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Expeditious Synthesis of the Marine Natural Products Prepolycitrin A and Polycitrins A and B through Heck Arylations

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New, efficient protocols for the syntheses of the marine natural products prepolycitrin A as well as polycitrins A and B were developed by employing the Heck–Matsuda arylation of maleic anhydride or dimethyl fumarate with aryldiazonium tetrafluoroborates. Both symmetrical and unsymmetrical 3,4-diarylmaleic anhydrides were easily and effectively prepared. Efficient bromination reactions that employed tribromoisocyanuric acid provided access to the polycitrin family of compounds. Under microwave irradiation in the presence of tyramine, the corresponding maleimides were obtained in high yields from the brominated 3,4-diarylmaleic anhydrides. This methodology provided for the concise synthesis of prepolycitrin A and the total syntheses of the marine alkaloids polycitrins A and B in overall yields of 37 and 47 % from maleic anhydride and dimethyl fumarate, respectively.

Introduction

Maleimides constitute an important and diverse class of bioactive compounds. Several relevant examples of these compounds include purpurone (**1**), which is a potent ATP-citrate lyase (ACL) inhibitor,[1] 1*H*-pyrrole-2,5-dione derivative **2**, which was recently reported as a selective COX-2 inhibitor (similar to celecoxib),[2] 1*H*-pyrrole-2,5-dione derivative **3**, which is a nontoxic inhibitor of multidrug resistance (MDR) in cancer cells,[3] and derivative **4**, which is an HIV integrase inhibitor.[4] Other maleimides include prepolycitrin A (**6**) as well as polycitrins A and B (i.e., **5** and **7**, respectively, see Figure 1). This interesting group of bioactive marine natural products was isolated from ascidians of the genus *Polycitor*.[5] The structural elucidation of these compounds was reported in 1994 by Kashman and co-workers,[5] who confirmed the presence of the unusual diarylmaleic anhydride or diarylmaleimide unit. In 1995, Steglich and co-workers[6] reported the biomimetic synthesis of prepolycitrin A and polycitrin A. Several years later (in 2000), Beccalli and co-workers[7] reported the first synthesis of the alkaloid polycitrin B, which was carried out in eight steps. In 2006, two new approaches to the preparation of polycitrin A were reported, that is, one by our group[8] and the other by Steglich and co-workers.[9] Despite the important biological and fluorescent properties displayed by these diarylated maleimides and maleic anhydrides (see Figure 1),[10] no further strategies to expedite the synthesis of this class of compounds have been reported.

We disclose our recent results regarding the efficient arylation of maleic anhydride and dimethyl fumarate through a Heck–Matsuda arylation with arenediazonium tetrafluoroborates as well as the application of this methodology to the concise and practical syntheses of prepolycitrin A (**6**), polycitrin A (**5**), and polycitrin B (**7**), which occurred with excellent overall yields.

Results and Discussion

Initial Studies

To achieve the efficient synthesis of the polycitrins, we reevaluated our previous results with regard to the Heck arylation of maleic anhydride using arenediazonium salts.[8] Our earlier work described a method that worked reasonably well for the arylation of maleic anhydride, which employed electron-rich arenediazonium salts. For electron-neutral and electron-deficient arenediazonium salts, the method was either ineffective or provided low yields of the desired diarylmaleic anhydrides. Because the Heck–Matsuda arylations potentially facilitate access to these key diarylmaleic anhydride frameworks,[11] we decided to reinvestigate our initial protocols and overcome the difficulties faced by the method's first iteration.

Palladium catalysts play a crucial role in Heck arylations, and, therefore, we decided to explore the new generation of highly reactive, air-stable palladium–phosphinous acid complexes, such as POPd and POPd1 (see Figure 2).[12]

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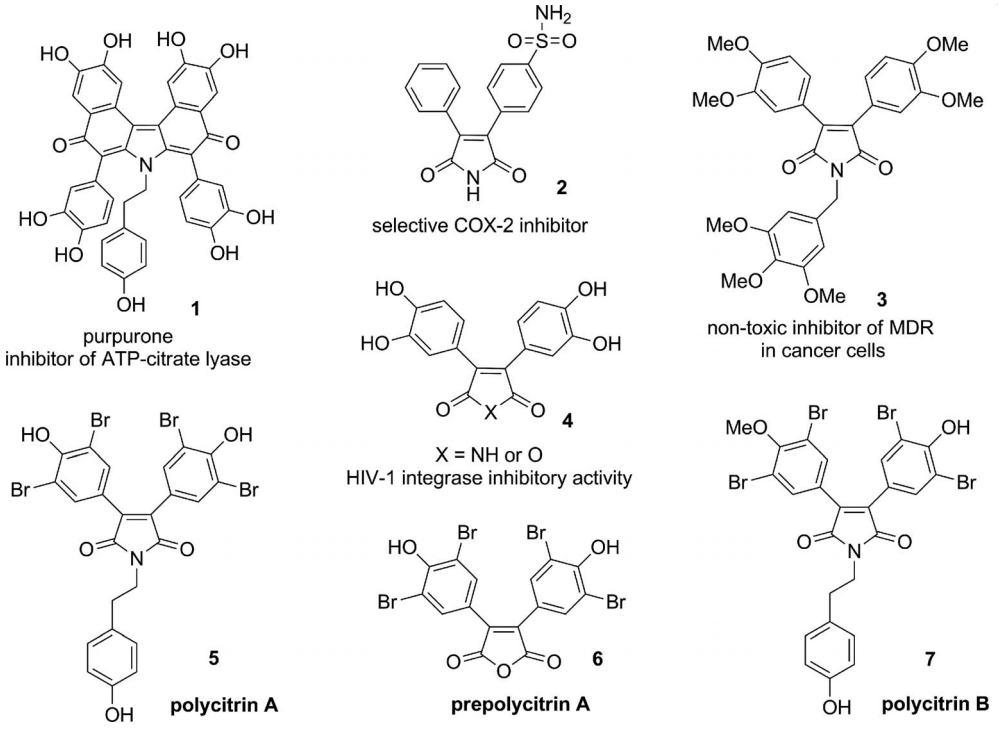


Figure 1. Bioactive diarylmaleimides and diarylmaleic anhydrides.

These catalysts have already demonstrated superior performance when employed in many coupling reactions.[13]

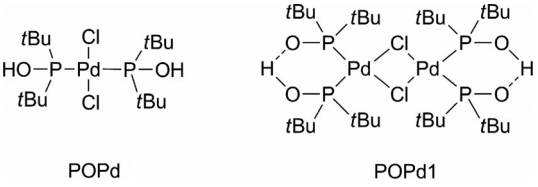
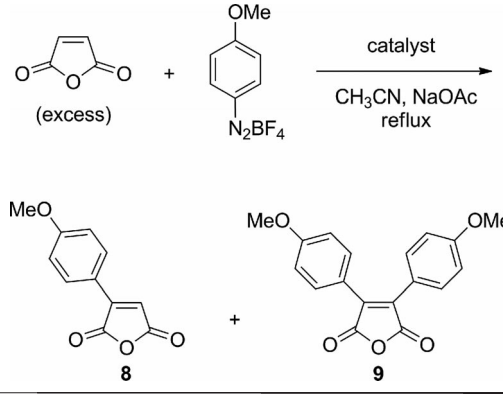


Figure 2. Palladium–phosphinous acid catalysts used in our studies.

We were initially reluctant to use these catalysts in Heck–Matsuda arylations because the presence of the chloride anion in the reaction medium might favor a neutral pathway over the desired cationic mechanism, which would drastically change the outcome of the reaction. At this stage, we were focused on the synthesis of a monoarylated

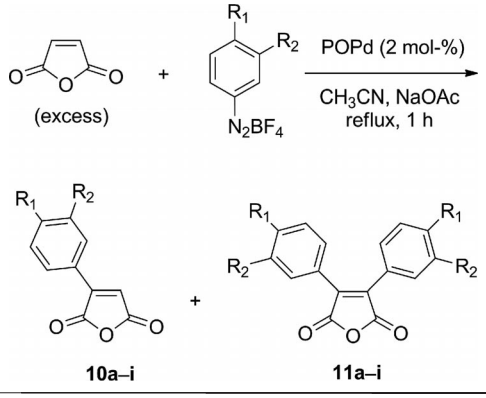
Table 1. Heck arylation of maleic anhydride using palladium–phosphinous acid catalysts.



Entry	Catalyst	% Yield	**8/9**[a]
1	POPd (2 mol-%)	95	95:5
2	POPd1 (2 mol-%)	73	90:10

[a] Ratio determined by capillary gas chromatography.

Table 2. Heck arylation of maleic anhydride using POPd.



Entry	Adduct R_1, R_2	Compound [% yield]	**10/11**[a]
1	Cl, H	**10a** (60)	99:01
2	Br, H	**10b** (52)	99:01
3	I, H	**10c** (50)	99:01
4	F, H	**10d** (78)	99:01
5	NO_2, H	**10e** (71)	85:15
6	OCF_3, H	**10f** (92)	90:10
7	CN, H	**10g** (40)[b]	90:10
8	SCH_3, H	**10h** (55)	90:10
9	OMe, OMe	**10i** (95)	95:05

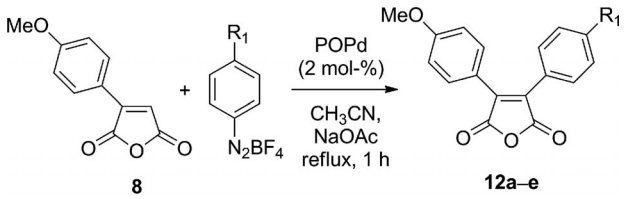
[a] Ratio determined by capillary gas chromatography. [b] During isolation, the hydrolysis of an aryl anhydride with electron-withdrawing groups may cause a significant decrease in yield.

maleic anhydride, which would provide the opportunity to prepare nonsymmetrical diarylmaleic anhydrides with a second Heck–Matsuda arylation. After exhaustive experimentation, we discovered that almost exclusive monoarylation could be achieved by employing a large excess amount of maleic anhydride. Good to excellent yields were obtained in refluxing acetonitrile with only 2 mol-% of POPd or POPd1 as described in Table 1. Intriguingly, even a large excess amount of maleic anhydride (50 equiv.) could not prevent the formation of small amounts of the diarylated maleic anhydride. POPd1 provided a lower overall yield and a larger amount of the diarylated side product. Therefore, POPd was chosen as the optimal Pd catalyst for the efficient arylation of maleic anhydride.

With these results on hand, the evaluation of the Heck–Matsuda reaction with a variety of aryldiazonium tetrafluoroborates, which included the previously low-performing electron-deficient and -neutral structures (see Table 2), could begin.

It was encouraging that a variety of aryldiazonium tetrafluoroborates provided access to the respective monoarylated maleic anhydride as the major or exclusive product in good to excellent yields. These results highlight the importance of choosing the correct Pd catalyst for the efficient Heck–Matsuda arylation of maleic anhydride. The insensitivity of the Heck reaction toward chloride anions in the reaction medium along with the fluorescence exhibited by many of the monoarylated maleic anhydrides were both surprising. With the exception of the product derived from benzenediazonium tetrafluoroborate, all other monoarylated maleic anhydrides exhibited intense blue fluorescence.

Table 3. Heck arylation of monoarylated maleic anhydride **8**.



Entry	R_1	Compound [% yield]
1	Cl	**12a** (65)
2	F	**12b** (30)
3	CF_3	**12c** (40)
4	SCH_3	**12d** (55)
5	OH	**12e** (69)[a]

[a] 2 equiv. of maleic anhydride **8** were used.

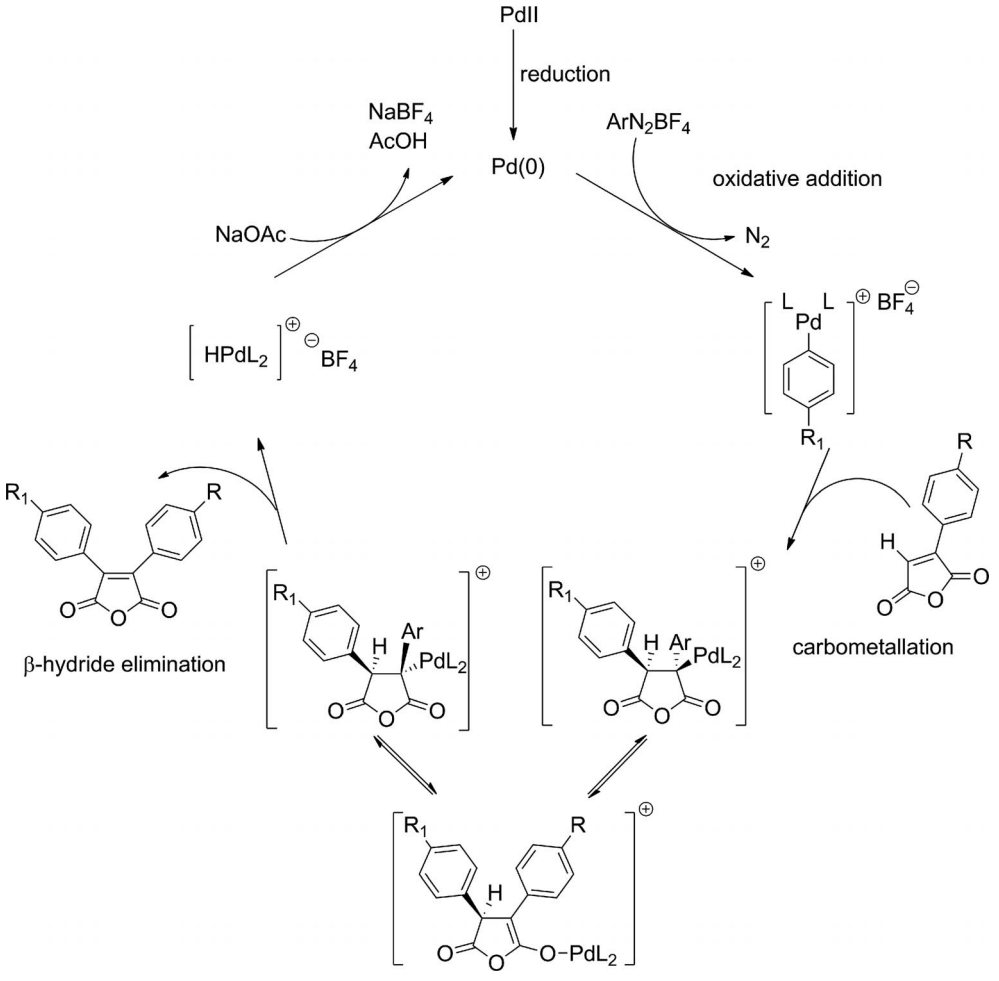


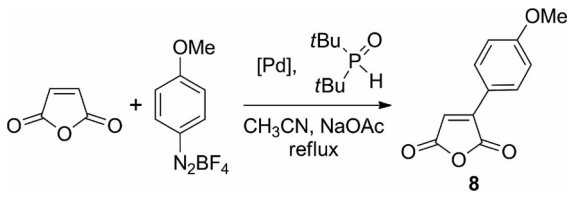
Figure 3. Proposed catalytic cycle.

POPd also effectively promoted the conversion of the monoarylated maleic anhydrides into the nonsymmetrical diarylated structures (see Table 3). A slight decrease in the yield was observed for the second Heck–Matsuda arylation, but this was most likely because of the steric interference caused by the two aromatic rings interacting with the planar maleic anhydride structure. To achieve the yields displayed in Table 3, it was necessary to use an excess amount of the diazonium salt (2 equiv.). An exception was in the case of R_1 = OH (see Table 3, Entry 5), in which 2 equiv. of maleic anhydride **8** were employed to provide a moderate 69% yield of diarylmaleic anhydride **12e**.

The Heck arylation of maleic anhydrides is interesting mechanistically, and a proposed reaction pathway is shown in Figure 3. For the mono- and diarylation of maleic anhydride, the isomerization of the carbopalladation intermediate occurs through a palladium(II) enolate. This inversion of configuration is necessary to account for the facile *syn* elimination, which occurs during the next stage.

In spite of the superior performance displayed by the POPd catalyst in the Heck–Matsuda arylations of maleic anhydride, the cost of this reagent is a considerable drawback when considering a more general application of the methodology. Therefore, we investigated the in situ formation of a similar palladium catalyst that could be as effective as POPd.[12] The phosphinous acid was prepared and subsequently combined with $Pd_2(dba)_3$ (dba = dibenzylideneacetone) or $Pd(OAc)_2$ to attempt the in situ formation of the catalyst. As shown in Table 4, $Pd(OAc)_2$ proved to be an effective Pd source, and the monoarylated (with 4-methoxyphenyl group) maleic anhydride was furnished in excellent yield (86%) by using only 4 mol-% of $Pd(OAc)_2$ under CO, which acts as a reducing agent (see Table 4, Entry 3). Even with 2 mol-% of $Pd(OAc)_2$ (see Table 4, Entry 5), the arylmaleic anhydride was produced in good 81% yield.

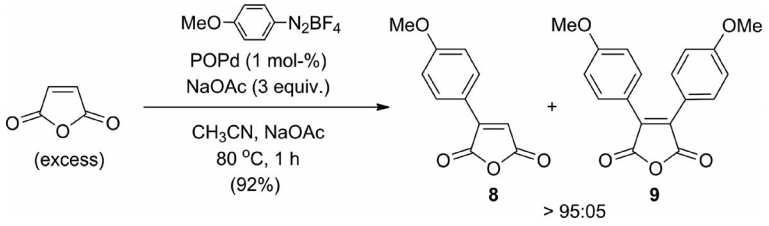
Table 4. Heck monoarylation of maleic anhydride with $Pd_2(dba)_3$-dba and $Pd(OAc)_2$ combined with phosphinous acid.



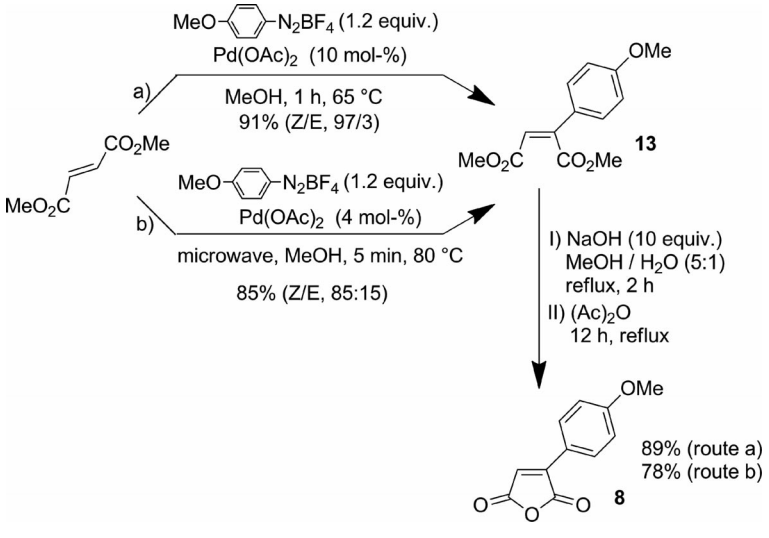
Entry	Pd source[a]	% Yield
1	$Pd_2(dba)_3$dba (2 mol-%)	30
2[b]	$Pd_2(dba)_3$dba (2 mol-%)	60
3[b]	$Pd(OAc)_2$ (4 mol-%)	86
4	$Pd(OAc)_2$ (4 mol-%)	58
5[b]	$Pd(OAc)_2$ (2 mol-%)	81

[a] 4 equiv. of phosphinous acid with respect to palladium. [b] Reactions conducted under CO.

It is also worth mentioning that the performance of the Heck–Matsuda arylation reactions can be carried out on a gram scale. The arylation of maleic anhydride was con-



Scheme 1. Synthesis of Heck adduct **8** from maleic anhydride on a 5 mmol scale with 1 mol-% of POPd.



Scheme 2. Synthesis of the Heck adduct **3** from dimethyl fumarate.

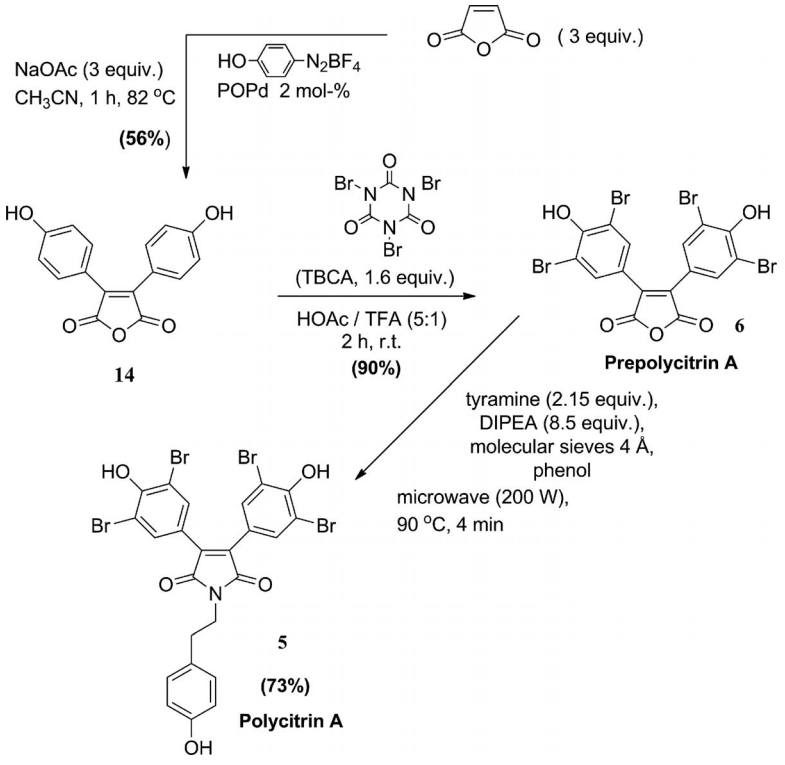
ducted with methoxyphenyldiazonium tetrafluoroborate on a 5 mmol scale with only 1 mol-% of POPd to provide the monoarylated Heck adduct almost exclusively in 92% yield (see Scheme 1).

The need for an excess amount of the maleic anhydride and the persistent occurrence of the diarylated products were a potential problem for widespread synthetic application. Therefore, new starting materials were investigated to obtain monoarylated maleic anhydride **8** exclusively. An alternative was found during the reaction of dimethyl fumarate with 4-methoxyphenyldiazonium tetrafluoroborate, which utilized $Pd(OAc)_2$ (10 mol-%) in refluxing methanol for 1 h.[14] These conditions provided the stereoselective synthesis of monoarylated dimethyl maleate **13** in an isolated yield of 91% (see Scheme 2, route a). Further investigation allowed for the decrease of the palladium catalyst loading to 4 mol-% when the reaction was carried out under microwave irradiation (see Scheme 2, route b). This reaction was completed in only 5 min and gave Heck adduct **13** in 85% yield with a *Z*/*E* ratio of 85:15. Basic hydrolysis of arylmaleate **13** with aqueous NaOH in methanol followed by the treatment of the crude mixture with acetic anhydride provided monoarylated maleic anhydride **8** in a 89% yield over two steps. For synthetic purposes, employing route a was optimal because of its higher yield and stereoselectivity.

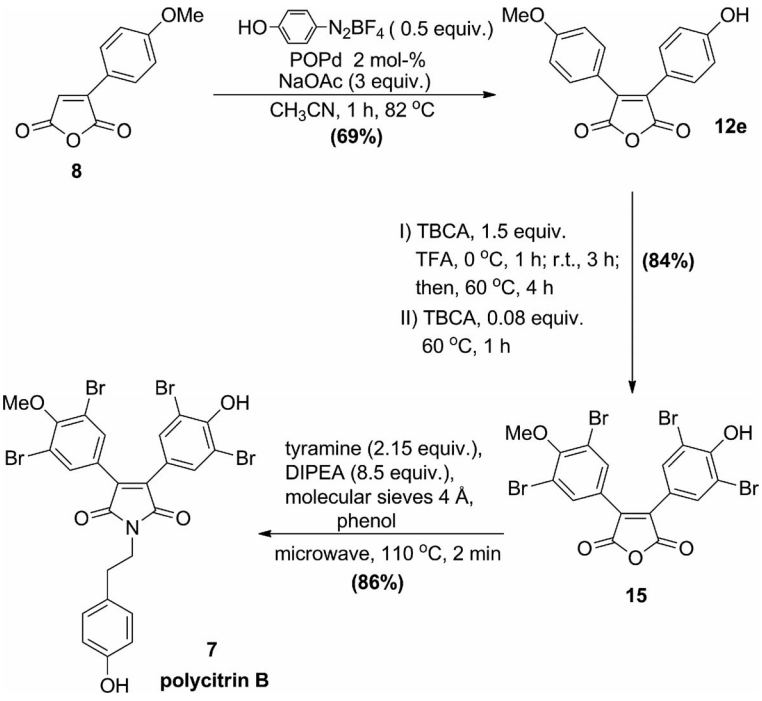
Synthesis of Prepolycitrin A and Polycitrin A

To perform a concise synthesis of these natural products, we decided to use the improved Heck–Matsuda arylation procedure described above. Instead of starting with 4-methoxyphenyldiazonium tetrafluoroborate as described previously,[8] we decided to initiate the synthesis with 4-hydroxyphenyldiazonium tetrafluoroborate[15] to obtain 3,4-di(4-hydroxyphenyl)maleic anhydride (**14**) in a single step. The diarylation of maleic anhydride with POPd was performed under different conditions, and the best procedure to obtain the diarylated Heck product was achieved by using an excess amount (3 equiv.) of maleic anhydride (see Scheme 3), instead of the usual excess amount of the aryldiazonium salt. Under these conditions, diarylated maleic anhydride **14** was obtained in an isolated yield of 56% (based on the aryldiazonium salt) along with some monoarylated product, which was easily removed by flash chromatography. When an excess amount of aryldiazonium salt (4 equiv.) was used, the diarylated Heck product was isolated in only 28% yield. Therefore, changing the maleic anhydride/aryldiazonium salt ratio to favor the maleic anhydride led to increased yields of the diarylated product (56% yield). These results suggest that under the conditions established in our protocol, the second arylation of the maleic anhydride is faster than the first and, additionally, the maleic anhydride seems to stabilize the palladium intermediates that are generated over the course of this reaction.

Although the yield for the desired diarylmaleic anhydride **14** was only moderate, the core structure of polycitrin A was obtained in a single step. Bromination of anhydride **14** was achieved by using tribromoisocyanuric acid (TBCA)[16] in a solution of acetic acid/trifluoroacetic acid (5:1) to complete the synthesis of prepolycitrin A (**6**) in 90% yield. The use of TBCA was advantageous because of its ease of handling and high reactivity. However, the reactivity of the



Scheme 3. Synthesis of the alkaloids prepolycitrin A and polycitrin A.



Scheme 4. The total synthesis of polycitrin B.

TBCA was significantly affected by the acidity of the reaction medium.[16b] In less acidic media (pH = 3–4), we observed the formation of a mixture of prepolycitrin A and its tribrominated intermediate, which was very difficult to separate by flash column chromatography. As we were able to prepare prepolycitrin A in gram quantities, we noticed a curious relationship between the color of our synthetic prepolycitrin A (an orange-red solid) and the actual color of the marine animal *Polycitor giganteus*, from which prepolycitrin A was first isolated (see picture in the Table of Contents).

To obtain polycitrin A, prepolycitrin A was initially heated with tyramine, Hunig's base, and phenol at 140 °C for 2 h. However, under these conditions the yields of the corresponding maleimide were always below 40%. We investigated this reaction under microwave irradiation. After examining several reaction conditions, it was possible to obtain polycitrin A (**5**) in good yield by employing tyramine, Hünig's base, and phenol at 90 °C under microwave irradiation (200 W, 4 min). The short irradiation time was critical to obtain good yields. This procedure allowed for the synthesis of polycitrin A in 73% yield from prepolycitrin A and in 37% overall yield from maleic anhydride, which is inexpensive.

Synthesis of Polycitrin B

The only reported total synthesis of polycitrin B was accomplished by Becalli et al.[7] These authors described a sequence of eight steps to synthesize this natural product in 30% overall yield. For the preparation of polycitrin B, we adopted a slightly different approach from the one described above for polycitrin A. We started as shown in Scheme 2 from (4-methoxyphenyl)maleic anhydride **8**, which was obtained from dimethyl fumarate. The Heck–Matsuda arylation of **8** with (4-hydroxyphenyl)diazonium tetrafluoroborate, 2 mol-% of POPd, and NaOAc as the base in acetonitrile at approximately 80 °C afforded the nonsymmetrical 3,4-diarylmaleic anhydride **12e** in an isolated yield of 69% (see Scheme 4). The use of 2 equiv. of the arylmaleic anhydride **8** was necessary to decrease the formation of side products (not identified). The bromination of the phenol-anisole moiety of anhydride **12e** by treatment with TBCA was carried out under strictly controlled conditions to avoid overoxidation. After several experiments, we determined that the addition of 1.5 equiv. of TBCA at 0 °C, a subsequent gradual temperature increase, and then a 4 h period at 60 °C followed by a second addition of 0.08 equiv. of TBCA (see Exp. Section for details) provided the tetrabrominated diarylmaleic anhydride **15** in 84% yield. Finally, conversion of the maleic anhydride into the maleimide was carried out as described for the synthesis of polycitrin A. The treatment of maleic anhydride **15** with tyramine, Hunig′s base, and phenol under microwave irradiation (110 °C, 2 min) afforded polycitrin B (**7**) in an excellent 86% isolated yield. The total synthesis of polycitrin B was accomplished in only five steps from dimethyl fumarate with an overall yield of 47%.

Conclusions

We developed a new and efficient protocol based on the Heck–Matsuda reaction for the synthesis of monoarylated maleic anhydrides as well as symmetrical and nonsymmetri-

cal diarylated maleic anhydrides. The mono- and diarylmaleic anhydrides are interesting fluorophores for biological studies as well as valuable starting materials for total syntheses. This method provided a new and straightforward synthesis for prepolycitrin A, which upon treatment with tyramine under microwave conditions, afforded polycitrin A. A new total synthesis of polycitrin B was also accomplished from monoaryl-substituted maleic anhydride **8**. Both syntheses feature the carefully controlled bromination reactions of the electron-rich aryl groups by employing TBCA as well as the efficient conversion of the diarylmaleic anhydride into the corresponding maleimide, which occurred under microwave conditions and with short reaction times. The total syntheses of prepolycitrin A and polycitrins A and B are simple and efficient compared to previously reported approaches. The more complex polycitrins A and B were synthesized through concise routes in overall yields of 37 and 47% from maleic anhydride and dimethyl fumarate, respectively.

Experimental Section

Typical Experimental Procedure for the Synthesis of Monoarylmaleic Anhydride: To a solution of POPd (5 mg, 2 mol-%) in CH_3CN (4 mL) were added maleic anhydride (0.98 g, 10 mmol), NaOAc (123 mg, 1.5 mmol), and the appropriate aryldiazonium tetrafluoroborate salt (0.5 mmol). The reaction mixture was heated to reflux for 1 h. The mixture was then cooled, and EtOAc (20 mL) was added. The organic phase was washed with saturated $NaHCO_3$ (3 × 15 mL) and then separated. The combined organic extracts were dried with Na_2SO_4. The solvent was removed under reduced pressure, and the crude residue was purified by flash column chromatography (silica gel, hexane/EtOAc) to give the corresponding monoarylated maleic anhydride in yields ranging from 50 to 95%. *Note:* Monoarylated maleic anhydrides that contain strong electron-withdrawing groups may undergo hydrolysis during isolation (washing with saturated $NaHCO_3$), which can cause a significant decrease in the yields. In those cases (e.g., compounds **10e** and **10g**), the crude product that was obtained after washing with $NaHCO_3$ and drying with Na_2SO_4 was dissolved in acetic anhydride (approximately 1 mL), and the resulting solution was heated at 100 °C for 90 min. After cooling to room temp., the acetic anhydride was removed in vacuo to provide a crude mixture, which was purified by flash chromatography as indicated above.

3-(4-Methoxyphenyl)-2,5-dihydrofuran-2,5-dione (8):[17] Orange solid (95% yield), m.p. 142–143 °C; ref.[17a] m.p. 142–143 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.90 (s, 3 H), 6.83 (s, 1 H), 7.00 (d, ^3J = 8.9 Hz, 2 H), 7.99 (d, ^3J = 8.9 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.7, 115.0, 121.1, 131.2, 146.4, 163.4, 164.2, 165.2 ppm. ^{13}C NMR (62.5 MHz, CD_3CN): δ = 56.4, 115.8, 120.9, 123.4, 132.0, 147.2, 164.1, 165.7, 166.7 ppm.

3,4-Di(4-methoxyphenyl)-2,5-dihydrofuran-2,5-dione (9):[18] Orange solid (56% yield), m.p. 169–171 °C; ref.[18] 170–171 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.85 (s, 6 H), 6.91 (d, ^3J = 9.0 Hz, 4 H), 7.57 (d, ^3J = 9.0 Hz, 4 H) ppm. ^{13}C NMR (CD_3CN, 62.9 MHz): δ = 55.4, 114.4, 119.9, 131.4, 135.7, 161.7, 165.4 ppm.

3-(4-Chlorophenyl)-2,5-dihydrofuran-2,5-dione (10a): Pale yellow solid (60% yield); m.p. 160–162 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.01 (s, 1 H), 7.49 (d, ^3J = 8.6 Hz, 2 H), 7.93 (d, ^3J = 8.6 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 124.6, 125.1, 129.7, 130.2, 139.2, 145.6, 163.2, 164.2 ppm. IR (KBr): $\tilde{\nu}$ = 3112, 1852, 1754, 1222 cm^{-1}. HRMS (ESI): calcd. for $C_{10}H_5ClO_3$ 207.9927; found 207.9927.

3-(4-Bromophenyl)-2,5-dihydrofuran-2,5-dione (10b): Yellow solid (52% yield); m.p. 167–168 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.02 (s, 1 H), 7.66 (d, ^3J = 8.7 Hz, 2 H), 7.93 (d, ^3J = 8.7 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 124.7, 125.7, 128.0, 130.4, 132.8, 145.9, 163.4, 164.4 ppm. IR (KBr): $\tilde{\nu}$ = 2958, 1822, 1757, 1275 cm^{-1}. HRMS (ESI): calcd. for $C_{10}H_5BrO_3$ 251.9422; found 251.9420.

3-(4-Iodophenyl)-2,5-dihydrofuran-2,5-dione (10c): Yellow solid (50% yield); m.p. 124 °C (decomp). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.04 (s, 1 H), 7.68 (d, ^3J = 8.5 Hz, 2 H), 7.87 (d, ^3J = 8.5 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 100.6, 124.9, 126.2, 130.3, 138.8, 146.0, 163.4 164.4 ppm. IR (KBr): $\tilde{\nu}$ = 3116, 1838, 1765, 1750, 1237 cm^{-1}. HRMS (ESI): calcd. for $C_{10}H_5IO_3$ 299.9283; found 299.9276.

3-(4-Fluorophenyl)-2,5-dihydrofuran-2,5-dione (10d): Yellow solid (78% yield); m.p. 127–129 °C (decomp). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.97 (s, 1 H), 7.18–7.24 (m, 2 H), 8.00–8.04 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 116.7, 117.0, 123.2, 124.0, 131.4, 131.6, 145.7, 163.3, 163.5, 164.5, 166.9 ppm. IR (KBr): $\tilde{\nu}$ = 3116, 1765, 1750 cm^{-1}. HRMS (ESI): calcd. for $C_{10}H_5FO_3$ 192.0223; found 192.0224.

3-(4-Nitrophenyl)-2,5-dihydrofuran-2,5-dione (10e):[19] Yellow solid (71% yield), m.p. 127–128 °C (decomp); ref.[19] m.p. 128–129 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.22 (s, 1 H), 8.17 (d, ^3J = 8.9 Hz, 2 H), 8.37 (d, ^3J = 8.9 Hz, 2 H) ppm.

3-(4-Trifluoromethoxyphenyl)-2,5-dihydrofuran-2,5-dione (10f): Orange solid (92% yield); m.p. 117–118 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.03 (s, 1 H), 7.36 (d, ^3J = 8.9 Hz, 2 H), 8.05 (d, ^3J = 8.9 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 121.3, 125.1, 125.5, 131.0, 131.7, 145.5, 163.3, 164.4 ppm. IR (KBr): $\tilde{\nu}$ = 3111, 1856, 1773, 1212 cm^{-1}. HRMS (ESI): calcd. for $C_{11}H_5F_3O_4$ 258.0140; found 258.0150.

3-(4-Cyanophenyl)-2,5-dihydrofuran-2,5-dione (10g): White solid (70% yield); m.p. 142–143 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.15 (s, 1 H), 7.82 (d, ^3J = 8.7 Hz, 2 H), 8.09 (d, ^3J = 8.7 Hz, 2 H) ppm. ^{1}H NMR {600 MHz, deuterated dimethyl sulfoxide ([D_6]-DMSO)}: δ = 6.54 (s, 1 H), 7.74 (d, ^3J = 8.5 Hz, 2 H), 7.93 (d, ^3J = 8.5 Hz, 2 H) ppm. ^{13}C NMR (150 MHz, [D_6]DMSO): δ = 112.8, 118.8, 121.3, 128.1, 133.4, 138.6, 146.6, 166.2, 168.5 ppm. IR (KBr): $\tilde{\nu}$ = 2958, 1773, 1712 cm^{-1}. HRMS (ESI): calcd. for $C_{11}H_5NO_3$ 199.0269; found 199.0264.

3-(4-Methylthiophenyl)-2,5-dihydrofuran-2,5-dione (10h): Yellow solid (55% yield); m.p. 127–128 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.54 (s, 3 H), 6.91 (s, 1 H), 7.30 (d, ^3J = 8.6 Hz, 2 H), 7.90 (d, ^3J = 8.6 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 121.3, 125.1, 125.5, 131.0, 131.7, 145.5, 163.3, 164 ppm. IR (KBr): $\tilde{\nu}$ = 1818, 1761, 1218 cm^{-1}. HRMS (ESI): calcd. for $C_{11}H_8O_3S$ 220.0194; found 220.0183.

3-(3,4-Dimethoxyphenyl)-2,5-dihydrofuran-2,5-dione (10i): Orange solid (95% yield); m.p. 164–166 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.95 (s, 3 H), 3.96 (s, 3 H), 6.85 (s, 1 H), 6.96 (d, ^3J = 8.5 Hz, 1 H), 7.48 (d, ^4J = 2.1 Hz, 1 H), 7.70 (dd, ^3J = 8.5 Hz, ^4J = 2.1 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 56.2, 111.2, 111.5, 119.9, 121.3, 123.9, 146.3, 149.6, 153.3, 164.1, 165.2 ppm. IR (KBr): $\tilde{\nu}$ = 2927, 1833, 1769, 1261 cm^{-1}. HRMS (ESI): calcd. for $C_{12}H_{10}O_5$ 234.0528; found 234.0527.

Typical Experimental Procedure for the Synthesis of Unsymmetrical Diarylmaleic Anhydride: To a solution of POPd (2 mg, 2 mol-%) in

CH_3CN (3 mL) were added 3-(4-methoxyphenyl)-2,5-dihydrofuran-2,5-dione (**8**, 0.04 g, 0.2 mmol), NaOAc (0.024 g, 0.3 mmol), and the appropriate diazonium tetrafluoroborate salt (0.4 mmol). The reaction mixture was heated to reflux for 1 h. EtOAc (10 mL) was then added, and the organic phase was subsequently washed with saturated $NaHCO_3$ (3× 7 mL) and separated. The combined organic extracts were dried with Na_2SO_4. The solvent was removed under reduced pressure, and the crude residue was purified by flash column chromatography (silica gel, hexane/EtOAc) to give the corresponding diarylated maleic anhydride in yields ranging from 30 to 69%.

3-(4-Chlorophenyl)-4-(4-methoxyphenyl)furan-2,5-dione (12a): Orange solid (65% yield); m.p. 167–170 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.85 (s, 3 H), 6.90 (d, ^3J = 8.9 Hz, 2 H), 7.38 (d, ^3J = 8.6 Hz, 2 H), 7.50 (d, ^3J = 8.6 Hz, 2 H), 7.54 (d, ^3J = 8.9 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.6, 114.7, 119.3, 126.2, 129.5, 131.0, 131.8, 134.5, 137.2, 138.2, 162.3, 165.0, 165.1 ppm. IR (KBr): $\tilde{\nu}$ = 2928, 1833, 1765, 1263 cm^{-1}. HRMS (ESI): calcd. for $C_{17}H_{11}ClO_4$ 314.0346; found 314.0330.

3-(4-Fluorophenyl)-4-(4-methoxyphenyl)furan-2,5-dione (12b): Yellow solid (30% yield); m.p. 141–142 °C (decomp). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.86 (s, 3 H), 6.91 (d, ^3J = 9.0 Hz, 2 H), 7.11 (t, ^3J = 8.7 Hz, 2 H), 7.54–7.60 (m, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.6, 114.6, 116.2, 116.5, 119.3, 123.8, 131.7, 134.6, 137.7, 162.1, 162.3, 165.0, 165.6 ppm. IR (KBr): $\tilde{\nu}$ = 2928, 1826, 1761, 1261 cm^{-1}. HRMS (ESI): calcd. for $C_{17}H_{11}FO_4$ 298.0641; found 298.0634.

3-(4-Trifluoromethoxyphenyl)-4-(4-methoxyphenyl)furan-2,5-dione (12c): Orange solid (40% yield); m.p. 157–160 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.86 (s, 3 H), 6.92 (d, ^3J = 9.0 Hz, 2 H), 7.56 (d, ^3J = 9.0 Hz, 2 H), 7.68 (s, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.6, 114.8, 119.0, 126.0, 126.1, 130.0, 131.4, 132.0, 132.4, 133.9, 139.6, 162.6, 164.7, 164.8 ppm. HRMS (ESI): calcd. for $C_{18}H_{11}F_3O_4$ 348.0609; found 348.0609.

3-(4-Methylthiophenyl)-4-(4-methoxyphenyl)furan-2,5-dione (12d):[2b] Orange solid (55% yield); m.p. 167–169 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.40 (s, 3 H), 3.85 (s, 3 H, OMe), 6.90 (d, ^3J = 8.8 Hz, 2 H), 7.22 (d, ^3J = 8.4 Hz, 2 H), 7.46 (d, ^3J = 8.2 Hz, 2 H), 7.57 (d, ^3J = 8.8 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.9, 55.5, 114.6, 119.8, 123.9, 125.7, 130.0, 131.6, 135.3, 136.7, 143.4, 162.0, 165.3, 165.4 ppm.

Synthesis of 3-(4-Hydroxyphenyl)-4-(4-methoxyphenyl)2,5-furan-2,5-dione (12e) on Gram Scale: To a stirred solution of POPd (0.049 g, 0.097 mmol), sodium acetate (2.380 g, 29.0 mmol), and **8** (1.976 g, 9.68 mmol) in acetonitrile (50 mL) was added 4-hydroxyphenyldiazonium tetrafluoroborate (1.007 g, 4.840 mmol). The resulting mixture was heated to reflux at 82 °C for 1 h and then subsequently cooled to room temperature. The solution was concentrated under reduced pressure, and the residue was filtered through silica gel (ethyl acetate). The solution was concentrated under reduced pressure, and the crude residue was purified by flash column chromatography (silica gel, hexane/EtOAc, 95:5) to afford **12e** (0.920 g, 3.11 mmol, 69%) as a yellow solid; m.p. 152–153 °C. ^{1}H NMR (250 MHz, CD_3CN): δ = 3.82 (s, 3 H), 6.85 (d, ^3J = 8.7 Hz, 2 H), 6.96 (d, ^3J = 8.8 Hz, 2 H), 7.40 (d, ^3J = 8.78 Hz, 2 H), 7.47 (d, ^3J = 8.8 Hz, 2 H), 7.48 (s, 1 H, OH) ppm. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.84 (s, 3 H), 6.84 (d, ^3J = 8.9 Hz, 2 H), 6.90 (d, ^3J = 9.0 Hz, 2 H), 7.48 (d, ^3J = 8.9 Hz, 2 H), 7.54 (d, ^3J = 9.0 Hz, 2 H) ppm. ^{13}C NMR (50 MHz, CD_3CN): δ = 56.2, 115.3, 116.6, 120.4, 121.2, 132.3, 132.6, 160.2, 162.5, 166.9 ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.5, 114.6, 116.1, 119.9, 120.1, 131.5, 135.9, 158.2, 161.8, 165.6 ppm. IR (KBr): $\tilde{\nu}$ = 398, 3438, 1846, 1823, 1757, 1745, 1623, 1605, 1589, 1508, 1437, 1350, 1273, 1236, 1175, 1122, 1095, 924, 841, 744, 575, 528 cm^{-1}. HRMS (ESI): calcd. for $C_{17}H_{12}O_5$ 296.0685; found 296.0672.

Preparation of Tribromoisocyanuric Acid:[16c] To a cold (ice bath, 0 °C) solution of cyanuric acid (1.61 g, 12.5 mmol), NaOH (1.50 g, 37.5 mmol), Na_2CO_3 (1.99 g, 18.75 mmol), and KBr (4.46 g, 37.5 mmol) in H_2O (180 mL) was added dropwise a solution of Oxone® (23.1 g, 37.5 mmol) in H_2O (150 mL). During the addition of the oxidant solution, a white solid precipitate appeared and formed a dense suspension, which was stirred for 24 h. The product was isolated by vacuum filtration, washed with cold H_2O, and then dried with P_2O_5 to give the product (86% yield). The m.p. was not determined as the reagent decomposed upon heating. FTIR (KBr): $\tilde{\nu}$ = 1741, 1724, 1660, 1405, 1339, 1197, 1146, 1051, 737, 717 cm^{-1}.

Dimethyl 2-(4-Methoxyphenyl)maleate (13)

By Using Conventional Heating: To a 250 mL round-bottomed flask that contained $Pd(OAc)_2$ (0.460 g, 2.05 mmol) in methanol (180 mL) was added dimethyl fumarate (2.972 g, 20.0 mmol). 4-Methoxyphenyldiazonium tetrafluoroborate (5.326 g, 24.0 mmol) was added with stirring, and the reaction mixture was heated to reflux (65 °C) for 1 h. The solution was cooled to room temp. and concentrated under reduced pressure. The resulting residue was filtered through a plug of silica gel (ethyl acetate). The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography (silica gel, hexanes/EtOAc, 90:10) to afford arylmaleate **13** (4.553 g, 18.19 mmol, 91%) as a colorless oil. The spectroscopic data obtained for compound **13** are consistent with those reported.[14b]

By Using Microwave Irradiation: To a microwave tube were added methanol (3 mL), $Pd(OAc)_2$ (0.003 g, 0.014 mmol), dimethyl fumarate (0.050 g, 0.35 mmol), the diazonium salt (0.093 g, 0.42 mmol), and a magnetic stir bar. The tube was then irradiated (80 °C, 300 W) with stirring for 5 min. After this period of time, the reaction mixture was submitted to the same procedure described above, which furnished the desired product **13** (85% yield; *Z*/*E* ratio, 85:15). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.77 (s, 3 H), 3.83 (s, 3 H), 3.95 (s, 3 H), 6.23 (s, 1 H), 6.90 (d, ^3J = 8.9 Hz, 2 H), 7.42 (d, ^3J = 8.9 Hz, 2 H) ppm. ^{13}C NMR (62.9 MHz, CD_3CN): δ = 52.50, 53.15, 56.22, 115.1, 115.5, 126.2, 129.5, 149.4, 162.9, 166.6, 169.4 ppm. IR (KBr): $\tilde{\nu}$ = 3462, 1815, 1757, 1609, 1578, 1543, 1472, 1398, 1342, 1329, 1310, 1267, 1253, 1244, 1159, 1148, 947, 893, 756, 621 cm^{-1}.

3-(4-Methoxyphenyl)-2,5-dihydrofuran-2,5-dione (8) from Dimethyl 2-(4-Methoxyphenyl)maleate (13): To a 125 mL round-bottomed flask that contained **13** (1.110 g, 4.437 mmol) were added methanol (50 mL) and NaOH (5 M solution, 10 mL). The reaction mixture was heated at reflux for 2 h. After cooling, the solvent was evaporated under reduced pressure to give a residue, which was suspended in water (25 mL). As the mixture was stirred, concentrated HCl (approximately 4.5 mL) was then added until the pH = 2. The obtained precipitate was extracted with ethyl acetate (3× 30 mL) in a 250 mL separatory funnel. The organic phase was separated, and the combined extracts were dried with anhydrous sodium sulfate and filtered. The solvent was evaporated under reduced pressure. To the residue was then added distilled acetic anhydride (70 mL), and the mixture was heated at reflux for 12 h. The solvent was then removed by using a rotary evaporator, and a yellow solid precipitate formed. This solid could be purified either by recrystallization or by silica gel chromatography. Recrystallization was performed by dissolving the crude solid in hot ethyl acetate (7 mL) followed by the slow addition of hexane until the solution displayed a slight turbidity. The mixture was cooled to room tem-

perature, when a needle-shaped yellow solid started to precipitate. The solid was filtered and washed with cold hexane and then was allowed to dry to furnish product **8** (0.780 g, 3.82 mmol, 86%). Alternatively, flash column chromatography [silica gel, 10% ethyl acetate in hexane] furnished the desired product **8** (0.852 g, 4.171 mmol, 94%).

3,4-Di(4-Hydroxyphenyl)-2,5-dihydrofuran-2,5-dione (14): To a stirred solution of POPd (0.050 g, 0.10 mmol), sodium acetate (1.230 g, 15.0 mmol), and maleic anhydride (1.467 g, 14.97 mmol) in acetonitrile (30 mL) was added 4-hydroxyphenyldiazonium tetrafluoroborate (1.038 g, 4.99 mmol). The resulting mixture was heated to reflux at 82 °C for 1 h and then cooled to room temperature. The solution was concentrated under reduced pressure in presence of silica gel (6.3 g), and the resulting residue was placed on a short silica gel column (ethyl acetate). The obtained solution was concentrated, and the residual maleic anhydride was removed under vacuum at 2 Torr (85 °C, 40 min). The crude residue was purified by flash column chromatography (silica gel, hexanes/EtOAc, 80:20) to afford **14** (0.395 g, 56% yield) as yellow solid and a small amount of the monoarylated side product 3-(4-hydroxyphenyl)-maleic anhydride (**14a**). The spectroscopic data for compound **14** are consistent with those reported.[6,20] M.p. 223 °C; ref.[20] m.p. 224 °C. ^{1}H NMR (250 MHz, [D$_6$]acetone): δ = 6.90 (d, ^3J = 8.7 Hz, 4 H), 7.47 (d, ^3J = 8.7 Hz, 4 H), 9.03 (s, 2 H, OH) ppm. ^{13}C NMR ([D$_6$]acetone, 62.9 MHz): δ = 116.6, 120.3, 132.5, 136.8, 160.6, 166.7 ppm.

3-(4-Hydroxyphenyl)-2,5-dihydrofuran-2,5-dione (14a): M.p. 199–200 °C (decomp). ^{1}H NMR (250 MHz, [D$_6$]acetone): δ = 7.00 (d, ^3J = 8.8 Hz, 2 H), 7.24 (s, 1 H), 8.03 (d, ^3J = 8.8 Hz, 2 H), 9.31 (s, 1 H, OH) ppm. ^{13}C NMR (62.9 MHz, CD$_3$CN): δ = 117.1, 120.2, 122.7, 132.2, 147.2, 161.9, 165.7, 166.7 ppm. IR (KBr): $\tilde{\nu}$ = 3395, 1841, 1740, 1594, 1573, 1504, 1242, 1174, 907, 837 cm^{-1}. HRMS (ESI): calcd. for $C_{10}H_7O_4$ 191.0344; found 191.0343.

3-(3,5-Dibromo-4-hydroxyphenyl)-4-(3,5-dibromo-4-methoxyphenyl)-2,5-furan-2,5-dione (15): To a 50 mL round bottomed flask that contained **12e** (0.253 g, 0.854 mmol) in trifluoroacetic acid (TFA, 20 mL) at 0 °C was added TBCA (0.468 g, 1.28 mmol), and the reaction mixture was stirred at this temperature for 1 h. The cooling bath was removed, and the reaction mixture was warmed to room temp. and then stirred for 3 h. Next, the mixture was heated to 60 °C and then stirred for 4 h. After this period of time, another portion of TBCA (0.024 g; 0.066 mmol) was added, and the reaction mixture was stirred for an additional hour. The reaction mixture was cooled, and the solvent was evaporated under vacuum. The crude reaction mixture was filtered through a plug of silica gel and then purified by flash column chromatography (10% ethyl acetate in hexane) to yield the desired product **15** (0.439 g, 0.717 mmol, 84%). The spectroscopic data that was obtained for compound **15** are consistent with those reported.[7] ^{1}H NMR (250 MHz, CD$_3$CN): δ = 3.91 (s, 3 H), 7.66 (s, 2 H), 7.70 (s, 2 H) ppm. ^{13}C NMR (62.9 MHz, CD$_3$CN): δ = 61.7, 111.2, 119.5, 122.1, 126.9, 134.6, 134.8, 136.0, 137.8, 154.1, 157.2, 165.4, 165.5 ppm. IR (KBr): $\tilde{\nu}$ = 3433, 1825, 1761, 1583, 1544, 1481, 1467, 1421, 1394, 1343, 1321, 1253, 1188, 1151, 1119, 1068, 993, 941, 878, 802, 756, 748, 727, 629, 613, 594 cm^{-1}.

Prepolycitrin A – 3,4-Di(3,5-dibromo-4-hydroxyphenyl)-2,5-dihydrofuran-2,5-dione (6): To a stirred solution of 3,4-di(4-hydroxyphenyl)-2,5-dihydrofuran-2,5-dione (**14**, 0.790 g, 2.80 mmol) in AcOH/trifluoroacetic acid (5:1, 22 mL) was slowly added TBCA (1.613 g, 4.41 mmol) at room temp. over a period of 2 h. After the complete addition of TBCA, the reaction mixture was stirred for an additional 30 min. Next, the solution was concentrated under reduced pressure in the presence of silica gel (2.2 g). The residue was placed on a short column of silica gel (ethyl acetate). The solution that was obtained was concentrated under vacuum. Purification of the residue by flash column chromatography (silica gel, hexanes/EtOAc, 80:20) afforded **6** (1.498 g, 90%) as an orange-red solid. The spectroscopic data obtained for this compound are consistent with those reported.[5b,6] There was a significant discrepancy between the reported melting points and the one recorded by us. Steglich and co-workers[6] reported a m.p. of 148–149 °C, whereas Rudi and co-workers[5b] described prepolycitrin A as a yellow oil. Because of these discrepancies, we used differential scanning calorimetry (DSC2910 TA Instrument, from 25 to 270 °C, at 10 °C min^{-1}) to determine the precise melting point of prepolycitrin A, m.p. 242.3 °C (DSC). ^{1}H NMR (250 MHz, [D$_6$]-acetone): δ = 7.81 (s, 4 H), 9.31 (br. s, 2 H, OH) ppm. ^{13}C NMR (62.9 MHz, [D$_6$]acetone): δ = 111.8, 122.6, 134.6, 136.2, 154.0, 165.6 ppm. IR (KBr): $\tilde{\nu}$ = 3462, 1815, 1757, 1608, 1578, 1543, 1483, 1466, 1398, 1329, 1310, 1267, 1254, 1148, 1115, 947, 893, 879, 756, 748, 716, 621, 590 cm^{-1}.

Polycitrin A (5): A mixture of the diarylmaleic anhydride **6** (0.036 g, 0.060 mmol), phenol (0.160 g), tyramine (0.019 g, 0.14 mmol), *N*,*N*-diisopropylethylamine (DIPEA, 0.096 mL, 0.55 mmol), and activated powdered molecular sieves (4 Å, 0.134 g) under nitrogen were placed in the microwave tube. The tube was heated to 90 °C over 1 min at 200 W and then maintained under these conditions for an additional 4 min. After the irradiation process, the reaction mixture was transferred to a 50 mL separatory funnel by using ethyl acetate (9 mL). The organic phase was washed with HCl (2 N solution, 5 mL), separated, and dried with anhydrous $MgSO_4$. After filtration, the organic solvent was removed under reduced pressure. The crude residue was then purified by flash chromatography (chloroform/hexanes, 1:1; pure chloroform; and then 1% methanol in chloroform). The fractions were collected, and the solvents were evaporated under vacuum to provide polycitrin A (0.031 g, 0.043 mmol, 72%) as a yellow solid. The spectroscopic data obtained for compound **5** are consistent with those reported for polycitrin A.[5,6] M.p. 180–181 °C; ref.[6,9] m.p. 180–182 °C. ^{1}H NMR (250 MHz, CD$_3$CN): δ = 2.86 (t, ^3J = 7.6 Hz, 2 H), 3.77 (t, ^3J = 7.6 Hz, 2 H), 6.77 (d, J = 8.4 Hz, 2 H), 7.08 (d, ^3J = 8.4 Hz, 2 H), 7.72 (s, 4 H) ppm. ^{13}C NMR (62.9 MHz, [D$_6$]acetone): δ = 34.7, 41.2, 112.0, 116.7, 124.1, 130.4, 131.2, 134.2, 135.2, 153.8, 157.4, 171.1 ppm. ^{13}C NMR (62.9 MHz, CD$_3$CN): δ = 34.3, 40.9, 111.4, 116.3, 124.0, 130.6, 131.0, 134.2, 134.6, 152.7, 156.7, 170.8 ppm. IR (KBr): $\tilde{\nu}$ = 3433, 1762, 1694, 1625, 1618, 1473, 1438, 1406, 1362, 1319, 1242, 1155, 1137, 1081, 1041, 995, 825, 800, 756, 730, 713, 621 cm^{-1}.

Polycitrin B (7): A mixture of diarylmaleic anhydride **15** (0.040 g, 0.065 mmol), phenol (0.160 g), tyramine (0.019 g, 0.14 mmol), *N*,*N*-diisopropylethylamine (0.096 mL, 0.55 mmol), and powdered molecular sieves (4 Å, 0.134 g) was placed in the microwave tube under nitrogen. The tube was heated to 110 °C over 1 min at 300 W and then maintained under these conditions for another 2 min. After the irradiation process, the reaction mixture was transferred to a 50 mL separatory funnel by using ethyl acetate (9 mL). The organic phase was washed with 4% HCl (9 mL), separated, and dried with anhydrous $MgSO_4$. After filtration, the organic solvent was removed under reduced pressure. The crude residue was then purified by flash column chromatography (chloroform/pentane, 1:2; pure chloroform; and then Et_2O/chloroform, 1:20). The fractions were collected and evaporated under reduced pressure to provide polycitrin B (0.041 g, 0.056 mmol, 86% yield) as a yellow solid. The spectroscopic data obtained for compound **7** are consistent with those reported for polycitrin B.[5a,7] ^{1}H NMR (250 MHz, [D$_6$]acetone): δ

= 2.86 (t, ^3J = 7.5 Hz, 2 H), 3.78 (t, ^3J = 7.5 Hz, 2 H), 3.92 (s, 3 H, OMe), 6.77 (d, ^3J = 8.2 Hz, 2 H), 7.08 (d, ^3J = 8.2 Hz, 2 H), 7.71 (s, 2 H), 7.76 (s, 2 H) ppm. ^{13}C NMR (62.9 MHz, [D$_6$]acetone): δ = 33.3, 39.9, 60.3, 110.6, 115.3, 117.8, 122.5, 127.6, 128.9, 129.7, 132.6, 133.8, 134.1, 134.3, 152.4, 155.2, 156.1, 169.4, 169.5 ppm. IR (KBr): $\tilde{\nu}$ = 3437, 1767, 1699, 1612, 1589, 1515, 1467, 1406, 1353, 1342, 1319, 1259, 1244, 1138, 1113, 1080, 993, 918, 879, 825, 756, 731, 631, 615, 594, 553 cm^{-1}.

Supporting Information (see footnote on the first page of this article): Copies of ^{1}H and ^{13}C NMR spectra for compounds **7** (polycitrin B), **8**, **9**, **10a**–**10i**, **12a**–**12e**, **13**, **14** and **15**, as well as IR spectra for compounds **12e** and **17**.

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