Pergamon

Tetrahedron 56 (2000) 5807–5811

TETRAHEDRON

A Novel Total Synthesis of Antibiotic Carbazole Alkaloid Carbazomycin G

Hitomi Hagiwara, Tominari Choshi, Hiroyuki Fujimoto, Eiichi Sugino and Satoshi Hibino*

Graduate School of Pharmacy and Pharmaceutical Sciences, Faculty of Pharmacy and Pharmaceutical Sciences, Fukuyama University, Fukuyama, Hiroshima 729-0292, Japan

Received 11 May 2000; accepted 12 June 2000

Abstract—A total synthesis of carbazomycin G (**1**) has been newly completed in seven steps. The 1,3-dioxygenated carbazole (**4**) via the 3-methoxy-1-methoxymethyloxycarbazole (**11**) as a synthetic precursor was synthesized by using the allene-mediated electrocyclic reaction of a 6π electron system generating from the **2**-propargylindole derivative (**10**), which was derived from the 3-vinylindole (**8**) in three steps. Finally, the oxidation of the phenol (**4**) followed by the addition of methyl lithium to the carbazole-1,4-quinone (**3**) provided carbazomycin G (**1**).

Introduction

Carbazomycin G (**1**) and H (**2**) were isolated from *Streptoverticillium ehimense* as a racemate by Nakamura and co-workers[1] together with carbazomycins A to F.[2] Carbazomycin G (**1**) possesses moderate antifungal activity against *Trichophyton* species.[1] Their structures, which have a unique quinol moiety, have been determined by spectroscopic and X-ray crystallographic analyses.[1] Total syntheses of both alkaloids have recently been developed by the Knölker group.[3] Two synthetic methodologies have been efficiently employed, one based on the iron-mediated C–C and C–N bond formation,[3a] and the other on palladium-catalyzed oxidative cyclization[3b] to carbazole-1,4-quinone as synthetic precursor. In the course of our study, we are developing the synthesis of biologically interesting condensed-heteroaromatic compounds, including natural products by the thermal electrocyclic reaction[4] of either conjugated hexatriene[5] or azahexatriene[6] systems incorporating the double bond of the principal aromatic or heteroaromatic ring. We recently reported the total synthesis of highly substituted carbazole alkaloids by the construction of the appropriate carbazole framework based on the allene-mediated electrocyclic reaction of the hexatriene system involving the indole 2,3-bond.[5] In the present paper, we describe the novel total synthesis of carbazomycin G (**1**) by application of this methodology. We envisaged that an electrocyclic reaction of a 2-allenylindole intermediate (**5**) derived from a 2-propargylindole derivative (**6**) would provide a 1,3-dioxygenated carbazole (**4**) as a synthetic precursor based on a retrosynthetic analysis (Scheme 1).

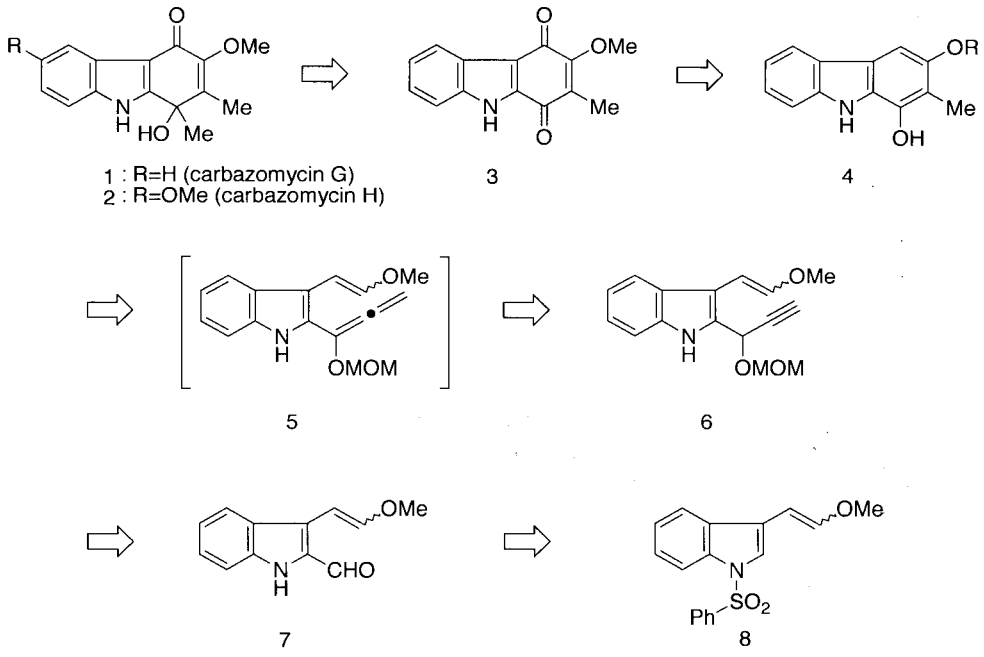
Results and Discussion

The required 3-(2-methoxyethenyl)indole-2-carbaldehyde (**7**) was initially prepared from the 3-(2-methoxyethenyl)-*N*-(phenylsulfonyl)indole (**8**).[7] Namely, treatment of a mixture of *E* and *Z*-isomer (**8**) (1:0.7) with LDA at −78 to 0°C for 3 h followed by addition of *N*,*N*-dimethylformamide (DMF) at −78 to 0°C for 3 h gave the 3-(2-methoxyethenyl)indole-2-carbaldehyde (**7**) (41%) having the *E*-stereochemistry along with unreactive *Z*-isomer (**8**) (14%). Based on the fact that no 3-[(*Z*)-methoxyethenyl]-indole-2-carbaldehyde, selective lithiation of *E* and *Z*-isomer (**8**) followed by formylation might have occurred. Further, based on the low recovery yield of unreactive *Z*-isomer (**8**), it would appear that the reactivity of the lithiated *Z*-isomer (**8**) with DMF was more weak than that of the *E*-isomer (**8**) with DMF due to the formation of a more stable 6-membered ring in the former. Although the yield of this reaction was moderate, the stereochemistry was extremely covenient for our key-step. Subsequently, Grignard reaction of **7** with ethynylmagnesium bromide at 0°C afforded the propargyl alcohol (**9**) (87%), which was treated with chloromethyl methyl ether (MOMCl) in the presence of ethyl diisopropylamine to yield the MOM-ether (**10**) (98%). The acetylene derivative (**10**) was subjected to an allene-mediated electrocyclic reaction using potassium *t*-butoxide in *t*-butanol and THF at 90°C to produce the desired 1,3-dioxygenated carbazole (**11**) (85%). Cleavage of MOM-ether of **11** with chlorotrimethylsilane and sodium iodide[8] at −20°C gave the phenol (**4**) (69%) as the synthetic precursor (Scheme 2).

Keywords: allenes; electrocyclic reactions; polycyclic heterocyclic compounds; quinonoid compounds.

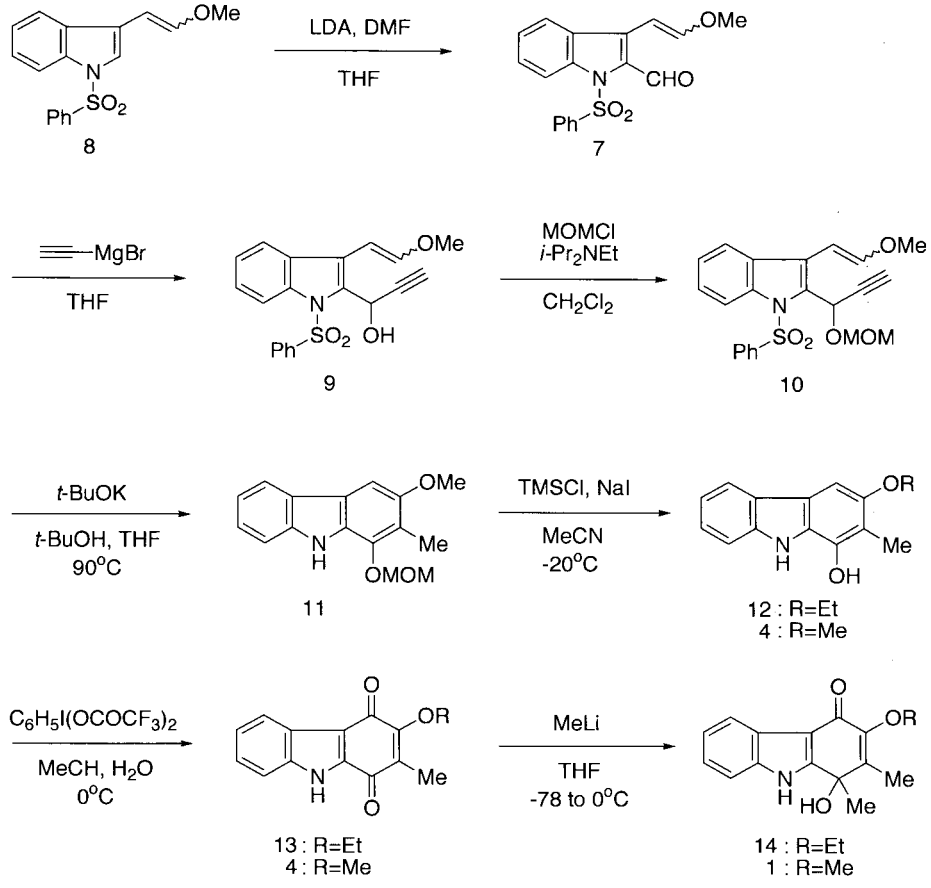
* Corresponding author. Tel.: +81-849-36-2111; fax: +81-849-36-2024; e-mail: hibino@fupharm.fukuyama-u.ac.jp

0040–4020/00/$ - see front matter
PII: S0040-4020(00)00543-3



Scheme 1.

Temporally, we examined an oxidation step and a final step using the previously reported 1-hydroxy-3-ethoxy-2-methylcarbazole (**12**)[5c] instead of **4**. Oxidations by Fremy's salt,[9] cerium ammonium nitrate,[10] and salcomine-molecular oxygen[11] did not work well in this case. Among them, the carbazole-1,4-quinone (**13**) was only obtained by a system of salcomine-molecular oxygen in DMF at room temperature in low yield (20%). However, we found that the oxidation to carbazole-1,4-quinone (**13**) from the phenol (**12**) proceeded in a good yield (73%) by using



Scheme 2.

[bis(trifluoroacetoxy)iodo]benzene[12] in an aqueous acetonitrile. Furthermore, the nucleophilic addition of the carbazole-1,4-quinone (**13**) with methyl lithium according to the Knölker's procedure[3] provided the carbazomycin G ethyl-congenor (**14**) in an excellent yield (98%).

Therefore, the oxidation of the true precursor, 1-hydroxy-3-methoxy-2-methylcarbazole (**4**), with [bis(trifluoroacetoxy)iodobenzene was carried out in a similar way to obtain the expected carbazole-1,4-quinone (**3**) in an excellent yield (98%). Finally, treatment of **3** with methyl lithium in the same manner gave carbazomycin G (**1**) regioselectively (87%) (Scheme 2). The spectral and physical data of synthetic carbazomycin G (**1**) were identical to the data reported for the natural product.[1] Thus a new total synthesis of carbazomycin G (**1**) was established in a seven-step sequence (17.5% overall yield) by the construction of the 1,3-dioxygenated carbazole nucleus (**12**) based on the allene-mediated electrocyclic reaction of the hexatriene system involving the indole 2,3-bond, together with the synthesis of carbazomycin G ethyl-congenor (**14**).

Experimental

All air-sensitive reactions were conducted in flame-dried glassware under an argon atmosphere unless otherwise stated. THF was freshly distilled from benzophenone ketyl. DMF, diisopropylamine and ethyl diisopropylamine were freshly distilled after drying over CaH_2. Silica gel (100 mesh, Merck Art 7734) was used for column chromatography. Melting points were measured by a Yanagimoto MP-500D micro melting points apparatus and were uncorrected. IR spectra were recorded on a Shimadzu FTIR-8500 spectrophotometer. ^1H and ^{13}C NMR spectra were taken with a JEOL-AL 300 using tetramethylsilane as an internal standard. All mass spectra were obtained by using Shimadzu 9020DF and QP5050 spectrometers equipped with an electrospray ionization source at 70 eV.

3-[(*E*)-2-Methoxyethenyl]-*N*-(phenylsulfonyl)indole-2-carbaldehyde (7). A stirred solution of 3-(2-methoxyethenyl)indole (**8**)[7] [a mixture of *E*/*Z* (1:0.7), 1.5 g, 4.79 mmol)] in THF (10 ml) was treated with a solution of LDA [prepared from diisopropylamine (1.4 ml, 10.5 mmol) and *n*-BuLi (2.52 mol/L in hexane, 4.2 ml, 10.5 mmol) in THF (10 ml)] at −78°C. The reaction temperature was gradually raised to 0°C during stirring for 3 h. A solution of DMF (0.9 ml, 12 mmol) in THF (2 ml) was added to the cooled mixture at −78°C. After stirring at 0°C for 2 h, the mixture was quenched with water. The EtOAc layer was washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography (silica gel, 50 g) using EtOAc–hexane (3:17 v/v) as an eluent to give the *E*-2-formylindole (**7**) (670 mg, 41%), mp 120–123°C (from EtOAc). IR (KBr) ν: 1641, 1356 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 3.79 (3H, s), 6.54 (1H, d, J=13 Hz), 7.26–7.71 (9H, m), 8.24 (1H, d, J=8 Hz), 10.57 (1H, s): MS *m*/*z*: 341 (M^+). Anal. calcd for $C_{18}H_{15}NO_4S$: C, 63.33; H, 4.43; N, 4.10. Found: C, 63.45; H, 4.51; N, 4.13.

2-(1-Hydroxyprop-2-yl)-3-[(*E*)-2-methoxyethenyl]-*N*-(phenylsulfonyl)indole (9). A stirred solution of ethynylmagnesium bromide (0.5 M in THF, 2.3 ml, 1.64 mmol) was added to the solution of the 2-formylindole (**7**) (372 mg, 1.09 mmol) in THF (15 ml) under cooling with ice. After stirring at the same temperature for 3 h, the reaction mixture was quenched with an aqueous NH_4Cl (saturated) solution and the mixture was extracted with EtOAc. The EtOAc layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography (silica gel, 15 g) using EtOAc–hexane (1:4 v/v) as an eluent to give the oily propargyl alcohol (**9**) (348 mg, 87%). IR (neat) ν: 3290, 2131, 1362 cm^{-1}; H NMR ($CDCl_3$) δ: 2.67 (1H, d, J=2.5 Hz), 3.77 (3H, s), 4.49 (1H, d, J=11 Hz), 5.83 (1H, d, J=13 Hz), 6.01 (1H, dd, J=2.5, 11 Hz), 6.99 (1H, d, J=13 Hz), 7.20–7.38 (4H, m), 7.47 (2H, t, J=7 Hz), 7.85(2H, d, J=7 Hz), 7.98 (1H, d, J=8 Hz); MS *m*/*z*: 367 (M^+). HRMS calcd for $C_{20}H_{17}NO_4S$: 367.0878; observed: 367.0891.

3-[(*E*)-2-Methoxyethenyl]-2-[(1-methoxymethyloxy)prop-2-yn-1-yl]-*N*-(phenylsulfonyl)indole (10). A stirred solution of MOMCl (0.27 ml, 3.6 mmol) was added to a solution of the propargyl alcohol (**9**) (163 mg, 0.44 mmol) and ethyl diisopropylamine (0.6 ml, 3.60 mmol) in CH_2Cl_2 (15 ml) at an ambient temperature, and the mixture was heated at 50°C for 12 h. After cooling to rt, the reaction mixture was quenched with water. The mixture was extracted with CH_2Cl_2. The CH_2Cl_2 layer was washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography (silica gel, 10 g) using EtOAc–hexane (1:9 v/v) as an eluent to give the oily MOM-ether (**10**) (183 mg, 98%). IR (neat) ν: 2123, 1373 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 2.64 (1H, d, J=2.5 Hz), 3.44 (3H, s), 3.74 (3H, s), 4.70 (1H, d, J=7 Hz), 4.99 (1H, d, J=7 Hz), 6.23 (1H, d, J=13 Hz), 6.61 (1H, d, J=2.5 Hz), 7.15–7.38 (5H, m), 7.47 (1H, t, J=6 Hz), 7.60 (1H, d, J=7 Hz), 7.81 (2H, d, J=6 Hz), 8.19 (1H, d, J=8 Hz); MS *m*/*z*: 411 (M^+). HRMS calcd for $C_{22}H_{21}NO_5S$: 411.1140; observed: 411.1157.

3-Methoxy-1-(methoxymethyloxy)-2-methylcarbazole (11). A stirred solution of the MOM-ether (**10**) (182 mg, 0.442 mmol) in THF (2 ml) was added to a solution of *t*-BuOK (149 mg, 1.33 mmol) in *t*-BuOH (6 ml) at an ambient temperature. The mixture was refluxed at 90°C for 12 h and cooled to rt. The mixture was quenched with an aqueous NH_4Cl (saturated) solution, which was extracted with EtOAc. The EtOAc layer was washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography (silica gel, 10 g) using EtOAc–hexane (1:19 v/v) as an eluent to give the oily carbazole (**11**) (102 mg, 85%). ^1H NMR ($CDCl_3$) δ: 2.31 (3H, s), 3.76 (3H, s), 3.95 (3H, s), 5.24 (2H, s), 7.17 (1H, t, J=7.9 Hz), 7.30 (1H, s), 7.37 (1H, t, J=7.9 Hz), 7.43 (1H, d, J=7.9 Hz), 7.99 (1H, d, J=7.9 Hz), 9.15(1H, br s); MS *m*/*z*: 271(M^+). HRMS calcd for $C_{16}H_{17}NO_3$: 271.1208; observed: 271.1196.

1-Hydroxy-3-methoxy-2-methylcarbazole (4). A stirred solution of TMSCl (0.19 ml, 1.52 mmol) was added to a suspension of the carbazole (**11**) (275 mg, 1.01 mmol) and NaI (228 mg, 1.52 mmol) in CH_3CN (10 ml) at −20°C. The mixture was stirred at −20°C for 10 min, and then

1.01 equiv. of NaI (151 mg) and TMSCl (0.13 ml) were added twice every 5 min to the mixture at −20°C, respectively, under monitoring with TLC. After the starting material disappeared, the reaction mixture was quenched with water and EtOAc at the same temperature, and then the mixture was extracted with EtOAc. The EtOAc layer was washed with 10% aqueous Na_2SO_3 solution and brine, dried over Na_2SO_4, and then concentrated. The residue was purified by column chromatography (silica gel, 20 g) using EtOAc–hexane (3:17 v/v) as an eluent to give the 1-hydroxycarbazole (**4**) (159 mg, 69%), mp 165–167°C (from Et_2O–hexane). IR (KBr) ν: 3398 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 2.34 (3H, br s), 2.99 (3H, s), 3.94 (3H, br s), 7.15 (1H, br s), 7.18 (1H, t, J=8 Hz), 7.37 (1H, t, J=8 Hz), 7.43 (1H, d, J=8 Hz), 7.99 (1H, d, J=8 Hz), 8.08 (1H, br s); MS m/z: 227 (M^+). Anal. Calcd for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77; N, 6.16. Found: C, 74.06; H, 5.84; N, 6.07.

3-Ethoxy-2-methylcarbazole-1,4-dione (13). [Bis(trifluoroacetoxy)iodo]benzene (283 mg, 0.66 mmol) was added to a stirred solution of the 1-hydroxycarbazole (**12**)[5c] (72 mg, 0.30 mmol) in CH_3CN (7 ml) and H_2O (3.5 ml) under cooling with ice and an N_2 atmosphere. After stirring at the same temperature for 1 h, the reaction mixture was quenched with an aqueous $NaHCO_3$ (saturated) solution and the mixture was extracted with 10% MeOH–$CHCl_3$. The $CHCl_3$ layer was washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography (silica gel, 40 g) using EtOAc–hexane as an eluent to give the carbazole-1,4-quinone (**13**) (56 mg, 73%), mp 209–211°C (from EtOAc–hexane). IR (KBr) ν: 3260, 1641 cm^{-1}; ^1H NMR (DMSO-d_6) δ:1.32 (3H, t, J=7 Hz), 1.91 (3H, s), 4.33 (2H, q, J=7 Hz), 7.30 (1H, t, J=7.9 Hz), 7.36 (1H, t, J=7.5 Hz), 7.52 (1H, d, J=7.9 Hz), 7.99 (1H, d, J=7.5 Hz), 12.85 (1H, br s); ^{13}C NMR ($CDCl_3$) δ: 181.3, 179.2, 158.0, 137.0, 135.7, 127.3, 126.6, 124.3, 124.2, 122.7, 114.9, 112.9, 70.0, 16.2, 9.68; MS m/z: 255(M^+). Anal. calcd for $C_{15}H_{13}NO_3$: C, 70.58; H, 5.13; N, 5.49. Found: C, 70.70; H, 5.11; N, 5.62.

3-Methoxy-2-methylcarbazole-1,4-dione (3). The above procedure was then carried out using 1-hydroxycarbazole (**4**) (25 mg, 0.11 mmol) and [bis(trifluoroacetoxy)iodo]-benzene (104 mg, 0.24 mmol) to give the carbazole-1,4-quinone (**3**) (27 mg, 98%), mp 257–259°C (EtOAc). IR (KBr) ν: 3260, 1641 cm^{-1}; ^1H NMR (DMSO-d_6) δ: 1.91 (3H, s), 4.03 (3H, s), 7.28–7.39 (2H, m), 7.52 (1H, d, J=8 Hz), 8.00 (1H, d, J=8 Hz), 12.86 (1H, br s); MS m/z: 241 (M^+). Anal. calcd for $C_{14}H_{11}NO_3$: C, 69.70; H, 4.60; N, 5.81. Found: C, 69.94; H, 4.72; N, 5.99.

3-Ethoxy-1-hydroxy-1,2-dimethylcarbazole-4-one (14). A stirred solution of methyllithium (1.09 mol/L in Et_2O, 0.36 ml, 0.39 mmol) was added to a solution of the carbazole-1,4-quinone (**13**) (10 mg, 0.039 mmol) at −78°C. After stirring at −78°C to rt for 3 h, the reaction mixture was quenched with an aqueous NH_4Cl (saturated) solution, and then the mixture was extracted with EtOAc. The EtOAc layer was washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography (silica gel, 20 g) using EtOAc–hexane (3:7 v/v) as an eluent to give carbazomycin G ethyl-congenor (**14**) (10 mg, 94%), mp 222–224°C (from EtOAc–hexane). IR (KBr) ν: 3200, 2930, 1690 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 1.25 (3H, t, J=7 Hz), 1.56 (3H, s), 1.98 (3H, s), 3.94 (2H, q, J=7 Hz), 5.91 (1H, s), 7.13–7.23 (2H, m), 7.43 (1H, d, J=7 Hz), 7.99 (1H, d, J=7 Hz), 12.2 (1H, s); ^{13}C NMR ($CDCl_3$) δ: 177.8, 154.3, 146.5, 141.0, 136.4, 123.8, 122.9, 121.5, 120.5, 112.0, 108.4, 67.3, 67.0, 28.0, 15.5, 10.5; MS m/z: 271 (M^+). Anal. calcd for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.32; N, 5.16. Found: C, 70.86; H, 6.39; N, 4.97.

Carbazomycin G (1). The above procedure was then carried out using the carbazole-1,4-quinone (**3**) (27 mg, 0.11 mmol) and methyllithium (1.09 mol/L, 1 ml, 1.12 mmol) to give carbazomycin G (**1**) (25 mg, 87%), mp 266–268°C (from EtOAc) (lit.,[1] mp 241–243°C and lit.,[3a] mp 266–268°C). IR (KBr) ν: 3204, 2926, 1611 cm^{-1}; ^1H NMR (DMSO-d_6) δ: 1.58 (3H, s), 1.99 (3H, s), 3.77 (3H, s), 5.95 (1H, s), 7.15–7.24 (2H, m), 7.44 (1H, d, J=7 Hz), 8.01(1H, d, J=7 Hz), 12.22 (1H, br s); ^{13}C NMR ($CDCl_3$) δ: 177.4, 154.2, 147.5, 140.7, 136.3, 123.7, 122.9, 121.4, 120.4, 112.0, 108.3, 67.2, 59.1, 27.8, 10.1; MS m/z: 257 (M^+).

Acknowledgements

This work was supported in part by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, Sports and Culture in Japan.

References

1. Kaneda, M.; Naid, T.; Kitahara, T.; Nakamura, S. *J. Antibiot.* **1988**, *41*, 602–608.

2. For the isolation of carbazomycins A–F see: (a) Sakano, K.; Kitahara, K.; Nakamura, S. *J. Antibiot.* **1980**, 33, 683–689. (b) Sakano, K.; Nakamura, S. *J. Antibiot.* **1980**, *33*, 961–966. (c) Kaneda, M.; Sakano, K.; Nakamura, S.; Kushi, Y.; Iitaka, Y. *Heterocycles* **1981**, 15, 993–998. (d) Yamasaki, K.; Kaneda, M.; Watanabe, K.; Ueki, Y.; Ishimaru, K.; Nakamura, S.; Nomi, R.; Yoshida, N.; Nakajima, T. *J. Antibiot.* **1983**, *36*, 552–558. (e) Kondo, S.; Katayama, M.; Marumo, B. *J. Antibiot.* **1986**, 39, 727–730. (f) Naid, T.; Kitahara, T.; Kaneda, M.; Nakamura, S. *J. Antibiot.* **1987**, *40*, 157–164.

3. (a) Knölker, H.-J.; Frohner, W. *Tetrahedron Lett.* **1997**, *38*, 4051–4054. (b) Knölker, H.-J.; Frohner, W. *J. Chem. Soc., Perkin Trans. 1* **1998**, 173–175.

4. (a) Woodward, R. B.; Hoffmann, R. *J. Am. Chem. Soc.* **1965**, *87*, 395–397. (b) Woodward, R. B.; Hoffmann, R. *The Conservation of Orbital Symmetry*; Chemie: Weinheim, 1970; Chapter 5. (c) Freming, I. *Frontier Orbital and Organic Chemistry*; Wiley: London, 1976. (d) Marvel, E. N. *Thermal Electrocyclic Reactions*; Academic Press: New York, 1980; Chapter 2. (e) Okamura, W. H.; de Lera, A. R. 1,3-Cyclohexadiene formations reactions; Trost, B. M., Freming, I., Paquette, L. A., Eds.; *Comprehensive Organic Synthesis*; Pergamon Press: New York, 1991; Vol. 5, pp 699–750. (f) Kawasaki, T.; Sakamoto, M. *J. Indian Chem. Soc.* **1994**, *71*, 443–457. (g) S. Hibino, S.; Sugino, E. Synthesis of [*b*]-annelated indoles by thermal electrocyclic reactions; C. J. Moody, Ed.; In *Advances in Nitrogen Heterocycles*; JAI Press: Greenwich, CT, 1995; Vol. 1, pp 205–227.

5. (a) Choshi, T.; Sada, T.; Fujimoto, H.; Nagayama, C.; Sugino,

E.; Hibino, S. *Tetrahedron Lett.* **1996**, *37*, 2593–2596. (b) Choshi, T.; Fujimoto, H.; Sugino, E.; Hibino, S. *Heterocycles* **1996**, *43*, 1847–1854. (c) Choshi, T.; Sada, T.; Fujimoto, H.; Nagayama, C.; Sugino, E.; Hibino, S. *J. Org. Chem.* **1997**, 62, 2535–2543. (d) Hagiwara, H.; Choshi, T.; Fujimoto, H.; Sugino, E.; Hibino, S. *Chem. Pharm. Bull.* **1998**, *46*, 1946–1949 and related references cited therein.

6. (a) Yoshioka, H.; Matsuya, Y.; Choshi, T.; Sugino, E.; Hibino, S. *Chem. Pharm. Bull.* **1996**, *44*, 709–714. (b) Choshi, T.; Matsuya, Y.; Okita, M.; Inada, K.; Sugino, E.; Hibino, S. *Tetrahedron Lett.* **1998**, 39, 2341–2344. (c) Kuwabara, N.; Hayashi, H.; Hiramatsu, N.; Choshi, T.; Sugino, E.; Hibino, S. *Chem. Pharm. Bull.* **1999**, *47*, 1805–1807. (d) Choshi, T.; Kuwada, T.; Fukui, M. Matsuya, Y.; Sugino, E. Hibino, S. *Chem. Pharm. Bull.* **2000**, *48*, 108–113.

7. Pfeuffer, L.; Pindur, U. *Helv. Chim. Acta* **1987**, *28*, 1419–1428.

8. Rigby, J. H.; Wilson, J. Z. *Tetrahedron Lett.* **1984**, *25*, 1429–1432.

9. Zimmer, H.; Lankin, D. C.; Horgan, S. W. *Chem. Rev.* **1990**, *71*, 229–246.

10. (a) Joseph, J. R., III; Callery, P. S.; Shulgin, A. T.; Castagnoli, N. J., Jr. *Org. Chem.* **1976**, 3627–3629. (b) Syper, L.; Kroc, K.; Mlochouski, J. *Synthesis* **1979**, 521–522. (c) Kubo, A.; Kitahara, Y.; Nakahara, S.; Numata, R. *Chem. Pharm. Bull.* **1983**, *31*, 341–343. (d) Kitahara, Y.; Nakai, T.; Nakahara, S.; Akazawa, M.; Shimizu, M.; Kubo, A. *Chem. Pharm. Bull.* **1991**, 39, 2256–2263.

11. (a) Bailes, R. H.; Calvin, M. *J. Am. Chem. Soc.* **1947**, *69*, 1886–1893. (b) VanDort, H. M.; Geursen, H. J. *Recl. Trav. Chim. Pays-Bas.* **1967**, *86*, 520–26. (c) Weinreb, S. M.; Hibino, S. *J. Org. Chem.* **1997**, *42*, 232–236. (d) Wakamatsu, T. T.; Nishi, T.; Ohnuma, T.; Ban, Y. *Synthetic Commun.* **1984**, *14*, 1167–1173.

12. (a) Barret, R.; Daudon, M. *Tetrahedron Lett.* **1990**, *31*, 4871–4872. (b) Moriarty, R. M.; Berglund, B. A.; Penmasta, R. *Tetrahedron Lett.* **1992**, *33*, 6065–6068. (c) Bergeron, D.; Brassard, P. *Heterocycles* **1992**, *34*, 1835–1845. (d) Bergeron, D.; Caron, B.; Brassard, P. *J. Org. Chem.* **1993**, *58*, 509–511.