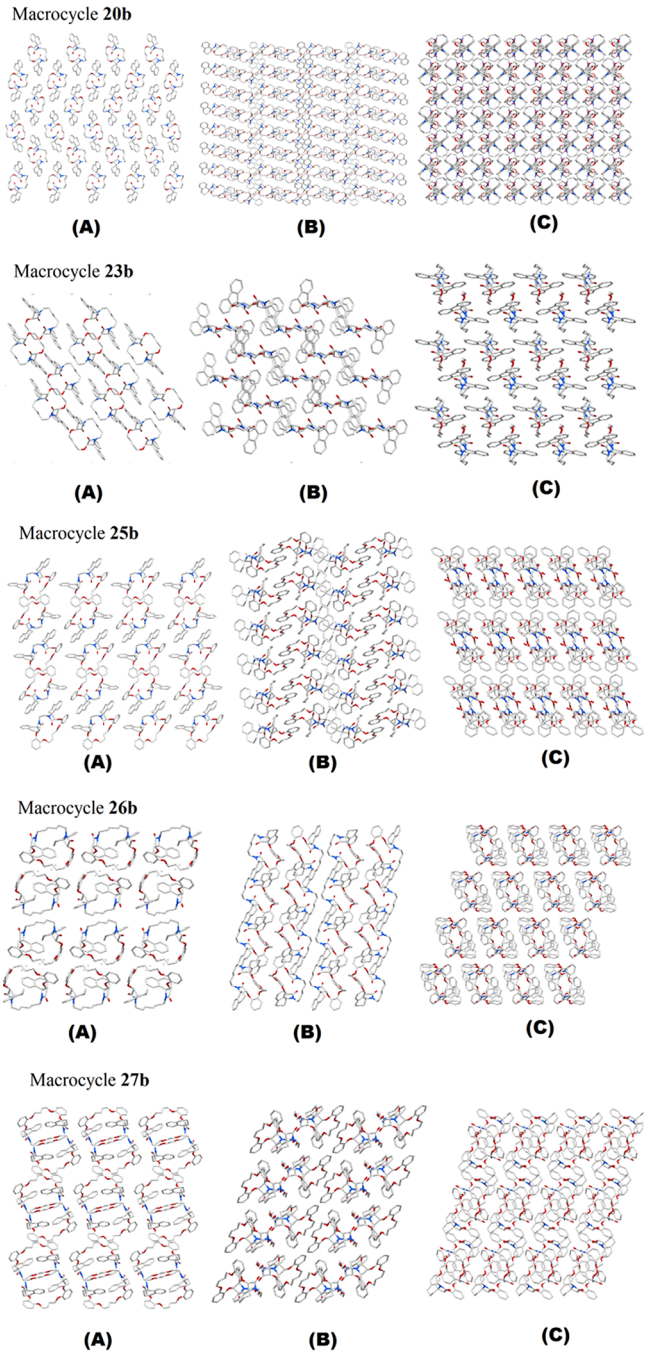

Figure 8. Packing patterns of *anti* **20b**, *anti* **23b**, *anti* **25b**, *anti* **26b**, and *anti* **27b** in their crystal network; view along the (A) a, (B) b, and (C) c directions. Color code: red—oxygen; blue—nitrogen, gray—carbon (hydrogens are hidden for clarity). The thermal ellipsoid representation (50% probability) of the crystal samples **20b**, **23b**, **25b**, **26b**, and **27b** are depicted in the Supporting Information. The molecular structure information of these compounds obtained from the single-crystal X-diffraction method is in good agreement with the predicted synthetic protocol and other characterization techniques like NMR and mass spectroscopy. Various crystallographic and refinement parameters of these crystals are provided in the Supporting Information.

Crystal Structure Analysis. Single crystals of **7b**, **10b**, **20b**, **23b**, **25b**, **26b**, and **27b** were grown by the slow solvent evaporation method. Single-crystal data collection was made on the Bruker X8 Prospector diffractometer by Cu-Kα radiation at room temperature. The reflection frames were then integrated with the Bruker SAINT Software package using a narrow-frame algorithm. Finally, the structure was solved using the Bruker SHELXTL Software Package and refined using SHELXL-2017/1. All non-hydrogen atoms were refined anisotropically.

Materials. All reagents were used with no further purification unless otherwise specified. Anhydrous solvents were either supplied from Sigma-Aldrich or dried as described by Perrin et al.[21]

General Procedures. *Synthesis of Diimines.* A mixture of the appropriate ketone (2 mmol) and the appropriate diamine (1 mmol) in toluene (50 mL) was heated under reflux for 3−15 h, and water was removed using a Dean−Stark apparatus. The solvent was removed in vacuo, and the reaction mixture was kept in an oven at 70 °C overnight to yield a pale-yellow viscous liquid, which was characterized and used in the subsequent step without further purification.

Diimine 1. White solid in 0.29 g (93%); mp 58−60 °C; ^{1}HNMR (600 MHz, $CDCl_3$-d6, 50 °C) δ = 8.23 (d, 2H, *J* 7.8), 7.32−7.30 (td, 2H, *J* 7.2, 1.2),7.25 (t, 2H, *J* 7.2), 7.14 (d, 2H, *J* 7.8), 3.97 (s, 4H), 2.79 (t, 4H, *J* 6.6), 2.74 (t, 4H, *J* 6.6), 1.96−1.92 (qui, 4H, *J* 6.0); ^{13}C{1H} NMR (150 MHz, $CDCl_3$-d6, 50 °C) δ = 165.5, 140.7, 135.0, 133.5, 128.9, 127.3, 126.8, 52.6, 39.3, 29.9, 23.5; EIMS *m*/*z* (%) 316 (M^+,4), 171 (8), 158 (100), 129 (14), 116 (5); HRMS (ESI) $[m]^+$ calcd for $C_{22}H_{24}N_2$ 316.1934, found 316.1934.

Diimine 2. Pale yellow solid in 0.33 g (89%); mp 68−70 °C; ^{1}HNMR (600 MHz, $CDCl_3$, 50 °C) δ = 8.29 (s, 2H), 7.33−7.23 (m, 6H), 7.16 (d, 2H, *J* 7.2), 3.52 (t, 4H, *J* 6.6), 2.83 (t, 4H, *J* 6.0), 2.63 (t, 4H, *J* 6.0), 1.99−1.95 (m, 4H), 1.82 (t, 4H, *J* 6.6), 1.56−1.51 (m, 4H); ^{13}C{1H} NMR (150 MHz, $CDCl_3$, 50 °C) δ = 164.2, 140.5, 133.6, 129.6, 128.4, 126.5, 125.7, 51.2, 39.3, 31.3, 30.0, 27.8, 22.8; EIMS *m*/*z* (%) 371 (M^+,3), 226 (100), 214 (32), 172 (22), 158 (46), 146 (36), 129 (20), 97 (7); HRMS (ESI) $[m]^+$ calcd for $C_{26}H_{32}N_2$ 372.2560, found 372.2560.

Diimine 3. White solid in 0.36 g (90%); mp 72−73 °C; ^{1}HNMR (600 MHz, $CDCl_3$, 50 °C) δ = 8.17 (d, 2H, *J* 7.8), 7.30−7.27 (td, 2H, *J* 7.2, 1.2), 7.22 (t, 2H, *J* 7.2),7.12 (d, 2H, *J* 7.8), 3.90 (t, 4H, *J* 6.6), 3.74 (s, 4H), 3.66 (t, 4H, *J* 6.6), 2.80 (t, 4H, *J* 6.6), 2.59 (t, 4H, *J* 6.6), 1.96−1.92 (qui, 4H, *J* 6.0); ^{13}C{1H} NMR (150 MHz, $CDCl_3$, 50 °C) δ = 165.8, 140.6, 134.9, 129.7, 128.4, 126.4, 125.8, 72.1, 70.8, 51.3, 29.9, 22.7; EIMS *m*/*z* (%) 404 (M^+,4), 232 (5), 216 (13), 172(25), 158 (100), 129 (36), 116 (15), 91 (7); HRMS (ESI) $[m]^+$ calcd for $C_{26}H_{32}O_2N_2$ 404.2458, found 404.2457.

Synthesis of β-Lactams. A solution of allyloxyacetyl chloride or *o*-allyloxyphenoxyacetyl chloride (4 mmol) in dry CH_2Cl_2 (5 mL) was purged with nitrogen and cooled to 0 °C, then a solution of TEA (8 mmol) in dry CH_2Cl_2 (5 mL) was added dropwise with a syringe. The mixture was stirred for 30 min, and a solution of the corresponding diimine (1 mmol) in dry CH_2Cl_2 (5 mL) was added dropwise over a period of 2 h. The reaction mixture was then stirred overnight at room temperature. The organic layer was washed with water and Na_2CO_3 solution (10%) till no effervescence and then dried over anhydrous Na_2SO_4. The solvent was then removed in vacuo, and the crude product was purified by chromatography with eluent petroleum ether (60−80)/EtOAc.

Compound 7a. Colorless oil in 0.14 g (29%); R_f = 0.55 (ethyl acetate/petroleum ether 2:3); ^{1}HNMR (600 MHz,

https://doi.org/10.1021/acsomega.2c05212
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$CDCl_3$, 50 °C) δ = 7.28−7.13 (m, 8H), 5.59−5.51 (m, 2H), 5.03−4.99 (m, 4H), 4.33 (s, 2H), 3.78−3.75 (tdd, 2H, *J* 1.2, 6.0, 12.0), 3.64−3.61 (tdd, 2H, *J* 1.2, 6.0, 12.6), 3.51−3.48 (m, 2H), 3.05−3.03 (m, 2H), 2.92−2.83 (m, 4H), 2.20−2.18 (m, 4H), 1.84−1.79 (m, 4H); $^{13}C\{1H\}$ NMR (150 MHz, $CDCl_3$, 50 °C) δ = 167.7, 139.1, 133.5, 132.2, 129.2, 128.3, 128.2, 125.7, 117.8, 90.7, 71.3, 67.6, 39.0, 32.5, 29.3, 21.2; EIMS *m*/*z* (%) 512 (M^+, 4), 453 (5), 396 (7), 200 (39), 185 (100), 159 (54), 129 (59), 91 (17); HRMS (ESI) $[m]^+$ calcd for $C_{32}H_{36}O_4N_2$ 512.2670, found 512.2674.

Compound ***7b***. White solid in 0.30 g (63%); mp 71−72 °C; R_f = 0.57 (ethyl acetate/petroleum ether 2:3); ^{1}HNMR (600 MHz, $CDCl_3$, 50 °C) δ = 7.28−7.26 (dd, 2H, *J* 1.2, 7.2), 7.25−7.22 (dt, 2H, *J* 1.2, 7.2), 7.18 (t, 2H, *J* 7.2), 7.13 (d, 2H, *J* 7.2), 5.56−5.50 (m, 2H), 5.02−4.96 (m, 4H), 4.25 (s, 2H), 3.73−3.70 (tdd, 2H, *J*1.2, 6.0, 12.0), 3.58−3.55 (tdd, 2H, *J* 1.2, 6.0, 12.6), 3.45−3.42 (m, 2H), 3.16−3.13(m, 2H), 2.92−2.83 (m, 4H), 2.19−2.14 (dt, 2H, *J* 3.0, 13.2), 2.09−2.06 (m, 2H), 1.89−1.87 (dd, 2H, *J* 3.0, 13.2), 1.82−1.78 (m, 2H); $^{13}C\{1H\}$ NMR (150 MHz, $CDCl_3$, 50 °C) δ = 167.1, 139.0, 133.4, 131.9, 129.2, 128.4, 128.3, 125.8, 118.1, 90.8, 71.3, 67.3, 38.6, 32.7, 29.3, 21.2; EIMS *m*/*z* (%) 512 (M^+, 4), 453 (5), 396 (7), 200(39), 185 (100), 159 (54), 129 (59), 91 (17); HRMS (ESI) $[m]^+$ calcd for $C_{32}H_{36}O_4N_2$ 512.2670, found 512.2674.

Compound ***8a,b***. Colorless oil in 0.51 g (90%); R_f = 0.73 (ethyl acetate/petroleum ether 2:3); ^{1}HNMR (600 MHz, $CDCl_3$, 50 °C) $\delta = \delta_H$(600 MHz, $CDCl_3$) 7.34−7.32 (td, 2H, *J* 1.8, 7.8), 7.22−7.17 (m, 4H), 7.12 (d, 2H, *J* 7.2), 5.58−5.51 (m, 2H), 5.02−4.96 (m, 4H), 4.28 (s, 1H), 4.27 (s, 1H), 3.74−3.71 (dd, 2H, *J* 6.0, 12.0), 3.58−3.55 (ddt, 2H, *J* 1.2, 6.0, 12.6), 3.20−3.16 (quin,2H, *J* 7.2), 2.93−2.86 (m, 6H), 2.16−2.11 (dt, 2H, *J* 3.0, 7.2), 2.09−2.06 (m, 2H), 1.85−1.80 (m, 4H), 1.63−1.38 (m, 4H), 1.26−1.23 (m, 4H); $^{13}C\{1H\}$ NMR (150 MHz, $CDCl_3$, 50 °C) δ = 167.1, 138.8, 133.5, 132.4, 129.0, 128.7, 128.1, 125.6, 117.9, 90.9, 71.3, 67.1, 39.8, 32.7, 29.4, 29.0, 27.0, 21.2; EIMS *m*/*z* (%) 568 (M+, 4), 510 (19), 452 (23), 411 (11), 373 (6), 283 (14), 200 (86), 159 (91), 131 (100), 91 (22); HRMS (ESI) $[m]^+$ calcd for $C_{36}H_{44}O_4N_2$ 568.3296, found 568.3295.

Compound ***9a,b***. Colorless oil in 0.55 g (92%); R_f = 0.74 (ethyl acetate/petroleum ether 2:3); ^{1}HNMR (600 MHz, $CDCl_3$, 50 °C) δ = 7.37−7.35 (d, 2H, *J* 7.2), 7.27−7.17 (m, 4H), 7.11−7.09 (d, 2H, *J* 7.2), 5.57−5.51 (m, 2H), 5.02−4.96 (m, 4H), 4.28 (s, 1H), 4.27 (s, 1H), 3.64−3.61 (m, 2H), 3.48−3.36 (m, 6H), 3.29−3.21 (m, 4H), 3.16−3.13 (m, 4H), 2.79−2.76 (m, 4H), 6.16−2.13 (t, 2H, *J* 16.2), 1.99−1.94 (m, 2H), 1.80−1.78 (m, 4H); $^{13}C\{1H\}$ NMR (150 MHz, $CDCl_3$, 50 °C) δ = 167.3, 138.8, 133.5, 132.6, 128.9, 128.6, 128.0, 125.5, 117.9, 91.0, 71.2, 70.1, 68.4, 67.3, 39.6, 32.2, 29.5, 21.2; EIMS *m*/*z* (%) 600 (M+, 13), 542 (25), 501 (20), 483 (15), 443 (9), 303 (38), 200 (96), 185 (100), 159 (93), 91 (27); HRMS (ESI) $[m]^+$ calcd for $C_{36}H_{44}O_6N_2$ 600.3194, found 600.3193.

Compound ***10a***. Colorless oil in 0.26 g (45%); R_f = 0.69 (ethyl acetate/petroleum ether 2:3); ^{1}HNMR (600 MHz, $CDCl_3$, 50 °C) δ =7.64−7.63 (dt, 4H, *J* 7.8, 0.6), 7.49 (d, 2H, *J* 7.2), 7.43−7.39 (m, 4H), 7.27−7.19 (m, 6H), 5.39−5.34 (m, 2H), 4.82−4.79 (m, 2H), 4.83 (s, 2H), 4.87−4.84 (m, 2H), 3.58−3.55 (ddt, 2H, *J* 12.0, 6.0, 1.2), 3.39−3.35 (ddt, 2H, *J* 12.6, 6.0, 1.2), 2.91−2.88 (m, 2H), 2.69−2.66 (m, 2H); $^{13}C\{1H\}$ NMR (150 MHz, $CDCl_3$, 50 °C) δ = 167.1, 142.1, 140.9, 140.4, 139.3, 132.8, 129.85, 129.81, 128.1, 127.8, 126.7, 123.3, 120.5, 120.2, 118.5, 89.2, 72.4, 71.9, 39.6; EIMS *m*/*z* (%) 580 (M^+, 6), 522 (8), 483 (5), 385 (7), 249 (56), 219 (43), 193 (37), 165 (100), 151 (3), 70 (4); HRMS (ESI) $[m]^+$ calcd for $C_{38}H_{32}O_4N_2$ 580.2357, found 580.2358.

Compound ***10b***. White solid in 0.26 g (45%); mp 181−182 °C; R_f = 0.70 (ethyl acetate/petroleum ether 2:3); ^{1}HNMR (600 MHz, $CDCl_3$, 50 °C) δ =7.64−7.63 (dd, 4H, *J* 7.8, 1.2), 7.56 (d, 2H, *J* 7.2), 7.43−7.38 (m, 6H), 7.31−7.28 (td, 2H, *J* 7.2, 0.6), 4.25−7.22 (td, 2H, *J* 7.2, 0.6), 5.42−5.35 (m, 2H), 4.90 (s, 2H), 4.87−4.79 (m, 4H), 3.61−3.57 (ddt, 2H, *J* 12.0, 6.0, 1.2), 3.40−3.37 (ddt, 2H, *J* 12.6, 6.0, 1.2), 2.92−2.88 (m, 2H), 2.68−2.64 (m, 2H); $^{13}C\{1H\}$ NMR (150 MHz, $CDCl_3$, 50 °C) δ = 167.3, 142.1, 141.1, 140.3, 139.5, 132.8, 129.8, 129.7, 128.3, 127.6, 126.6, 123.9, 120.4, 120.2, 118.5, 89.2, 72.6, 71.9, 40.0; EIMS *m*/*z* (%) 580 (M+, 5), 522 (7), 483 (4), 385 (6), 249 (58), 219 (47), 193 (39), 165 (100), 151 (3), 70 (4); HRMS (ESI) $[m]^+$ calcd for $C_{38}H_{32}O_4N_2$ 580.2357, found 580.2355.

Compound ***11a,b***. White solid in 0.55 g (82%); mp 135−136 °C; R_f = 0.77 (ethyl acetate/petroleum ether 2:3); ^{1}HNMR (600 MHz, $CDCl_3$, 50 °C) δ = 7.69 (d, 4H, *J* 7.8), 7.58 (d, 2H, *J* 7.2), 7.43 (t, 4H, *J* 7.2), 7.37 (t, 2H, *J* 7.2), 7.33−7.29 (m, 4H), 5.44−5.38 (m, 2H), 4.91 (s, 1H), 4.90 (s, 1H), 4.89−4.81 (m,4H), 3.59−3.56 (m, 2H), 3.39−3.35 (m, 2H), 2.94−2.89 (m, 2H), 2.82−2.77 (quin, 2H, *J* 6.6), 1.00 (quin, 4H, *J* 6.6), 0.85 (quin, 4H, *J* 7.2); $^{13}C\{1H\}$ NMR (150 MHz, $CDCl_3$, 50 °C) δ = 166.99 (166.97), 142.45 (142.43), 140.97 (140.94), 140.36 (140.34), 140.0, 132.8, 129.75 (129.71), 128.08 (128.07), 127.5, 126.7, 123.17 (123.15), 120.5, 120.2, 118.5, 89.4, 72.4, 71.9, 40.65 (40.62), 28.1, 26.45 (26.43); EIMS *m*/*z* (%) 636 (M+, 4), 578 (10), 539 (11), 441 (4), 305 (10), 234 (42), 193 (26),165 (100); HRMS (ESI) $[m]^+$ calcd for $C_{42}H_{40}O_4N_2$ 636.2983, found 636.2981.

Compound ***12a,b***. Pale yellow oil in 0.53 g (80%); R_f = 0.61 (ethyl acetate/petroleum ether 2:3); ^{1}HNMR (600 MHz, $CDCl_3$, 50 °C) δ = 7.67−7.65 (m, 4H), 7.61−7.60 (dt, 2H, *J* 7.8, 1.2), 7.44−7.39 (m, 6H), 7.32−7.29 (m, 4H), 5.42−5.36 (m, 2H), 4.91 (s, 1H), 4.90 (s, 1H), 4.88−4.86 (dd,2H, *J* 10.2, 1.2), 4.83−4.80 (dd, 2H, *J* 17.4, 1.2), 4.37−4.28 (m, 2H), 3.37−3.34 (m, 2H), 3.19−3.17 (m, 2H), 3.10−3.00 (m, 6H), 2.91−2.86 (m, 4H); $^{13}C\{1H\}$ NMR (150 MHz, $CDCl_3$, 50 °C) δ = 167.02 (167.01), 142.48 (142.47), 140.98 (140.96), 140.28 (140.27), 139.99 (139.98), 132.7, 129.6, 129.5, 127.99 (127.98), 127.47 (127.45), 126.67 (126.66), 123.2, 123.1, 120.4, 120.1, 118.5, 89.6, 72.6, 71.8, 69.7, 67.73 (67.72), 40.2; EIMS *m*/*z* (%) 668 (M^+, 15), 610 (7), 571 (16), 473 (3), 337 (22), 234 (61), 219 (52), 193 (35), 165 (100), 70 (7); HRMS (ESI) $[m]^+$ calcd for $C_{42}H_{40}O_6N_2$ 668.2881, found 668.2882.

Compound ***13a***. Pale yellow oil in 0.27 g (78%); R_f = 0.69 as (ethyl acetate/petroleum ether 2:3); ^{1}HNMR (600 MHz, $CDCl_3$, 50 °C) δ = 7.37−7.35 (dd, 2H, *J* 7.8, 1.8), 7.29−7.23 (m, 4H), 7.14 (d, 2H, *J* 7.2), 6.92−6.89 (td, 2H, *J* 7.8, 1.8), 6.82−6.81 (dd, 2H, *J* 9.6, 1.2), 6.75−6.72 (td, 2H, *J* 7.8, 1.2), 6.51−6.49 (dd, 2H, *J* 7.8, 1.2), 5.92−5.86 (m, 2H), 5.28−5.25 (dq, 2H, *J* 10.8, 1.8), 5.18−5.16 (dq, 2H, *J* 17.4, 1.2), 5.10 (s, 2H), 4. 34−4.28 (m, 4H), 3.67−3.65 (m, 2H), 3.10−3.07 (m, 2H), 2.85−2.82 (m, 2H), 2.72−2.69 (dd, 2H, *J* 16.8, 4.2), 2.33(d, 2H, *J* 13.2), 2.21−2.16 (td, 2H, *J* 13.2, 3.0), 1.98−1.94 (m, 2H), 1.62−1.59 (m, 2H); $^{13}C\{1H\}$ NMR (150 MHz, $CDCl_3$, 50 °C) δ = 167.2, 149.6, 147.4, 139.8, 133.5, 132.7, 129.4, 128.3, 127.9, 125.9, 123.9, 121.8, 120.5, 117.2, 116.0, 90.8, 70.4, 68.0, 39.3, 32.7, 29.2, 20.9; EIMS *m*/*z* (%) 696 (M^+, 15), 547 (95), 507 (17), 397 (18), 292 (26), 255 (100),

https://doi.org/10.1021/acsomega.2c05212
ACS Omega 2022, 7, 36795−36803

212 (51), 171 (55), 129 (57), 91 (19); HRMS (ESI) $[m]^+$ calcd for $C_{44}H_{44}O_6N_2$ 696.3194, found 696.3195.

Compound ***13b***. Pale yellow oil in 0.27 g (78%); R_f = 0.67 as (ethyl acetate/petroleum ether 2:3); ^{1}HNMR (600 MHz, $CDCl_3$, 50 °C) δ = 7.42−7.40 (dd,2H, *J* 7.2, 1.8), 7.29−7.24 (m, 4H), 7.14−7.12 (dd, 2H, *J* 9.0, 6.6), 6.91−6.88 (td, 2H, *J* 7.8, 1.8), 6.82−6.80 (dd, 2H, *J* 7.8, 1.2), 6.70−6.67 (td, 2H, *J* 7.8, 1.8), 6.30−6.29 (dd, 2H, *J* 7.8, 1.2), 5.93−5.87 (m, 2H), 5.29−5.26 (dq, 2H, *J* 17.4, 1.2), 5.19−5.17 (dq, 2H, *J* 10.8, 1.8), 5.02 (s, 2H), 4.36−4.30 (m, 4H), 3.60−3.57 (q, 2H, *J* 5.4), 3.25−3.22 (q, 2H, *J* 5.4), 2.84−2.81 (m, 2H), 2.68−2.64 (dd, 2H, *J* 16.8, 4.8), 2.19−2.14 (m, 2H), 1.93−1.90 (dt, 2H, *J* 9.6, 3.6), 1.51−1.49 (m, 2H); ^{13}C{1H} NMR (150 MHz, $CDCl_3$, 50 °C) δ = 166.6, 149.7, 147.2, 139.6, 133.4, 132.4, 129.3, 128.4, 128.2, 125.9, 124.1, 121.7, 120.8, 117.3, 115.9, 91.0, 70.4, 67.7, 38.8, 32.9, 29.1, 20.9; EIMS *m*/*z* (%) 696 (M^+, 6), 605 (5), 547 (31), 507 (14), 419 (15), 397 (23), 292 (56), 255 (85), 212 (74), 185 (83), 129 (100), 91 (45); HRMS (ESI) $[m]^+$ calcd for $C_{44}H_{44}O_6N_2$ 696.3194, found 696.3195.

Compound ***14a,b***. Pale yellow oil in 0.66 g (88%); R_f = 0.63 as (ethyl acetate/petroleum ether 2:3); ^{1}HNMR (600 MHz, $CDCl_3$, 50 °C) δ = 7.47−7.45 (m, 2H), 7.27−7.25 (m, 4H), 7.13−7.11 (m, 2H), 6.90−6.88 (td, 2H, *J* 7.2, 1.2), 6.82−6.80 (dd, 2H, *J* 7.8, 1.2), 6.72−6.69 (td, 2H, *J* 7.2, 1.2), 6.41−6.39 (dt, 2H, *J* 7.8, 1.2), 5.92−5.88 (m, 2H), 5.29−5.26 (dd, 2H, *J* 17.4, 1.8), 5.19−5.17 (dd, 2H, *J* 10.8, 1.2), 5.03 (s, 1H), 5.02 (s, 1H), 4.34−4.30 (qt, 4H, *J* 6.6, 1.8), 3.34−3.29 (m, 2H), 2.97−2.92 (m, 2H), 2.83−2.79 (m, 2H), 2.69−2.65 (dd, 2H, *J* 16.8, 4.8), 2.14−2.09 (td, 2H, *J* 12.0, 1.8), 1.93−1.91 (m, 4H), 1.58−1.55 (m, 6H), 1.32−1.30 (m, 4H); ^{13}C{1H} NMR (150 MHz, $CDCl_3$, 50 °C) δ = 166.5, 149.6, 147.5, 139.4, 133.5, 132.9, 129.1, 128.4, 128.2, 125.7, 123.8, 121.8, 120.60 (120.61), 117.3, 116.1, 91.0, 70.4, 67.4, 39.9, 32.9, 29.2, 29.0, 27.08 (27.09), 20.9; EIMS *m*/*z* (%) 752 (M^+, 5), 603 (84), 562 (36), 453 (32), 413 (56), 373 (86), 311 (71), 292 (32), 214 (36), 171 (51), 158 (56), 144 (100), 129 (71), 115 (31), 91 (19); HRMS (ESI) $[m]^+$ calcd for $C_{48}H_{52}O_6N_2$ 752.3820, found 752.3820.

Compound ***15a,b***. Pale yellow oil in 0.67 g (86%); R_f = 0.60 as (ethyl acetate/petroleum ether 2:3); ^{1}HNMR (600 MHz, $CDCl_3$, 50 °C) δ = 7.49−7.47 (m, 2H), 7.27−7.19 (m, 4H), 7.09−7.08 (m, 2H), 6.83−6.82 (td, 2H, *J* 7.8, 1.2), 6.79 (d, 2H, *J* 7.8), 6.68 (t, 2H, *J* 7.8), 6.37−6.36 (dd, 2H, *J* 7.2, 1.2), 5.92−5.85 (m, 2H), 5.28−5.16 (m, 4H), 5.02 (s, 1H), 5.01 (s, 1H), 4.32−4.28 (qd, 4H, *J* 10.2, 4.8), 3.56−3.23 (m, 12H), 2.77−2.73 (td, 2H, *J* 11.4, 5.4), 2.65−2.62 (dd, 2H, *J* 13.2, 3.6), 2.18 (t, 2H, *J* 14.4), 1.89−1.85 (m, 4H), 1.51−1.49 (m, 2H); ^{13}C{1H} NMR (150 MHz, $CDCl_3$, 50 °C) δ = 166.6, 149.5, 147.3, 139.3, 133.4, 133.0, 128.9, 128.3, 127.9, 125.5, 123.8, 121.6, 120.4, 117.1, 115.9, 91.0, 70.2, 70.0, 68.3, 67.5, 39.6, 32.3, 29.2, 20.7; EIMS *m*/*z* (%) 784 (M^+, 5), 635 (93), 594 (20), 485 (20), 445 (30), 405 (35), 343 (46), 292 (35), 274 (8), 212 (100), 158 (72), 144 (61), 91 (17); HRMS (ESI) $[m]^+$ calcd for $C_{48}H_{52}O_8N_2$ 784.3718, found 784.3715.

General Procedures of RCM. Grubb's catalyst II (6.0 mg, 5 mol %) was added into a solution of the appropriate bis-β-lactam (0.5 mmol) in DCM (10 mL). The reaction mixture was heated to 40 °C in an oil bath overnight. After completion, the solvent was removed in vacuo, and the product was purified by column chromatography using (2:3) ethyl acetate/petroleum ether.

Compound ***20a,b***. Pale yellow solid in 0.48 g (90%); mp 172−173 °C; R_f = 0.71 as (ethyl acetate/petroleum ether 2:3); ^{1}HNMR (600 MHz, $CDCl_3$, 50 °C) δ = 7.27−7.14 (m, 8H), 5.94−5.93 (m, 2H), 4.89 (s, 2H), 4.22 (d, 2H, *J* 12), 3.80−3.77 (m, 2H), 3.70−3.64 (td, 2H, *J* 13.2, 3.0), 2.89−2.87 (m, 4H), 2.79−2.75 (dt, 2H, *J* 14.4, 3.0), 2.44−2.41 (m, 2H), 2.13−2.07 (m, 4H), 1.87−1.77 (m, 4H), 1.61−1.56 (m, 2H), 1.44−1.34 (m, 4H); ^{13}C{1H} NMR (150 MHz, $CDCl_3$, 50 °C) δ = 170.5, 139.6, 134.0, 133.2, 129.5, 127.8, 127.0, 125.9, 90.7, 73.2, 68.3, 37.1, 33.8, 29.6, 29.5, 25.7, 21.5; EIMS *m*/*z* (%) 540 (M^+, 36), 523 (7), 469 (15), 452 (31), 411(29), 373 (14), 311 (69), 271 (22), 228 (21), 185 (47), 129 (100), 91 (38); HRMS (ESI) $[m]^+$ calcd for $C_{34}H_{40}O_4N_2$ 540.2983, found 540.2983.

Compound ***21a,b***. Yellow oil in 0.51 g (88%); R_f = 0.72 as (ethyl acetate/petroleum ether 2:3); ^{1}HNMR (600 MHz, $CDCl_3$, 50 °C) δ = 7.30−7.16 (m, 8H), 5.85−5.84 (m, 2H), 4.70 (s, 2H), 4.17 (d, 2H, *J* 11.4), 3.78−3.66 (m, 4H), 3.60−3.58 (dd, 2H, *J* 10.2, 1.8), 3.51−3.24 (m, 6H), 2.89−2.77 (m, 6H), 2.23−2.10 (m, 6H), 1.86−1.82 (m, 2H); ^{13}C{1H} NMR (150 MHz, $CDCl_3$, 50 °C) δ = 168.9, 158.9, 139.5, 133.1, 129.4, 127.9, 127.7, 125.8, 89.0, 71.4, 70.8, 68.4, 39.8, 33.2, 29.5, 21.5; EIMS *m*/*z* (%) 572 (M^+, 10), 530 (4), 501 (6), 443 (8), 413 (14), 343 (60), 303 (24), 211 (54), 185 (100), 172 (34), 129 (73), 91 (24); HRMS (ESI) $[m]^+$ calcd for $C_{34}H_{40}O_6N_2$ 572.2881, found 572.2881.

Compound ***23a,b***. White solid in 0.55 g (90%); mp 310−311 °C; R_f = 0.71 as (ethyl acetate/petroleum ether 2:3); ^{1}HNMR (600 MHz, $CDCl_3$, 50 °C) δ = 8.29−8.28 (m, 2H), 7.73 (d, 2H, *J* 7.2), 7.71−7.69 (m, 2H), 7.53 (d, 2H, *J* 7.2), 7.47−7.44 (m, 6H), 7.38−7.36 (td, 2H, *J* 7.2, 1.2), 6.05−6.04 (m, 2H), 5.70 (s, 2H), 4.27 (d, 2H, *J* 12.6), 3.79−3.70 (m, 4H), 2.50−2.47 (dt, 2H, *J* 15.0, 3.0), 1.99−1.95 (quin, 2H, *J* 6.0), 1.23−1.21 (m, 2H), 1.09−1.07 (m, 4H); ^{13}C{1H} NMR (150 MHz, $CDCl_3$, 50 °C) δ = 171.4, 143.7, 142.0, 140.7, 140.6, 133.2, 129.55, 129.52, 128.3, 127.5, 126.2, 125.4, 120.2, 119.9, 88.5, 73.9, 73.0, 37.8, 27.8, 24.6; EIMS *m*/*z* (%) 608 (M^+, 18), 551 (10), 481 (4), 415 (21), 345 (23), 305 (13), 219 (6), 180 (16), 165 (100), 129 (3), 83 (3); HRMS (ESI) $[m]^+$ calcd for $C_{40}H_{36}O_4N_2$ 608.2670, found 608.2668.

Compound ***24a,b***. Yellow oil in 0.55 g (87%); R_f = 0.75 as (ethyl acetate/petroleum ether 2:3); ^{1}HNMR (600 MHz, $CDCl_3$, 50 °C) δ = 8.04 (d, 2H, *J* 7.2), 7.74 (d, 2H, *J* 7.2), 7.69 (d, 2H, *J* 7.8), 7.56 (d, 2H, *J* 7.8), 7.54−7.51 (td, 2H, *J* 7.2, 1.2), 7.48−7.45 (m, 4H), 7.38−7.35 (td, 2H, *J* 7.8, 1.2), 5.76−5.74 (m, 2H), 5.49 (s, 2H), 4.17 (d, 2H, *J* 13.2), 4.04−3.99 (td, 2H, *J* 11.4, 3.6), 3.64−3.61 (ddd, 2H, *J* 12.0, 6.0, 3.0), 3.39−3.33 (m, 4H), 3.21−3.18 (m, 2H), 2.85−2.81 (td, 2H, *J* 10.8, 2.4), 2.65−2.62 (dt, 2H, *J* 15.0, 3.0); ^{13}C{1H} NMR (150 MHz, $CDCl_3$, 50 °C) δ = 169.2, 143.5, 142.0, 139.9, 139.7, 132.9, 129.6, 129.5, 128.9, 127.3, 126.7, 125.6, 120.2, 119.7, 87.8, 72.4, 72.0, 70.3, 66.6, 39.9; EIMS *m*/*z* (%) 640 (M^+, 64), 570 (11), 447 (8), 377 (35), 246 (68), 219 (72), 165 (100), 114 (5),70 (30); HRMS (ESI) $[m]^+$ calcd for $C_{40}H_{36}O_6N_2$ 640.2568, found 640.2567.

Compounds ***25a***. Pale yellow oil in 0.31 g (50%); R_f = 0.74 as (ethyl acetate/petroleum ether 2:3); ^{1}HNMR (600 MHz, $CDCl_3$, 50 °C) δ = 7.42−7.40 (dd, 2H, *J* 7.2, 1.2), 7.32−7.27 (m, 4H), 7.20 (d, 2H, *J* 7.2), 7.0−6.97 (td, 2H, *J* 7.8, 1.8), 6.90−6.88 (dd, 2H, *J* 8.4, 1.2), 6.63−6.60 (td, 2H, *J* 7.8, 1.2), 6.41 (t, 2H, *J* 1.8), 5.75−5.74 (dd, 2H, *J* 7.8, 1.2), 4.66 (d, 2H, *J* 11.4), 5.31 (s, 2H), 4.57 (d, 2H, *J* 11.4), 3.84 (d, 2H, *J* 11.4), 2.95 (d, 2H, *J* 12.6), 2.85−2.78 (m, 2H), 2.71−2.67 (dd, 2H, *J*

https://doi.org/10.1021/acsomega.2c05212
ACS Omega 2022, 7, 36795−36803

17.4, 5.4), 2.07−2.02 (td, 2H, *J* 13.2, 3.0), 1.90−1.87 (m, 4H), 1.24−1.19 (m, 2H); ^{13}C{1H} NMR (150 MHz, $CDCl_3$, 50 °C) δ = 168.2, 150.6, 146.5, 139.6, 134.4, 129.3, 128.4, 128.1, 127.4, 127.1, 126.0, 124.9, 122.8, 120.7, 113.3, 91.0, 70.1, 67.7, 40.7, 31.2, 29.9, 20.8; EIMS *m*/*z* (%) 668 (M^+, 14), 559 (7), 507 (16), 457 (8), 397 (53), 357 (9), 255 (52), 212 (100), 185 (93), 171 (51), 120 (57), 91 (16); HRMS (ESI) $[m]^+$ calcd for $C_{42}H_{40}O_6N_2$ 668.2881, found 668.2883.

Compounds ***25b***. White solid in 0.26 g (43%); mp 244−246 °C; R_f = 0.75 as (ethyl acetate/petroleum ether 2:3); ^{1}HNMR (600 MHz, $CDCl_3$, 50 °C) δ = 7.42−7.40 (dd, 2H, *J* 7.2, 1.2), 7.32−7.27 (m, 4H), 7.20 (d, 2H, *J* 7.2), 7.0−6.97 (td, 2H, *J* 7.8, 1.8), 6.90−6.88 (dd, 2H, *J* 8.4, 1.2), 6.63−6.60 (td, 2H, *J* 7.8, 1.2), 6.41 (t, 2H, *J* 1.8), 5.75−5.74 (dd, 2H, *J* 7.8, 1.2), 4.66 (d, 2H, *J* 11.4), 5.26 (s, 2H), 4.57 (d, 2H, *J* 11.4), 3.84 (d, 2H, *J* 11.4), 2.95 (d, 2H, *J* 12.6), 2.85−2.78 (m, 2H), 2.71−2.67 (dd, 2H, *J* 17.4, 5.4), 2.07−2.02 (td, 2H, *J* 13.2, 3.0), 1.90−1.87 (m, 4H), 1.24−1.19 (m, 2H); ^{13}C{1H} NMR (150 MHz, $CDCl_3$, 50 °C) δ = 168.1, 150.6, 146.5, 139.6, 134.4, 129.3, 128.4, 128.1, 127.4, 127.1, 126.0, 124.9, 122.8, 120.7, 113.3, 92.1, 70.1, 68.1, 40.7, 31.2, 29.2, 21.3; EIMS *m*/*z* (%) 668 (M^+, 14), 559 (7), 507 (16), 457 (8), 397 (53), 357 (9), 255 (52), 212 (100), 185 (93), 171 (51), 120 (57), 91 (16); HRMS (ESI) $[m]^+$ calcd for $C_{42}H_{40}O_6N_2$ 668.2881, found 668.2883.

Compounds ***26a***. Pale yellow oil in 0.17 g (23%); R_f = 0.77 as (ethyl acetate/petroleum ether 2:3); ^{1}HNMR (600 MHz, $CDCl_3$, 50 °C) δ = 7.58−7.56 (dd, 2H, *J* 7.8, 0.6), 7.33 (t, 2H, *J* 7.8), 7.14−7.16 (td, 2H, *J* 7.8, 1.2), 7.07 (d, 2H, *J* 7.2), 6.93−6.89 (td, 2H, *J* 7.2, 1.8), 6.83−6.81 (td, 2H, *J* 7.2, 1.2), 6.64−6.61 (td, 2H, *J* 7.8, 1.8), 6.13 (t, 2H, *J* 2.4), 6.05−6.04 (dd, 2H, *J* 7.8, 1.2), 5.28 (s, 2H), 4.53−4.48 (m, 2H), 3.37−3.33 (m, 2H), 3.02−2.99 (m, 2H), 2.82−2.76 (m, 2H), 2.65−2.61 (dd, 2H, *J* 16.8, 3.6), 2.15−2.13 (dd, 2H, *J* 13.2, 3.0), 2.06−2.04 (m, 2H), 1.91−1.88 (m, 2H), 1.60−1.57 (m, 4H),1.47−1.45 (m, 6H); ^{13}C{1H} NMR (150 MHz, $CDCl_3$, 50 °C) δ = 166.9, 150.0, 146.6, 139.6, 133.1, 128.9, 128.7, 128.2, 128.0, 125.9, 123.9, 121.0, 120.6, 113.8, 90.8, 68.6, 67.6, 39.1, 32.4, 29.4, 28.6, 26.3, 21.0; EIMS *m*/*z* (%) 724 (M^+, 16), 615 (10), 562 (38), 453 (88), 413 (52), 311 (82), 283 (29), 185 (56), 171 (72), 121 (100), 91 (21); HRMS (ESI) $[m]^+$ calcd for $C_{46}H_{48}O_6N_2$ 724.3507, found 724.3504.

Compounds ***26b***. White solid in 0.49 g (68%); mp 258−260 °C; R_f = 0.78 as (ethyl acetate/petroleum ether 2:3); ^{1}HNMR (600 MHz, $CDCl_3$, 50 °C) δ = 7.55−7.53 (dd, 2H, *J* 7.8, 1.2), 7.33 (t, 2H, *J* 7.8), 7.28−7.25 (td, 2H, *J* 7.8, 1.2), 7.08 (d, 2H, *J* 7.2), 6.93−6.89 (td, 2H, *J* 7.2, 1.8), 6.83−6.81 (td, 2H, *J* 7.2, 1.2), 6.69−6.66 (td, 2H, *J* 7.8, 1.8), 6.25−6.24 (dd, 2H, *J* 7.8, 1.2), 6.13 (t, 2H, *J* 2.4), 5.26 (s, 2H), 4.53−4.48 (m, 2H), 3.37−3.33 (m, 2H), 3.02−2.99 (m, 2H), 2.82−2.76 (m, 2H), 2.65−2.61 (dd, 2H, *J* 16.8, 3.6), 2.15−2.13 (dd, 2H, *J* 13.2, 3.0), 2.06−2.04 (m, 2H), 1.91−1.88 (m, 2H), 1.60−1.57 (m, 4H), 1.47−1.45 (m, 6H); ^{13}C{1H} NMR (150 MHz, $CDCl_3$, 50 °C) δ = 166.7, 149.8, 146.8, 139.4, 132.8, 129.1, 128.9, 128.7, 128.2, 126.0, 123.9, 121.2, 120.4, 114.5, 90.6, 68.9, 67.4, 39.3, 32.9, 29.4, 28.7, 26.5, 21.0; EIMS *m*/*z* (%) 724 (M^+, 16), 615 (10), 562 (38), 453 (88), 413 (52), 311 (82), 283 (29), 185 (56), 171 (72), 121 (100), 91 (21); HRMS (ESI) $[m]^+$ calcd for $C_{46}H_{48}O_6N_2$ 724.3507, found 724.3504.

Compounds ***27a***. Pale yellow oil in 0.17 g (22%); R_f = 0.78 as (ethyl acetate/petroleum ether 2:3); ^{1}HNMR (600 MHz, $CDCl_3$, 50 °C) δ = 7.57−7.55 (dd, 2H, *J* 7.8, 1.2), 7.31−7.27 (m, 4H), 7.09−7.08 (dd, 2H, *J* 7.2, 0.6), 6.92−6.90 (td, 2H, *J* 7.2, 1.2), 6.82−6.80 (dd, 2H, *J* 8.4, 1.2), 6.68−6.65 (td, 2H, *J* 7.8, 1.2), 6.25−6.23 (dd, 2H, *J* 8.4, 1.8), 6.05 (t, 2H, *J* 3.0), 5.18 (s, 2H), 4.45 (d, 2H, *J* 0.6), 3.60−3.20 (m, 12H), 2.77−2.75 (m, 2H), 2.65−2.62 (dd, 2H, *J* 16.8, 4.8), 2.22−2.15 (td, 2H, *J* 13.2, 2.4), 1.97 (d, 2H, *J* 13.2), 1.90−1.87 (m, 2H), 1.62−1.51 (m, 2H); ^{13}C{1H} NMR (150 MHz, $CDCl_3$, 50 °C) δ = 166.7, 149.9, 146.7, 139.5, 133.0, 129.0, 128.8, 128.6, 128.2, 125.8, 124.1, 121.3, 121.2, 114.5, 91.1, 70.4, 68.9, 68.5, 67.6, 40.1, 32.4, 29.3, 20.9; EIMS *m*/*z* (%) 756 (M^+, 55), 647 (23), 595 (28), 485 (21), 445 (41), 343 (80), 303 (24), 212 (76), 185 (100), 158 (76), 121 (72), 70 (15); HRMS (ESI) $[m]^+$ calcd for $C_{46}H_{48}O_8N_2$ 756.3405, found 756.3405.

Compounds ***27b***. White solid in 0.53 g (70%); mp 268−270 °C; R_f = 0.79 as (ethyl acetate/petroleum ether 2:3); ^{1}HNMR (600 MHz, $CDCl_3$, 50 °C) δ = 7.55−7.53 (dd, 2H, *J* 7.8, 1.2), 7.28 (t, 2H, *J* 7.8), 7.24−7.21 (td, 2H, *J* 7.8, 1.2), 7.08 (d, 2H, *J* 7.8), 6.94−6.91 (td, 2H, *J* 7.8, 1.8), 6.84−6.83 (dd, 2H, *J* 7.8, 1.8), 6.60−6.57 (td, 2H, *J* 7.8, 1.8), 6.15 (t, 2H, *J* 3.0), 5.90−5.89 (dd, 2H, *J* 9.6, 1.8), 5.25 (s, 2H), 4.54 (s, 4H), 3.67−3.44 (m, 10H), 3.19−3.15 (m, 2H), 2.79−2.73 (m, 2H), 2.58−2.54 (dd, 2H, *J* 16.8, 4.8), 2.19−2.14 (td, 2H, *J* 13.2, 3.0), 1.99 (d, 2H, *J* 13.8), 1.93−1.91 (m, 2H), 1.48−1.35 (m, 2H); ^{13}C{1H} NMR (150 MHz, $CDCl_3$, 50 °C) δ = 166.7, 150.4, 146.2, 139.8, 133.2, 129.1, 128.6, 128.5, 128.1, 125.8, 124.4, 122.1, 121.1114.0, 91.2, 70.4, 68.9, 68.4, 67.9, 40.1, 32.4, 29.3, 20.9; EIMS *m*/*z* (%) 756 (M^+, 54), 647 (23), 595 (28), 485 (21), 445 (41), 343 (80), 303 (24), 212 (76), 185 (100), 158 (76), 121 (72), 70 (15); HRMS (ESI) $[m]^+$ calcd for $C_{46}H_{48}O_8N_2$ 756.3405, found 756.3405.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.2c05212.

X-ray data of seven samples (ZIP)

NMR and HRMS (ESI) spectral data of diimines (**1**−**3**) and compounds **7**−**15a**,**b**, **20a**,**b**, **21a**,**b**, and **23**−**27a**,**b**; single-crystal X-ray diffraction studies of macrocycles **7b**, **10b**, **20b**, **23b**, **25b**, **26b**, and **27b** (PDF)

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Notes

The authors declare no competing financial interest.

https://doi.org/10.1021/acsomega.2c05212
ACS Omega 2022, 7, 36795−36803

■ ACKNOWLEDGMENTS

The investigators gratefully acknowledge the financial support of this project by the Research Administration of Kuwait University through a research grant (Sc 01/18). The analytical services provided by the RSPU Unit general facilities of the Faculty of Science through research grants GFS (GS 01/01, GS 01/03, GS 01/05, and GS 03/08) are highly appreciated. We are grateful to Dr. Ali Husain for his valuable input in drawing the chemical structures, schemes, and artwork.

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ACS Omega 2022, 7, 36795−36803