HETEROCYCLES, Vol. 96, No. 3, 2018, pp. 483 - 489. © 2018 The Japan Institute of Heterocyclic Chemistry
Received, 25th December, 2017, Accepted, 5th February, 2018, Published online, 21st February, 2018
DOI: 10.3987/COM-17-13864

A PRACTICAL SYNTHESIS OF THE CYCLIC BUTYLENE TEREPHTHALATE TRIMER

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Abstract – This paper described a practical synthetic approach for the cyclic butylene terephthalate trimer (**7**). The key step was a ring-closing metathesis, using Grubbs' second-generation catalyst to form the macrocyclic ring. The advantages of this procedure included short reaction steps, simple operations and good yields.

Polybutylene terephthalate (PBT) is a thermoplastic engineering polymer widely used as an insulator in the electrical and electronics industries. PBT is a thermoplastic crystalline polymer and a type of polyester, with an excellent balance of properties and processing characteristics.[1] During the manufacturing of PBT, some cyclic butylene terephthalates are inevitablely produced as impurities (Figure 1).[2] Despite of existing in a small amount, these cyclic butylene terephthalates can affect the quality of PBT. Thus, pure cyclic butylene terephthalates are always needed as standard reagents during the quality analysis of PBT.

To the best of our knowledge, few synthetic procedures have been reported for these cyclic butylene terephthalate oligomers. Although an old German paper systematically describes the synthesis of these cyclic oligomers, these synthetic routes involve long steps, resulting in low efficiency and yields.[3] This defect can be ascribed to laborious protections and de-protections of hydroxyl and carboxylic acid groups in their synthetic method. Another Chinese patent also needs long steps to prepare the cyclic trimer,[4] which is a tedious process. In the abovementioned synthetic methods, these large ring lactones are commonly constructed by the condensation of the corresponding carboxylic acids with alcohols. Moreover, since the abovementioned paper and patent are written in German or Chinese, they are difficult to read for most audiences in the world.

It is well known that Ru-catalyzed ring-closing metathesis (RCM) has proven to be an efficient, straightforward and reliable method to synthesize large rings.[5-9] The commercially available Grubbs' first- and second-generation catalysts are commonly used for these transformations. For those linear substrates, template-directed olefin metathesis is often employed to generate the close proximity of the olefins and facilitate the formation.[10] Thus, it was occurred to us that these cyclic butylene terephthalates might be synthesized by ring-closing metathesis. Herein, we report a novel and facile synthesis of the cyclic trimer **7** via template-directed ring-closing metathesis.

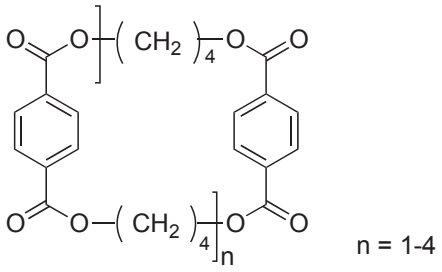
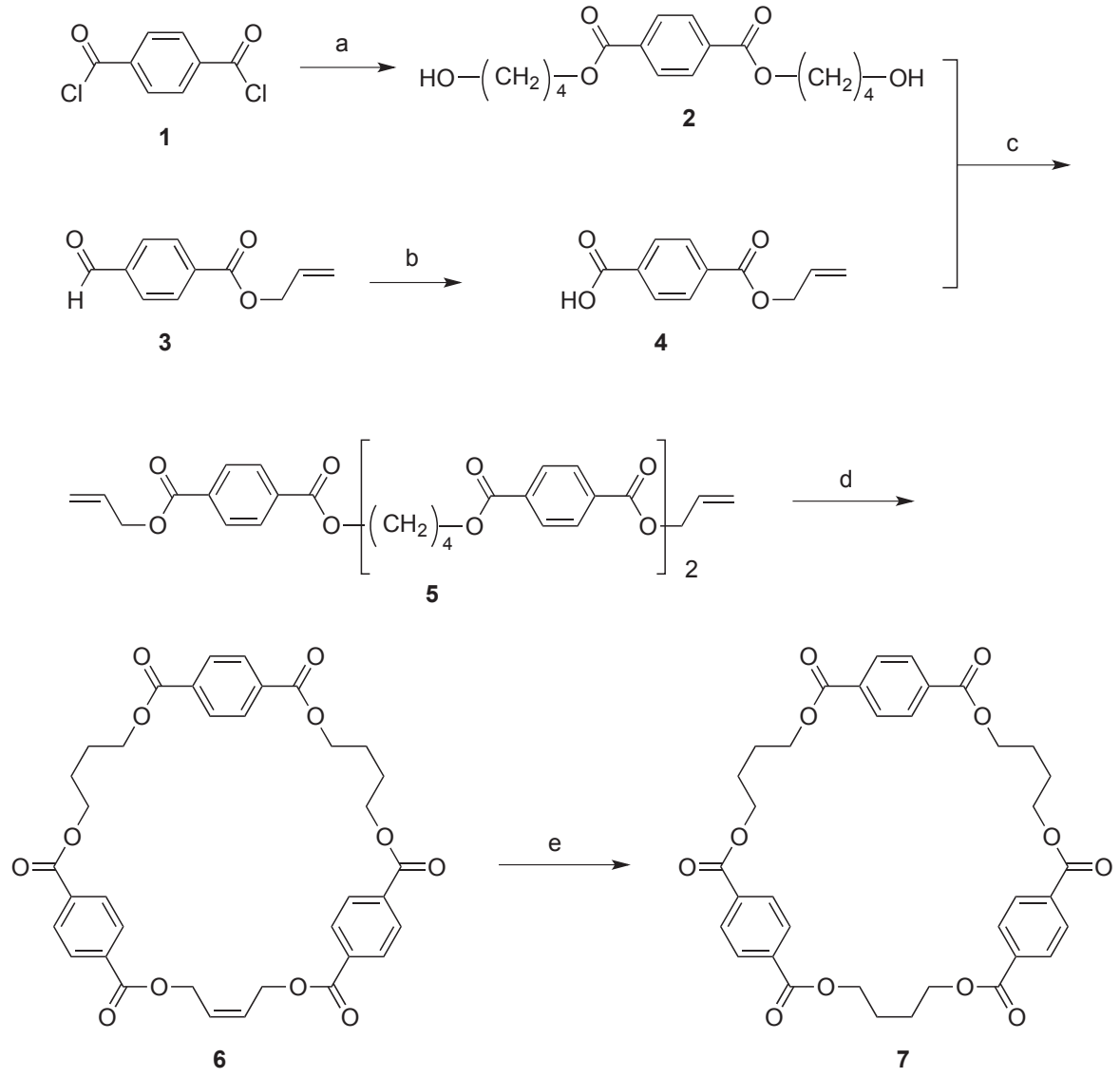


Figure 1. Cyclic butylene terephthalates oligomers

Our synthesis of the cyclic butylene terephthalate trimer (**7**) was outlined in Scheme 1. The commercially available starting material terephthaloyl chloride (**1**) was directly condensed with an excess of 1,4-butanediol.[11] Since 1,4-butanediol was highly soluble in water, the excessive 1,4-butanediol could be washed with water. After crystallization, the diol **2** was obtained in 90% yields. Although the compound **4** could be prepared by the condensation of terephthalic acid with allyl bromide according to the published methods,[12] it was found by us that this direct esterification was of low selectivity and low yields. Thus, an alternative method was devised. The acid **4** could be prepared by the oxidation of the aldehyde **3**, which was prepared by the condensation of 4-formylbenzoic acid with allyl bromide in high yields. Under the mild oxidative conditions, the aldehyde was selectively oxidized to give the acid in a yield of 94%, while the terminal double bond remained unchanged. Subsequently, the condensation of **2** and **4** proceeded smoothly to afford the linear intermediate **5** in a good yield.

With the diolefin **5** in hand, the ring-closing metathesis was attempted. As the solvents and catalysts would play important roles,[13] the olefin metathesis reactions of diolefins **5** were examined in various organic solvents and Grubbs' catalysts (Table 1). Thus, the metathesis reaction of diolefin **5** using 10 mol% of the first generation catalyst in dichloromethane was performed at reflux to furnish macrotetralide **6** in very low yields (Table 1, Entry 1). The reaction conditions were optimized by using other solvents and increasing the amounts of catalysts. A marginal improvement in the yield (18%) was observed when the reaction was performed in chloroform and the amount of catalysts was increased to 30 mol% (Table 1, Entry 4). When Grubbs' second-generation catalyst was used, the yields could be slightly

improved. However, the best yield was only 30% (Table 1, Entry 7). In all the cases, the starting material **5** was recovered in a range of 42–65% yield.



Scheme 1. Reagents and conditions: a) 1,4-butanediol, Py, 90%; b) 30% H_2O_2, KH_2PO_4, $NaClO_2$, 94%; c) EDC, DMAP, $CHCl_3$, 75%; d) Grubbs' second-generation catalyst, Ti(O*i*Pr)$_4$, $CHCl_3$, 58%; e) Pd/C, H_2, THF, 95%.

Since a few reports demonstrated that RCM reactions in the presence of Lewis acid could increase the yields,[14] we examined the feasibility of this strategy. The reaction was carried out with different metal ions such as $TiCl_4$, LiCl, Ti(O*i*Pr)$_4$, $ZnCl_2$ and $AlCl_3$. Besides, the reaction was further optimized with regard to mol% and temperature (Table 2). The optimized reaction conditions employed 30 mol% of Ti(O*i*Pr)$_4$ and 30 mol% of Grubbs' second-generation catalyst to afford **6** in 58% yield (Table 2, Entry 3), with 25% starting material recovered. The moderate yields might be ascribed to the linear structure and the long distance between the two terminal double bonds. Even under the assistance of Lewis acids, the

two double bonds were still difficult to approach each other, resulting in the low conversion. At last, the compound **6** was hydrogenated to afford the target molecular **7** in almost quantitative yields. The structure of the cyclic trimer **7** was comfirmed by ^{1}H NMR, ^{13}C NMR and HRMS (ESI) (see the supporting information). Since the structure of **7** has three symmetric axes, some NMR signals are overlapping. The assignment of NMR signals is illustrated in Figure 2.

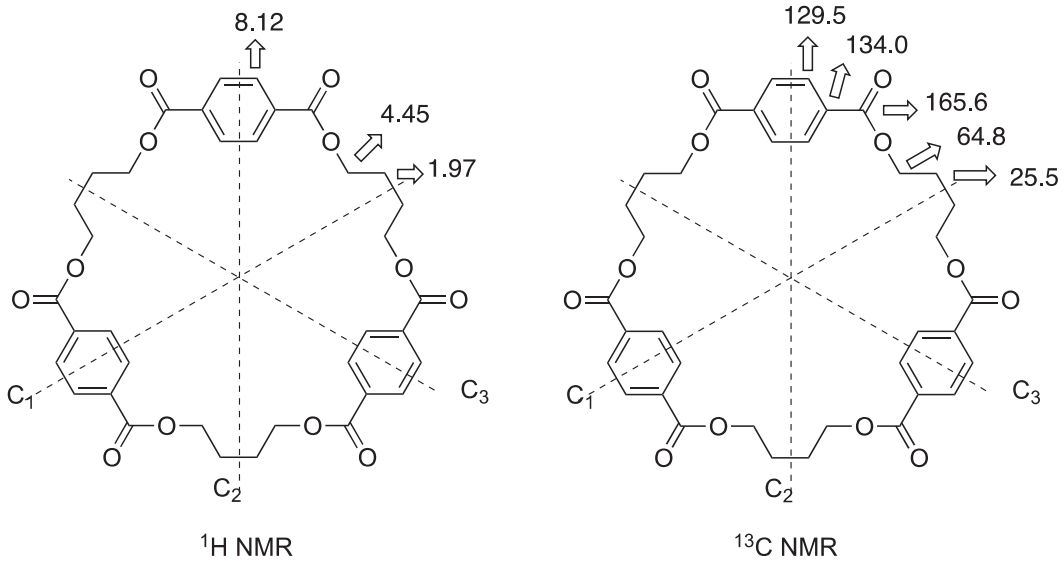


Figure 2. The assignment of NMR signals of the cyclic trimer **7**

Table 1. Effect of catalysts and solvents on the ring-closing metathesis[a]

Entry	Grubbs' Catalyst	Amount (mol%)	Solvent	Temperature (°C)	Yield (%)[b]
1	1st	10	CH_2Cl_2	40	8
2	1st	30	CH_2Cl_2	40	15
3	1st	10	$CHCl_3$	60	13
4	1st	30	$CHCl_3$	60	18
5	1st	30	toluene	90	11
6	2nd	10	$CHCl_3$	60	15
7	2nd	30	$CHCl_3$	60	30
8	2nd	30	dichloroethane	80	28
9	2nd	30	toluene	80	21

[a] Reagents and conditions: Grubbs' catalyst 1 or 2, degassed solvents under Ar for 20 h.
[b] Isolated yield.

Table 2. Effect of metal ions on the ring-closing metathesis[a]

Entry	Metal ion	Amount (mol%)	Temperature (°C)	Yield (%)[b]
1	-	-	60	30
2	$Ti(OiPr)_4$	10	20	31
3	$Ti(OiPr)_4$	30	20	58
4	$TiCl_4$	30	20	26
5	LiCl	30	20	46
6	$AlCl_3$	30	20	38
7	$ZnCl_2$	30	20	33

[a] Reagents and conditions: Grubbs' catalyst 2, degassed chloroform under Ar for 20 h.
[b] Isolated yield.

In summary, we have developed a six-step synthesis of the cyclic butylene terephthalate trimer (**7**) from easily available terephthaloyl chloride (**1**) and 4-formylbenzoic acid allyl ester (**3**). The key step is an olefin metathesis reaction using Grubbs' second-generation catalyst with titanium isopropoxide as a cocatalyst. This procedure has the advantages of short reaction steps, simple operations and fairly good overall yields.

EXPERIMENTAL

Starting materials, reagents and chemicals were purchased from commercial suppliers and used without further purification. The progress of reactions was monitored by silica gel thin layer chromatography (TLC) plates, visualized under UV. Flash column chromatography was performed using Qingdao Haiyang silica gel (200-300) with distilled solvents. ^{1}H NMR spectra were recorded on a Bruker DRX-500 (500 MHz) or DRX-400 (400 MHz) spectrometer. ^{13}C NMR spectra were obtained on a JNM-EX400 (100 MHz) spectrometer. High-resolution mass data were obtained on a MicrOTOF II spectrometer. Melting points were measured on a SGW X-4 (INESA) temperature apparatus and were uncorrected. IR spectra were obtained using KBr disks on the FTIR Bruker Tensor 27.

Bis(4-hydroxybutyl)terephthalate (2). Pyridine (30.6 g, 0.39 mol) was add dropwise into a solution of the compound **1** (19.7 g, 97 mmol) and 1,4-butanediol (69.9 g, 0.77 mol) in THF (70 mL) at 0 ºC. Then the mixture was stirred at room temperature for 4 h. The solvent was removed under reduced pressure. The residue was extracted with CH_2Cl_2 (250 mL), washed with water (200 mL), 1 M HCl (200 mL) and saturated aqueous $NaHCO_3$ solution (200 mL). The organic phase was dried over anhydrous Na_2SO_4 and concentrated to give crude product, which was triturated with a mixture of petroleum ether and EtOAc

(5 : 1, petroleum ether : EtOAc) to give the compound **2** as a white solid (27.3 g) in 90% yield. mp 68-71 ºC (lit.[3] 72 ºC); ^{1}H NMR ($CDCl_3$, 400 MHz), δ 8.10 (s, 4H), 4.40 (t, J = 6.5 Hz, 4H), 3.74 (t, J = 6.4 Hz, 4H), 1.94-1.85 (m, 4H), 1.78-1.70 (m, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz), δ 165.9, 134.1, 129.5, 65.2, 62.3, 29.2, 25.2; HRMS (ESI): *m/z* calcd for $C_{16}H_{22}NaO_6$ $(M + Na)^+$: 333.1309, found: *m/z* = 333.1292.

4-((Allyloxy)carbonyl)benzoic acid (4). To a mixture of the compound **3** (5.8 g, 31 mmol), 30% hydrogen peroxide (5.2 g, 46 mmol) and KH_2PO_4 (8.3 g, 61 mmol) in a solution of water (20 mL) and MeCN (20 mL) was added dropwise a solution of 80% $NaClO_2$ (5.5 g, 49 mmol) in water (20 mL) at 0 ºC. The mixture was stirred at room temperature for 4 h. Then $NaHSO_3$ was added to quench the reaction. The mixture was filtrated to give the solid crude product, which was oven-dried and triturated with a mixture of petroleum ether and EtOAc (3 : 1, petroleum ether : EtOAc) to give the compound **4** as a white solid (5.9 g) in 94% yield. mp 148-150 ºC; ^{1}H NMR (DMSO-d_6, 500 MHz), δ 13.31 (br, 1H), 8.05-8.09 (m, 4H), 6.02-6.09 (m, 1H), 5.40-5.44 (m, 1H), 5.28-5.30 (m, 1H), 4.83 (d, J = 5.4 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz), δ 170.2, 164.3, 133.8, 132.0, 130.9, 129.2, 128.7, 117.8, 65.1.

Bis(4-(4-allylterephthaloyloxy)butyl)terephthalate (5). To a mixture of the compound **2** (1.43 g, 4.6 mmol) and the compound **4** (2.37 g, 12 mmol) in $CHCl_3$ (20 mL), was added DMAP (0.28 g, 2.3 mmol), EDCI (3.53 g, 18 mmol). The mixture was stirred at 60 ºC for 24 h. The reaction mixture was washed with 1 M HCl (50 mL) water (50 mL), dried over anhydrous Na_2SO_4, and concentrated in vacuo to give the crude product. After purification by column chromatography on silica gel ($CHCl_3$), the compound **5** was obtained as a white solid (2.37 g) in 75% yield. mp 138-140 ºC; ^{1}H NMR ($CDCl_3$, 500 MHz), δ 8.11-8.15 (m, 12H), 6.03-6.11 (m, 2H), 5.43-5.47 (m, 2H), 5.32-5.35 (m, 2H), 4.86-4.88 (m, 4H), 4.46 (br, 8H), 2.00 (br, 8H). ^{13}C NMR ($CDCl_3$, 100 MHz), δ 165.8, 165.7, 165.4, 134.1, 134.0, 131.9, 129.6, 129.5, 118.7, 66.0, 64.9, 25.5; HRMS (ESI): *m/z* calcd for $C_{38}H_{38}NaO_{12}$ $(M + Na)^+$: 709.2255, found: *m/z* = 709.2236.

Macrotetralide (6). The compound **5** (1.5 g, 2.2 mmol) was stirred in $CHCl_3$ (10 mL). A solution of Grubbs II catalyst (0.56 g, 0.66 mmol) in $CHCl_3$ (10 mL) was added dropwise, then Ti(O*i*Pr)$_4$ (0.19 g, 0.66 mmol) was dropped in. The mixture was stirred at room temperature for 20 h. The reaction mixture was washed with water (50 mL), dried over anhydrous Na_2SO_4. Concentration in vacuo gave crude product, which was purified by column chromatography on silica gel (40 : 1, $CHCl_3$: EtOAc) to give the compound **6** as a white solid (0.83 g) in 58% yield. mp 172-174 ºC; ^{1}H NMR ($CDCl_3$, 500 MHz), δ 8.12-8.15 (m, 12H), 6.07 (br, 2H), 4.92 (br, 4H), 4.45 (br, 8H), 1.97 (br, 8H). ^{13}C NMR ($CDCl_3$, 100 MHz), δ 165.7, 165.6, 165.3, 134.1, 134.0, 133.8, 129.7, 129.6, 127.7, 64.9, 64.8, 64.5, 25.5, 25.4; HRMS (ESI): *m/z* calcd for $C_{36}H_{34}NaO_{12}$ $(M + Na)^+$: 681.1942, found: *m/z* = 681.1987.

Cyclic butylene terephthalate trimer (7). A mixture the compound **6** (1.2 g, 1.8 mmol) and 20% Pd/C (0.24 g, 2.3 mmol) in THF (20 mL) was hydrogenated at room temperature for 8 h. The catalyst was then flittered off and filtrate was evaporated to dryness to give the compound **7** as a white solid (1.14 g) in 95% yield. mp 155-157 ºC; ^{1}H NMR ($CDCl_3$, 500 MHz), δ 8.12 (s, 12H), 4.45 (br, 12H), 1.97 (br, 12H). ^{13}C NMR ($CDCl_3$, 100 MHz), δ 165.6, 134.0, 129.5, 64.9, 25.5; HRMS (ESI): *m/z* calcd for $C_{36}H_{36}NaO_{12}$ $(M + Na)^+$: 683.2099, found: *m/z* = 683.2063.

ACKNOWLEDGEMENTS

This research was financially supported by The National Key Technology R&D Program (No. 2015BAK45B00), Shanghai Science and Technology Council (No. 14142201200). We also thank the Laboratory of Organic Functional Molecules, Sino-French Institute of ECNU for support.

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