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Thermally reactive phenylethynyl-terminated bis(benzylester) and bis(amide) monomers based on semi-enzymatically produced 6-phenylethynyl picolinic acid

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Abstract

The synthesis and isolation of 6-phenylethynyl picolinic acid (PEPCA; IUPAC name: 6-(2-phenylethynyl)pyridine-2-carboxylic acid) was first demonstrated when *Acinetobacter* sp. strain F4 was used to biotransform diphenylacetylene to the ring-fission product that underwent facile ring closure to form PEPCA in the presence of ammonium ions. Here, the structure and properties of PEPCA were confirmed by comparison with those of PEPCA that was chemically synthesized. In the chemical route, commercially available 6-bromopicolinic acid was first converted to methyl 6-bromopicolinate using methyl iodide and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU). The resulting methylester was coupled with phenylacetylene by the palladium-catalyzed reaction to yield methyl 6-phenylethynyl picolinate, which was then hydrolyzed by sodium carbonate to afford PEPCA. Both enzymatically and chemically synthesized PEPCA were used to prepare its thermally reactive bis(benzylester) and bis(amide) derivatives. Thus, three phenylethynyl-terminated bis(amide) derivatives were synthesized by treating PEPCA with 1,3-phenylenediamine, 4,4′-oxydianiline or 4,4′-(hexafluoroisopropylidene)dianiline via dicyclohexylcarbodiimide (DCC)-mediated amidation. The bis(benzylester) derivative was prepared from PEPCA and α,α′-dibromo-*p*-xylene. All the intermediates and final products were characterized by FT-IR, NMR, MS and elemental analysis. The thermal properties of PEPCA and the reactive derivatives were characterized by DSC and TGA. The exothermic peaks of three bis(amide) derivatives were at least 20–40 °C lower than typically reported for the phenylethynyl compounds. Lowered reaction temperatures observed for the thermally-induced free radical polymerization of phenylethynyl groups were attributed to the strong electron-withdrawing capability of the pyridine moiety. Bis(amide) derivatives exhibited excellent thermal stability after previously cured at 300 °C for 30 min and 350 °C for 30 min.
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1. Introduction

The phenylethynyl (or phenylacetylenyl) group is one of the most important synthons in the development of heat resistant polymers primarily because of its thermal reactivity at relatively high temperatures (typically > 300 °C), that allows wider processing window, and because of its thermally stable cured or cross-linked structures. Furthermore, phenylethynyl-terminated (PET) resins can be fabricated without the evolution of volatiles, and the cured resins, retain mechanical performance under severe operating conditions [1,2]. Similar to the thermal reaction chemistry of acetylene-terminated (AT) resins [3], the cure mechanism is most probably dominated by the thermally-induced addition reaction of the phenylethynyl termini of the oligomers that drives chain-extension and network formation processes. While cured AT resins are generally quite brittle, cured PET resins are tougher than their AT counterparts, which suggests that much higher degree of linear addition must have occurred at the early stage of the PET curing process prior to the network formation. In addition to serving as terminal reactive groups or crosslinkable pendants, the phenylethynyl group has also been

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utilized as thermally reactive pendants that can undergo efficient intramolecular cyclization as an effective means to improve melt-processibility, solvent resistance and/or significantly advance the softening temperatures of the original aromatic polymers after heat treatment [4–7].

Historically, the production of plastics and polymer fibers has been the exclusive domain of the organic chemists. However, during the past decades, the explosive growth of biotechnology has extended to organic polymer chemistry as well. The reasons for this trend include the recognition of the rapidly increasing capabilities of biotechnology, the demonstrated ability of microorganisms to supplement existing chemistry synthesis technology and the desire to create new polymer materials with improved performance. These are, of course, in addition to the increasing awareness of the need for green chemistry by the chemical industry.

Substituted picolinic acids are useful as feedstocks for the synthesis of a variety of pharmaceuticals, agricultural chemicals, and dyes [8]. Several relatively simple substituted picolinic acids were synthesized biochemically [9]. Recently, we described a simple enzymatic route to a more complex molecule, 6-phenylethynyl picolinic acid (PEPCA) which might serve as a building block material for high performance polymers [10]. More recently, Shindo et al. used a recombinant *Escherichia coli* strain to convert more complex aromatic and heterocyclic. Compounds with a benzene ring to a picolinic acid with the assistance of a recombinant *E. coli* strain[11]. We previously suggested [10] that the strong electron-withdrawing properties of the pyridine moiety would increase the reactivity of PEPCA in a Diels–Alder reaction if PEPCA were to serve as a dienophile or simply undergo a thermally induced free-radical polymerization. Thus, its potential utility as a dienophile, a thermosetting function, or a crosslinker would make PEPCA an attractive alternative to a functionalized phenylacetylene as a endcapping agent or reactive pendants for high-performance network polymers for aerospace [12] and electronic packaging applications [13].

The objectives of this work are to validate the structure and certain chemical properties of PEPCA synthesized biologically and to assess its applicability as a thermally reactive functional group in new high-performance-polymer development.

2. Experimental

2.1. Materials

All chemicals were reagent-grade and purchased from Aldrich Chemical Inc. and used as received, unless otherwise specified.

2.2. Instrumentation

The melting points (mp) of all compounds were determined on a Mel-Temp melting point apparatus and are uncorrected. Proton and carbon-13 nuclear magnetic resonance (^{1}H NMR and ^{13}C NMR) spectra were measured at 300 MHz on a Bruker AVANCE 300 spectrometer. Elemental analysis and mass spectral analysis were performed by System Support Branch, Materials Directorate, Air Force Research Lab, Dayton, Ohio. Infrared (IR) spectra were recorded on a Nicolet Nexus 470 Fourier transform spectrophotometer. Differential scanning calorimetry (DSC) analysis was performed in nitrogen with a heating rate of 10 °C/min using a Perkin–Elmer model 2000 thermal analyzer equipped with differential scanning calorimetry cell. High-pressure differential scanning calorimetry (HP-DSC) analysis was performed in nitrogen with a heating rate of 10 °C/min and a pressure of 525 psi using a TA Thermal Analyzer Q1000 equipped with differential scanning calorimetry cell. Themogravimetric analysis (TGA) was conducted in helium (He) and air atmospheres at a heating rate of 10 °C/min using a TA Hi-Res TGA 2950 themogravimetric analyzer.

2.3. 6-Phenylacetylene picolinic acid (PEPCA, **3**, biological route) [10]

Growth on toluene and addition of diphenylacetylene (DPA) in hexane was as before [10]. The culture fluid was clarified by centrifugation then either an equal volume of ammonium hydroxide or 40 g/L of ammonium chloride was added. After 8 h at 70 °C, sulfuric acid was added to the ammonium hydroxide treated mixtures to adjust the pH to slightly acidic. The solution was repeatedly passed through a discovery DPA6S solid phase extraction column and then the PEPCA was eluted from the column with methanol. The methanol was removed in a rotary evaporator and the residue was extracted with ethyl acetate, which was then removed in a rotary evaporator to yield a yellow solid. The residue was recrystallized from heptane/toluene mixture (70:30) to yield white needles, mp 144–146 °C. The characterization of the PEPCA produced by the above method was reported previously [10].

2.4. Methyl 6-chloropicolinate (**5**)

Into a 100 mL three-necked, round-bottomed flask equipped with a magnetic stirrer, an addition funnel, a condenser and nitrogen inlet and outlet were added 6-bromopicolinic acid (Aldrich; 2.02 g, 10 mmol) and methanol (50 mL). Thionyl chloride (11.8 g, 100 mmol) was added dropwise at room temperature over a period of 30 min. Then the mixture was heated to reflux for 4 h. Excess methanol and thionyl chloride were removed under reduced pressure. The resulting solid was dissolved in methylene chloride. The mixture was washed with dilute ammonium hydroxide solution (10% in water). The organic layer was separated and washed twice with water. It was then dried over magnesium sulfate and filtered. Methylene chloride was removed in a rotary-evaporator. The white residue was recrystallized from heptane to afford 1.71 g (80%) of white crystals, mp 92.5–93.5 °C. Anal. Calcd for $C_7H_6ClNO_2$: C, 49.00%; H, 3.52%; N, 8.16. Found: C, 49.22%; H, 3.62%; N, 7.91%. FT-IR (KBr, cm^{-1}): 2967 (methyl), 1723 (carbonyl). Mass spectrum (*m/e*): 171, 173 (M^+).

2.5. Methyl 6-bromopicolinate (**6**)

Into a 250 mL three-necked, round-bottomed flask equipped with a magnetic stirrer and nitrogen inlet and outlet were placed 6-bromopicolinic acid (1.00 g, 4.95 mmol), methyl iodide (0.70 g, 4.95 mmol), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 0.75 g, 4.95 mmol) and a mixture of benzene (100 mL) and acetonitrile (100 mL) solvents. The mixture was stirred at room temperature for 5 h and then washed twice with water. The organic layer was separated and dried over magnesium sulfate. Following filtration, the solvent was evaporated to yield 0.95 g (89%) of a white solid mp 91–92 °C. The white solid was further recrystallized from heptane to yield 0.88 g (82% yield) white crystals, mp 93–94 °C (Lit. [14] 93–94 °C). Anal. Calcd for $C_7H_6BrNO_2$: C, 38.92%; H, 2.80%; N, 6.48. Found: C, 39.62%; H, 2.72%; N, 6.22. FT-IR (KBr, cm^{-1}): 2964 (methyl), 1721 (carbonyl). Mass spectrum (*m/e*): 215, 217 (M^+). ^1H NMR ($CDCl_3$, δ in ppm): 4.01 (s, 3H, COOC*H*$_3$), 7.28–7.76 (m, 2H, Ar–*H*), 8.09–8.12 (dd, 1H, Ar–*H*). ^{13}C NMR ($CDCl_3$, δ in ppm):53.19, 124.09, 131.86, 139.23, 142.11, 148.71, 164.43.

2.6. Methyl 6-phenylacetylene picolinate (M-PEPCA, **7**)

Methyl 6-bromopicolinate (1.1 g, 5.1 mmol), phenylacetylene (0.62 g, 3.1 mmol), triphenylphosphine (0.050 g), cuprous iodide (0.14 g), bis(triphenylphosphine) palladium dichloride (0.070 g) and triethylamine (25 mL) were added to a 100 mL three-necked round-bottomed flask equipped with a magnetic stirrer and nitrogen inlet and outlet. The mixture was heated to reflux for 4 h. The mixture was poured into water and methylene chloride was added to extract the precipitate. The organic phase was separated and evaporated to dryness under reduced pressure. The resulting solid residue was recrystallized from heptane to afford 0.50 g (83%) of white crystals, mp 67.5–68.5 °C. Anal. Calcd for $C_{15}H_{17}NO_2$: C, 75.94%; H, 4.67%, N, 5.90%. Found: C, 76.34%; H, 4.59%; N, 5.47%. FT-IR (KBr, cm^{-1}): 2950 (methyl), 2219 (ethynyl), 1724 (carbonyl). Mass spectrum (*m/e*): 237 (M^+). ^1H NMR ($CDCl_3$, δ in ppm): 4.03 (s, 3H, COOC*H*$_3$), 7.35–7.39 (m, 3H, Ar–*H*), 7.59–7.63 (m, 2H, Ar–*H*), 7.69–7.72 (d, 1H, Ar–*H*), 7.82–7.88 (t, 1H, Ar–*H*), 8.08–8.11 (d, 1H, Ar–*H*). ^{13}C NMR ($CDCl_3$, δ in ppm): 53.13, 88.03, 90.45, 121.96, 124.00, 128.41, 129.24, 130.42, 132.15, 137.28, 143.76, 148.33, 165.32. UV–vis (THF; λ_{max} in nm): 283, 300.

2.7. 6-Phenylacetylene picolinic acid (PEPCA, **3**, chemical route)

Methyl 6-phenylacetylene picolinate (1.2 g, 5.1 mmol), sodium carbonate (2.1 g, 15.3 mmol) and methanol (50 mL) were added to a 100 mL three-necked round-bottomed flask equipped with a magnetic stirrer and nitrogen inlet and outlet. The mixture was heated to reflux for 4 h and was allowed to cool to room temperature. The filtrate was neutralized with acetic acid and diluted with water. Methylene chloride was added, and organic phase was separated, followed by drying over magnesium sulfate. The mixture was filtered and the solvent was evaporated to dryness under reduced pressure. The white residue was recrystallized from heptane/toluene (70:30) to yield 0.90 g (79%) of white needles, mp 146–147 °C (Lit. [10] 144–146 °C). Anal. Calcd for $C_{14}H_9NO_2$: C, 75.33%; H, 4.06%, N, 6.27%. Found: C, 75.34%; H, 4.01%; N, 5.97%. FT-IR (KBr, cm^{-1}): 2208 (ethynyl), 1695 (carbonyl). Mass spectrum (*m/e*): 223 (M^+). ^1H NMR (DMSO-d_6, δ in ppm): 7.40–7.44 (m, 3H, Ar–*H*), 7.61–7.64 (m, 2H, Ar–*H*), 7.75–7.78 (d, 1H, Ar–*H*), 7.92–7.98 (t, 1H, Ar–*H*), 8.16–8.19 (d, 1H, Ar–*H*). ^{13}C NMR (DMSO-d_6, δ in ppm): 86.94, 91.45, 121.35, 122.68, 128.56, 129.70, 131.08, 132.15, 138.60, 142.29, 146.35, 163.83. UV–vis (THF; λ_{max} in nm): 283, 301.

2.8. α,α'-Bis(6-phenylacetylene picolinate)-p-xylene (BIS-E, **9**)

Into a 100 mL three-necked round-bottomed flask equipped with a magnetic stirrer and nitrogen inlet and outlet were placed 6-phenylacetylene picolinic acid (0.126 g, 0.563 mmol), α,α'-dibromo-*p*-xylene (0.0742 g, 0.281 mmol), DBU (0.0857 g, 0.563 mmol) and benzene (10 mL). The mixture was agitated at room temperature for 24 h, then filtered to remove the solid. The filtrate was collected and washed with water three times. The organic layer was separated and dried over magnesium sulfate. The mixture was filtered and the filtrate was collected. The solvent was removed under reduced pressure. The solid was recrystallized from heptane/toluene mixture (70:30) to afford 0.14 g (91%) of yellow crystals, mp 192–194 °C. Anal. Calcd for $C_{36}H_{24}N_2O_4$: C, 78.82%; H, 4.41%, N, 5.11%. Found: C, 78.61%; H, 4.39%; N, 4.96%. FT-IR (KBr, cm^{-1}): 2932 (–CH_2–); 2214 (ethynyl), 1734 (carbonyl). Mass spectrum (*m/e*): 548 (M^+). ^1H NMR ($CDCl_3$, δ in ppm): 5.47 (s, 4H, C*H*$_2$), 7.50–7.53 (m, 6H, Ar–*H*), 7.51 (s, 4H, Ar–*H*), 7.59–7.62 (m, 6H, Ar–*H*), 7.67–7.69 (d, 2H, Ar–*H*), 7.78–7.84 (t, 2H, Ar–*H*), 8.04–8.05 (d, 2H, Ar–*H*). ^{13}C NMR ($CDCl_3$, δ in ppm): 67.12, 88.12, 90.42, 121.93, 124.14, 128.41, 128.81, 129.04, 130.45, 132.12, 135.81, 137.16, 143.84, 148.31, 164.52. UV–vis (THF; λ_{max} in nm): 284, 300.

2.9. 1,3-Bis(6-phenylacetylene picolinamide)benzene (BIS-A1, **11a**)

Into a 100 mL three-necked round-bottomed flask equipped with a magnetic stirrer and nitrogen inlet and outlet were placed 6-phenylethynyl picolinic acid (0.304 g, 1.36 mmol), 1,3-benzenediamine (0.0742 g, 0.682 mmol), *N*,*N*′-dicyclohexylcarbodiimide (DCC, 0.280 g, 1.36 mmol), 4-dimethylaminopyridine (DMAP, 0.050 g) and methylene chloride (5 mL). The mixture was agitated at room temperature for 24 h, then filtered to remove the solid. The filtrate was collected and the solvent was removed under a reduced pressure. The solid was recrystallized from heptane/toluene mixture (60:40) to afford 0.25 g (71%) of yellow crystals, mp 205–206.5 °C. Anal. Calcd for $C_{34}H_{22}N_4O_2$: C, 78.75%; H, 4.28%, N, 10.80%. Found: C, 78.46%; H, 4.22%; N, 10.95%.

FT-IR (KBr, cm^{-1}): 3344 (N–H); 2213 (ethynyl), 1702, 1671 (carbonyl). Mass spectrum (*m/e*): 518 (M^+). ^1H NMR (DMSO-d_6, δ in ppm): 7.38–7.42 (t, 1H, Ar–*H*), 7.50–7.53 (m, 6H, Ar–*H*), 7.68–7.72 (m, 6H, Ar–*H*), 7.91–7.94 (dd, 2H, Ar–*H*), 8.11–8.19 (m, 4H, Ar–*H*), 8.50 (s, 1H, Ar–*H*), 10.53 (s, 2H, Ar–*H*). ^{13}C NMR (DMSO-d_6, δ in ppm): 88.34, 89.65, 112.83, 116.38, 121.07, 122.00, 128.89, 129.71, 130.20, 131.79, 138.37, 138.72, 141.13, 150.65, 161.97. UV–vis (THF; λ_{max} in nm): 285, 303.

2.10. 4,4′-Bis(6-phenylacetylene picolinamide)phenoxybenzene (BIS-A2, **11b**)

Compound **11b** was synthesized from 6-phenylethynyl picolinic acid (0.304 g, 1.36 mmol), 4,4′-oxydianiline (0.136 g, 0.682 mmol), DCC (0.280 g, 1.36 mmol), DMAP (0.050 g) and methylene chloride (5 mL) using the same procedure used for **11a** to afford 0.32 g (77%) of white crystals, mp 182–185 °C. Anal. Calcd for $C_{40}H_{26}N_4O_3$: C, 78.67%; H, 4.29%, N, 9.17%. Found: C, 78.32%; H, 4.27%; N, 8.96%. FT-IR (KBr, cm^{-1}): 3354 (N–H); 2218 (ethynyl), 1678 (carbonyl), 1220 (ether). Mass spectrum (*m/e*): 610 (M^+). ^1H NMR (DMSO-d_6, δ in ppm): 7.05–7.08 (d, 4H, Ar–*H*), 7.49–7.52 (m, 6H, Ar–*H*), 7.54–7.58 (d, 4H, Ar–*H*), 7.91–7.94 (m, 6H, Ar–*H*), 8.10–8.18 (m, 4H, Ar–*H*), 10.58 (s, 2H, Ar–*H*). ^{13}C NMR (DMSO-d_6, δ in ppm): 88.40, 89.66, 118.64, 121.08, 122.07, 122.23, 128.96, 129.76, 130.20, 131.80, 133.79, 138.72, 141.15, 150.83, 153.10, 161.97. UV–vis (THF; λ_{max} in nm): 285, 302.

2.11. 2,2-Bis[4-(6-phenylacetylene picolinamide)phenylene]-hexafluoropropane (BIS-A3, **11c**)

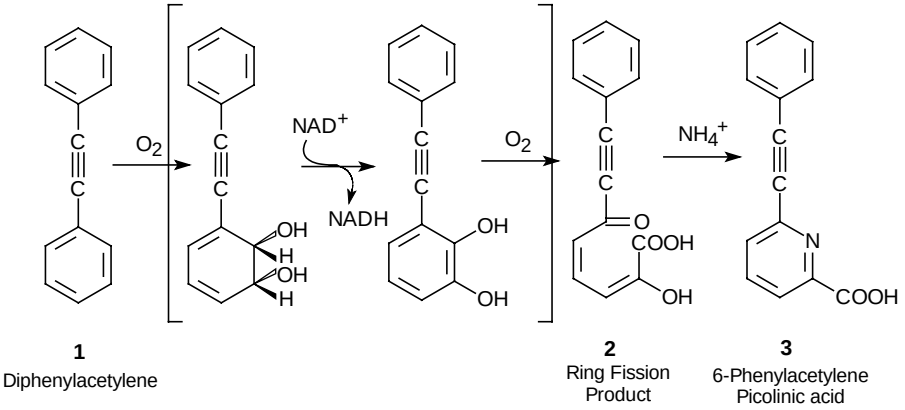
Compound **11c** was synthesized from 6-phenylethynyl picolinic acid (0.205 g, 0.920 mmol), 4,4′-(hexafluoroisopropylidene)dianiline (0.153 g, 0.460 mmol), DCC (0.200 g, 0.964 mmol), DMAP (0.050 g) and methylene chloride (5 mL) following the same procedure used for **11a** to yield 0.27 g (78%) of white crystals, mp 189–191 °C. Anal. Calcd for $C_{43}H_{26}F_6N_4O_2$: C, 69.35%; H, 3.52%, N, 7.52%. Found: C, 69.27%; H, 3.44%; N, 7.69%. FT-IR (KBr, cm^{-1}): 3344 (N–H); 2218 (ethynyl), 1688 (carbonyl), 1173 (C–F). Mass spectrum (*m/e*): 744 (M^+). ^1H NMR (DMSO-d_6, δ in ppm): 7.38–7.42 (t, 1H, Ar–*H*), 7.50–7.53 (m, 6H, Ar–*H*), 7.68–7.72 (m, 6H, Ar–*H*), 7.91–7.94 (dd, 2H, Ar–*H*), 8.11–8.19 (m, 4H, Ar–*H*), 8.50 (s, 1H, Ar–*H*), 10.53 (s, 2H, Ar–*H*). ^{13}C NMR (DMSO-d_6, δ in ppm): 66.81, 88.35, 89.76, 113.25, 118.64, 120.42, 121.06, 122.24, 128.94, 129.76, 130.03, 130.26, 130.43, 131.78, 138.76, 139.11, 141.22, 150.54, 162.51. UV–vis (THF; λ_{max} in nm): 286, 302.

3. Results and discussion

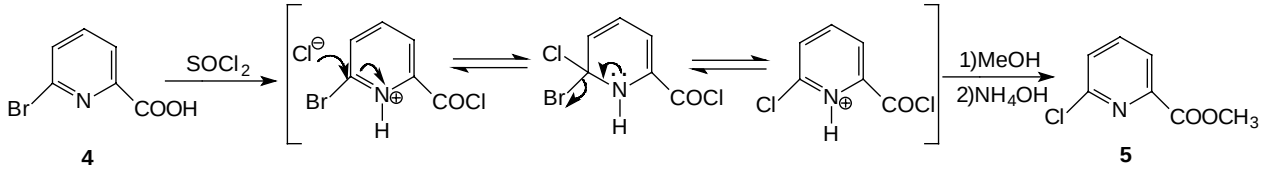
3.1. Synthesis

Initially, 6-phenylethynyl picolinic acid (PEPCA) was synthesized from diphenylacetylene (tolan) using enzymatic catalysis. Surprisingly, even though PEPCA is not a very complex organic molecule, there was no record of its isolation, characterization and identification in the literature prior to our report [10]. *Acinetobacter* sp. strain F4 catalyzed the overall conversion of diphenylacetylene (**1**) to a yellow metabolite, which was identified as a putative *meta* ring fission product (2-hydroxy-8-phenyl-6-oxoocta-2,4-dien-7-ynoic acid, designated as RFP, **2**). The RFP was easily converted to PEPCA (**3**) by treatment with ammonium hydroxide and the whole process could be accomplished in a one-pot operation. The proposed transformation pathway from DPA to PEPCA is shown in Scheme 1 [10].

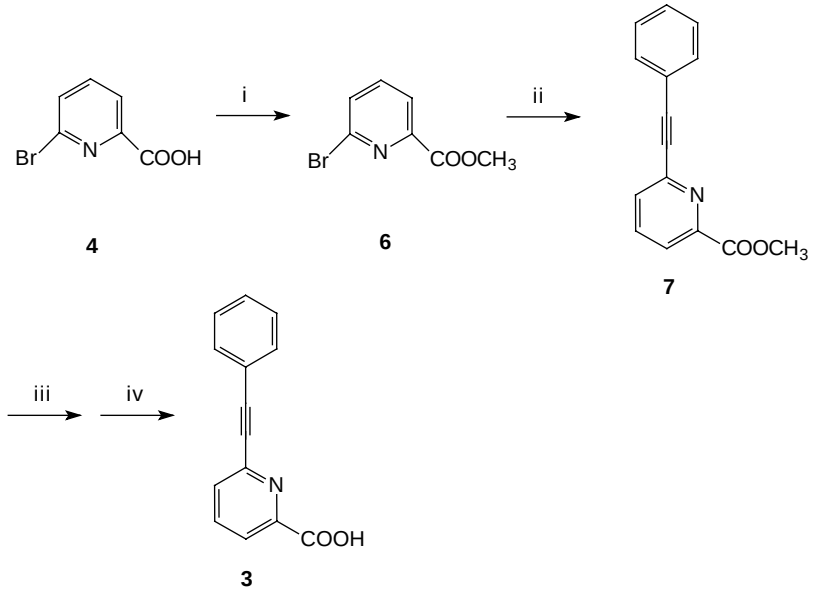
For validation purposes, we devised a scheme to prepare PEPCA from the commercially available 6-bromopicolinic acid. Our initial synthetic scheme called for the conversion of the starting acid to the corresponding methyester so as to avoid the interference of COOH group in the Pd-catalysed ethynylation with phenylacetylene. We found that when bromopicolinic acid (**4**) was treated with thionyl chloride and methanol, methyl 6-chloropicolinate [15] (**5**) was obtained in good yield instead of the desired methyl 6-bromopicolinate (**6**), indicating that the effective bromide–chloride exchange had taken place. Apparently, an aromatic nucleophilic substitution reaction played an important role in the reaction. Presumably,



Scheme 1. Proposed transformation pathway from DPA to 6-phenylacetylene picolinic acid via biological route. The toluene dioxygenase, toluene dihydrodiol dehydrogenase, and 3-methylcatechol 2,3-dioxygenase of *Acinetobacter* sp. strain F4 convert DPA to the ring fission product 2-hydroxy-6-phenylacetylene muconic semialdehyde. The ring fission product is chemically converted to 6-phenylacetylene picolinic acid by addition of ammonia [10].



Scheme 2. Proposed mechanism for the formation of methyl 6-chloropicolinate.

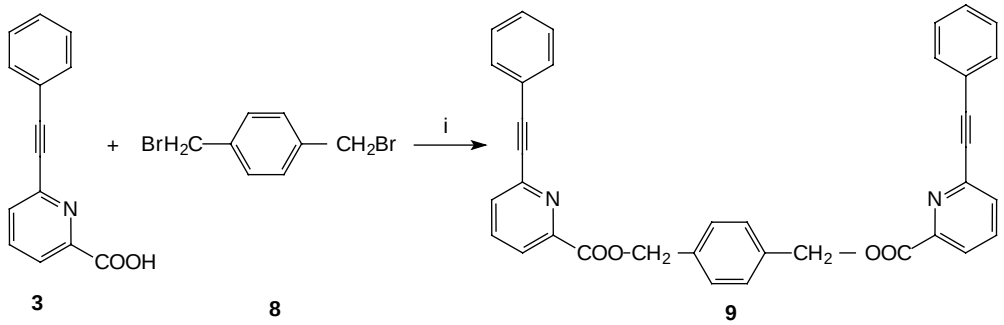


Scheme 3. Chemical synthesis of 6-phenylacetylene picolinic acid (i) methyl iodide, DBU, acetonitrile, 12 h; (ii) phenylacetylene, $PdCl_2(PPh_3)_2$, CuI, PPh_3, NEt_3, reflux, 4 h; (iii) Na_2CO_3, MeOH, Reflux, 4 h; (iv) acetic acid.

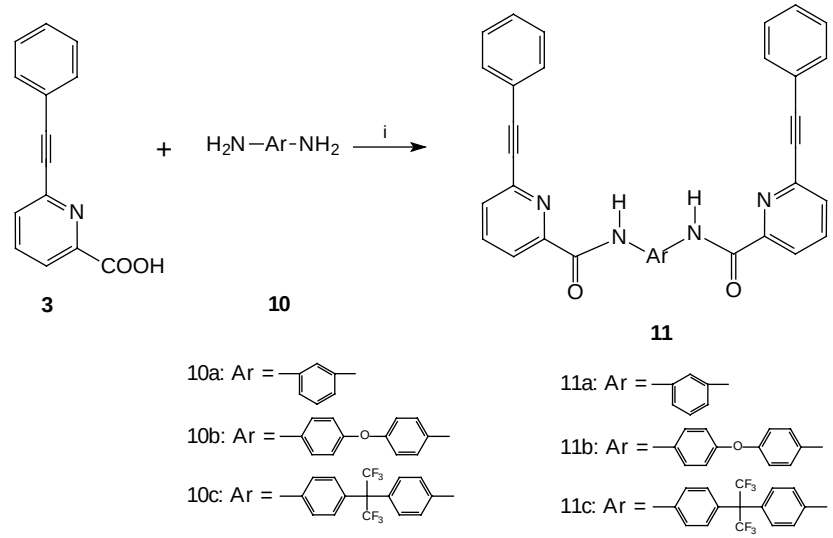
a large amount of hydrogen chloride was generated during the reaction protonated the pyridine nitrogen, which activated the α-bromide as a leaving group to such an extent that even a weak nucleophile such as chloride anion was able to displace it. A proposed mechanism is depicted in Scheme 2.

PEPCA was synthesized according to the revised reaction conditions as shown in Scheme 3. Because the starting bromopicolinic acid is sensitive to acidic conditions, the standard esterification catalysts such as sulfuric acid or tin(IV) and titanium(IV) compounds are not suitable. Thus, 6-bromopicolinic acid (**4**) was methylated to methyl 6-bromopicolinate (**6**) with methyl iodide in a mixture of benzene and acetonitrile in conjunction with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as the base to first deprotonate the acid. The reaction was monitored by TLC and it was completed in 4 h. Compound **6** was coupled with phenylacetylene with the assistance of a palladium catalyst to yield methyl 6-phenylethynyl picolinate (M-PEPCA, **7**), which was then hydrolyzed by sodium carbonate and neutralized with acetic acid to 6-phenylethynyl picolinic acid (PEPCA, **3**).

Both the enzymatically and chemically synthesized batches of PEPCA were used to prepare derivatives and yielded identical products. Thus, the bis(benzylester), i.e. α,α′-bis(6-phenylacetylene picolinate)-*p*-xylene (BIS-E, **9**), was synthesized from PEPCA and α,α′-dibromo-*p*-xylene (**8**) in benzene with the aid of DBU (Scheme 4). The other three bis(amide)s (BIS-A1-3, **11a–c**) were prepared from the treatment of PEPCA (**3**) treated with 1,3-phenylenediamine, 4,4′-oxydianiline or 4,4′-(hexafluoroisopropylidene)dianiline



Scheme 4. Synthesis of BIS-E; (i) α,α′-dibromo-*p*-xylene, DBU, benzene, room temperature, 24 h.



Scheme 5. Synthesis of BIS-A's; (i) DCC, DMAP, room temperature, 24 h.

(**10a–c**), using N,N′-dicyclohexylcarbodiimide (DCC) and 4-dimethylaminopyridine (DMAP); (Scheme 5).

3.2. Infrared spectra

PEPCA prepared by both enzymatic and chemical methods had similar melting points. The chemically synthesized PEPCA displayed a melting point of 146–147 °C while the bio-prepared PEPCA showed a melting point of 144–146 °C. Practically identical FT-IR spectra (Fig. 1(a) and (b)) and essentially the same H-and ^{13}C NMR spectra (data not shown) confirmed that the same compound was prepared by both routes. FT-IR spectra displayed broad peaks around 2500–3500 cm^{-1}, which was due to the O–H stretch of

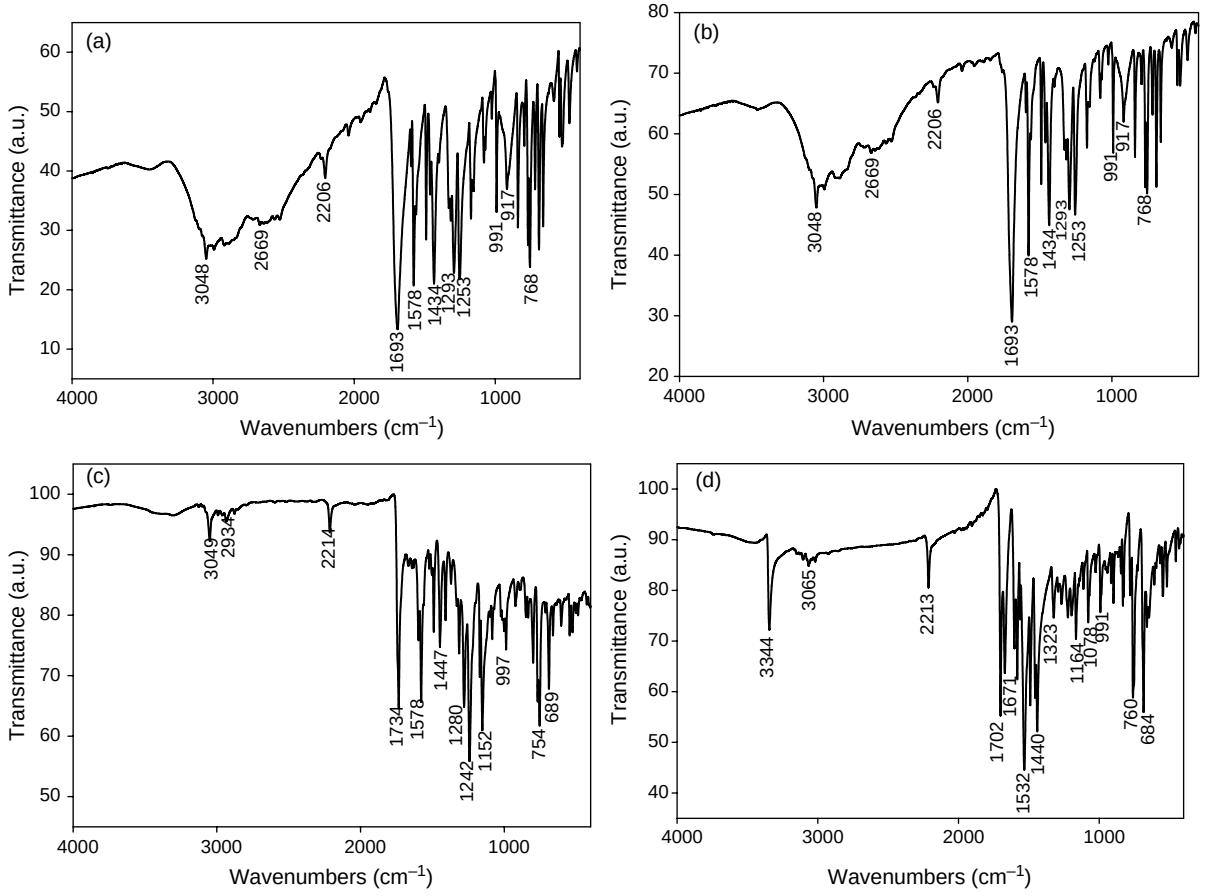


Fig. 1. FT-IR spectra of (a) PEPCA (biological synthesis); (b) PEPCA (chemical synthesis); (c) BIS-E; (d) BIS-A1.

carboxylic acid. The stretch frequency of the carbon–carbon triple bond appeared at 2213 cm^{-1}. The strong peak at 1693 cm^{-1} was attributed to carbonyl vibration of the carboxylic acid moiety.

BIS-E (**9**) exhibited a band at 2934 cm^{-1} assignable to the methylene groups. The vibration band of the ester carbonyl groups was found at 1734 cm^{-1} (Fig. 1(c)). BIS-E also exhibited a characteristic peak at 1242 cm^{-1} due to C–O vibration of the ester linkage. BIS-A1 (**11a**) was prepared from PEPCA and 1,3-phenylenediamine using DCC as a dehydrating agent. BIS-A1 displayed an N–H stretch at 3344 cm^{-1}. The carbonyl vibration band was split into two bands at 1671 and 1702 cm^{-1} due to two resonant structures of amides (Fig. 1(d)). After the carboxylic acid moiety of PEPCA had been converted into amide or ester, respectively, in each cases, the carboxylic acid broad band between 2500 and 3500 cm^{-1} disappeared and their carbonyl stretches were shifted to the positions characteristic of amides and esters.

3.3. UV–vis spectra

The UV–vis spectra of M-PEPCA, PEPCA, BIS-E and BIS-A1-3 in THF are shown in Fig. 2. Two absorption bands were observed and the maxima were very close, ranging from 283 to 286 nm for the first band and from 300 to 303 nm for the second band. The UV–vis spectra of M-PEPCA, PEPCA and BIS-E were almost identical, indicating that the 6-phenylethynyl-picolinic component is the major contributor to the UV absorption peaks. The xylene spacer of BIS-E was unable to conjugate with the 6-phenylethynyl-picolinic component, therefore, there is no difference in the spectra of PEPCA and M-PEPCA. The UV–vis spectrum of BIS-A1-3 was similar to that of PEPCA. However, the BIS-A1-3 peaks are broader and extend into longer wavelengths. The evidence shows that the spacers of BIS-As are somewhat in conjugation with the 6-phenylethynyl-picolinic unit through the amide bond, which causes the peaks to shift towards longer wavelengths.

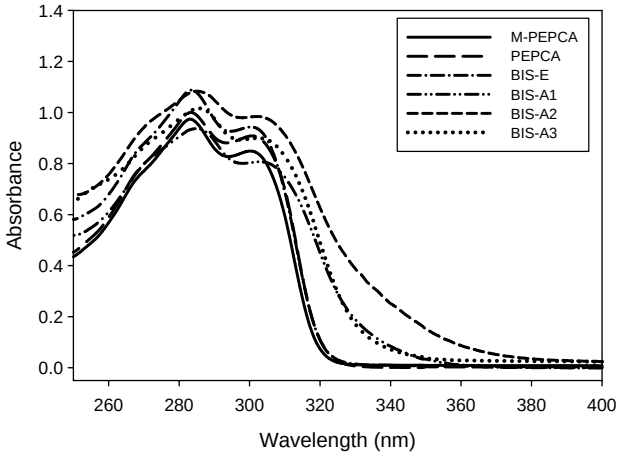


Fig. 2. UV–vis spectra of M-PEPCA, PEPCA, BIS-E and BIS-A1-3 in THF solution.

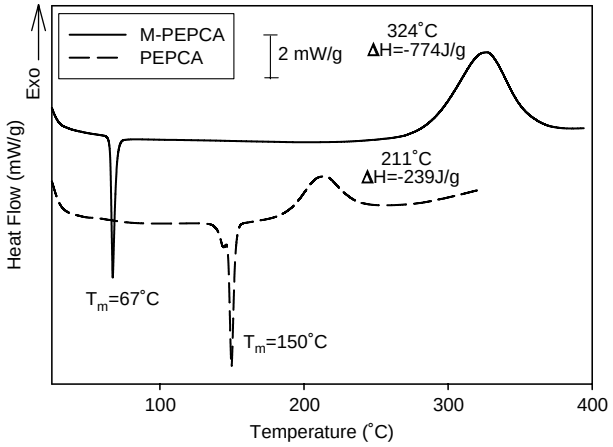


Fig. 3. HP-DSC thermograms of M-PEPCA and PEPCA.

3.4. Thermal properties

M-PEPCA, PEPCA, BIS-E and BIS-A's were investigated with differential scanning calorimetry (DSC) and themogravimetric analysis (TGA). Because M-PEPCA and PEPCA sublimed easily upon heating, their DSC runs were conducted in a pressurized cell (at 525 psi N_2; designated as HP-DSC). M-PEPCA exhibited a melting peak at 67 °C and an exotherm with onset temperature at 277 °C and peak temperature at 324 °C. Both onset and peak values for the M-PEPCA are 20–69 °C lower than those of the phenylethynyl-terminated imide model compounds reported [16]. PEPCA displayed a melting endotherm at 150 °C and an exotherm with onset temperature at 186 °C and peak value at 211 °C (Fig. 3). The peak value of the exotherm was so low that we suspected it was not from the polymerization of the phenylethynyl end groups. Typically, the cure-exotherm maxima of the phenylethynyl groups are around 350–400 °C [17]. In addition, the exothermic enthalpy of PEPCA, 329 J/g, was much lower than that of M-PEPCA, 774 J/g. Therefore, we tentatively conclude that the exotherm of PEPCA with the peak value at 211 °C did not originate from the thermally-induced addition reaction of phenylethynyl groups. While we are not certain about the chemical basis of this exotherm, we suspect that the acidic proton was likely to be

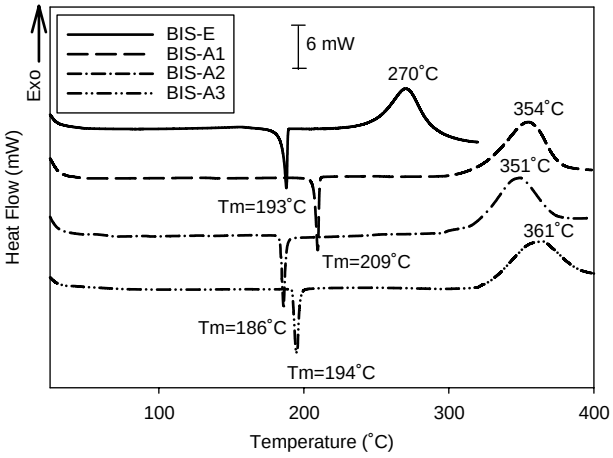


Fig. 4. DSC thermograms of BIS-E and BIS-A1-3.

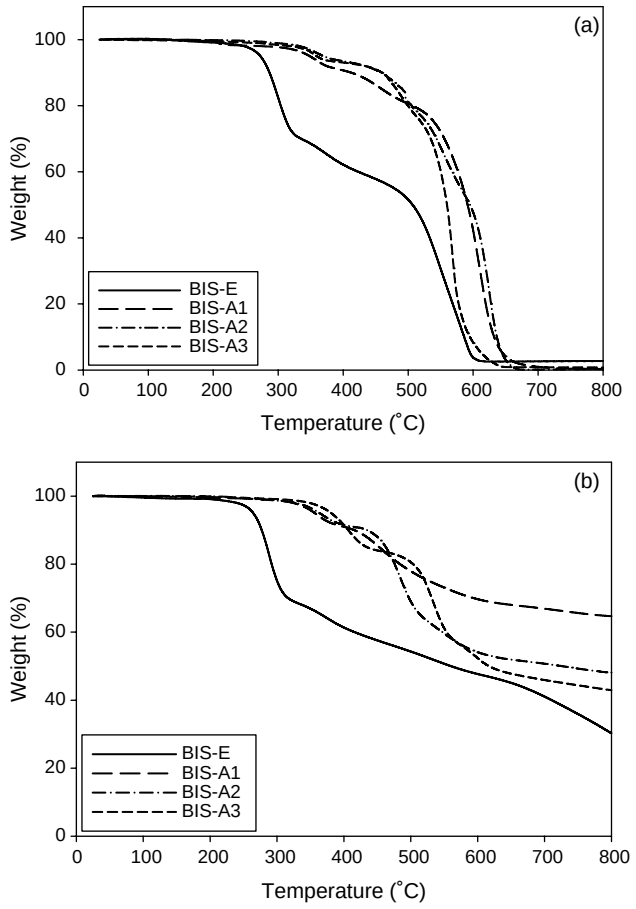


Fig. 5. TGA thermograms of BIS-E and BIS-A1-3 before being cured (a) in air; (b) in nitrogen.

involved to trigger some electrophilic addition–substitution processes. This explanation seems to be supported by the comparison with the DSC profile of the methylester analog.

The DSC scans of the bis(benzylester) and bis(amide) derivatives, BIS-E and BIS-As, were conducted under normal nitrogen atmosphere because their molecular weights are high enough to prevent them from sublimation during heating scans The exotherm of BIS-E appeared with the onset temperature of 244 °C and maximized at 270 °C (Fig. 4). However, the TGA curve showed that BIS-E started to degrade around 240 °C and suffered a 5% weight loss at 273 and 265 °C in air and nitrogen, respectively (Fig. 5). Apparently, the curing and degradation of BIS-E were concurrent in the thermal zone of 240–270 °C at the heating rate used (10 °C/min for both DSC and TGA). Therefore, to resolve the competing kinetics between the curing and degradation processes, we monitored the curing process for BIS-A1 by following the change of its T_g with time as the materials was held isothermally at 275 °C in a DSC cell. We observed the T_g at 87 °C after 30 min of heating at 275 °C. However, it increased dramatically to 162 °C within the 8 h, and then slowly to 187 °C in 16 h. After 32 h, the T_g increased more slowly, reaching 192 °C in 32 h (Fig. 6). These data indicate that BIS-E could thermally polymerize, probably with onset temperature ~240 °C. Nevertheless, it is also evident that the cured bis(benzylester) would not be thermally stable because of the two methylene units of xylene moiety.

In comparison with the bis(benzylester) analog, the bisamides exhibited much better thermal and thermo-oxidative stabilities (Fig. 5). Their 5% weight loss ranged from 358 to 370 °C in air and from 362 to 381 °C in nitrogen. Their exothermic peaks and onset temperatures ranged from 351 to

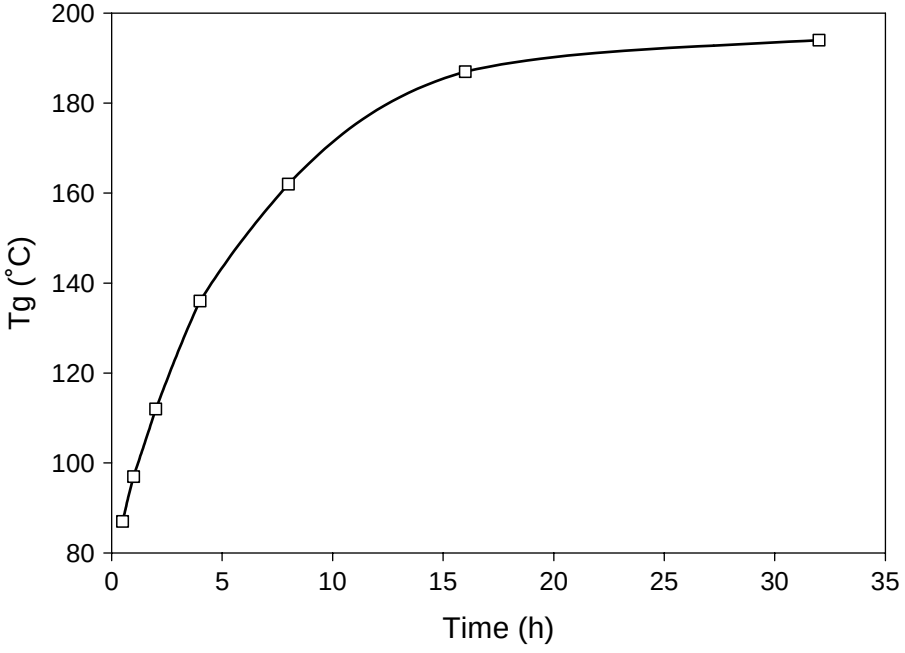


Fig. 6. T_g of BIS-A1 as a function of time at 275 °C.

Table 1
Thermal properties of M-PEPCA, PEPCA, bis(benzylester) and bis(amide)s

Compound	DSC					TGA			
	T_m		Exotherm			In air		In nitrogen	
	T_m (°C)	ΔH_{endo} (J/g)	Onset	Peak (°C)	ΔH_{exo} (J/g)	$T_{5\%}$[a] (°C)	Char[b] (%)	$T_{5\%}$[a] (°C)	Char[b] (%)
M-PEPCA	67	132	277	324	774	–	–	–	–
PEPCA	150	147	186	211	239	–	–	–	–
BIS-E	193	119	244	270	428	273	2.74	265	30.2
BIS-A1	209	134	319	354	613	358	0.33	362	64.7
BIS-A2	186	103	317	351	588	370	0.36	364	48.1
BIS-A3	194	96	324	361	547	360	0.77	381	42.9

[a] Temperature at which 5% weight loss occurred on TGA thermogram obtained with a heating rate of 10 °C/min.
[b] Char yield at 800 °C.

361 °C and from 317 to 324 °C, respectively, while their enthalpy values ranged from 547 to 613 J/g (Fig. 4 and Table 1). Considering that the DSC maxima of the thermal polymerization of the phenylethynyl end groups were generally observed at temperatures ~380–400 °C [3], the exothermic peak values of M-PEPCA and BIS-A's are at least 20–40 °C lower. Apparently, the strong electron-withdrawing capability of the pyridine moiety did lower the reaction temperatures during thermally-induced polymerization of phenylethynyl groups. Previous studies on other phenylethynyl-terminated reactive oligomers [18,19] have also shown that the electron-withdrawing substituents can reduce the cure temperature as well as accelerate the cure kinetics. It should also be noted that replacing phenyl group with a naphthyl or an anthracenyl group could effectively lowered the onset temperature by 30–80 °C [20]. Additionally, we observed that a hyperbranched poly(aromatic-ether-ketone-imide) containing a phenylethynyl group *ortho* to an aromatic keto-carbonyl group displayed a much lower exothermic peak temperature, i.e. 254 °C, than its *m*- and *p*-analogs [21]. The thermal properties of M-PEPCA, PEPCA, BIS-E and BIS-As are summarized in Table 1.

The thermal and thermo-oxidative stabilities of the BIS-A1-3 that was previously cured at 300 °C for 30 min and 350 °C for 30 min were evaluated with TGA. The cured samples displayed excellent thermal stability both in air and nitrogen. Their 5% weight loss ranged from 446 to 467 °C in air and from 466 to 482 °C in nitrogen (Fig. 7 and Table 2). Thus, the thermal decomposition temperatures were higher than those of the uncured samples by about 80 °C in air and 100 °C in nitrogen. The continuing rise of the BIS-A1's T_g (Fig. 6) indicated that the curing process of BIS-A1 was slow. It was assumed that BIS-A's were unable to be fully cured during the TGA scan, resulting in lower thermal stability than the cured samples.

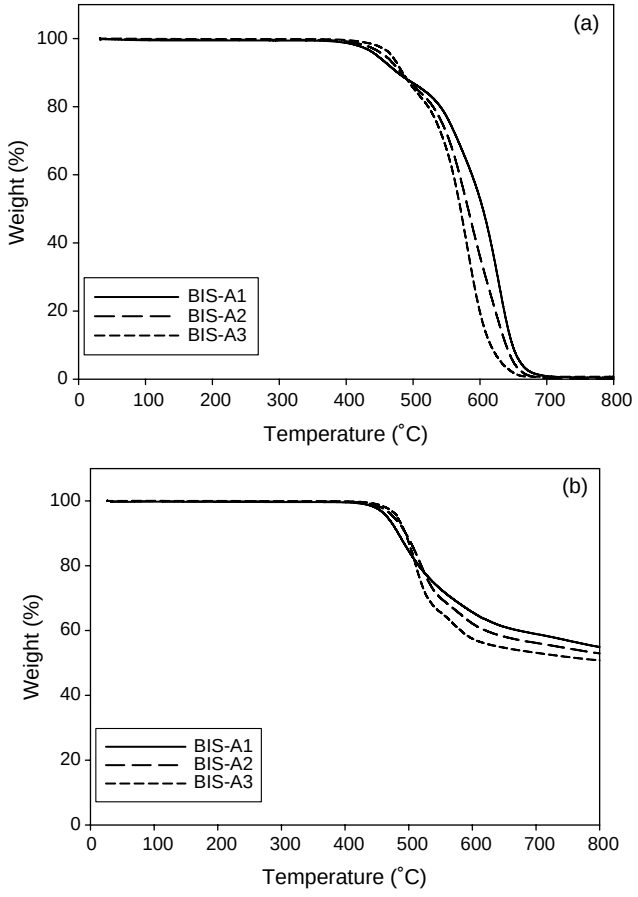


Fig. 7. TGA thermograms of BIS-A1-3 after having being cured at 300 °C for 30 min and 350 °C for 30 min (a) in air; (b) in nitrogen.

4. Conclusion

6-Phenylethynyl picolinic acid (PEPCA) was first prepared via a biological route. The chemical synthesis of PEPCA via

Table 2
Thermal properties of DSC-cured bis(amide) samples

Compound	T_g[a] (°C)	In air		In nitrogen	
		$T_{5\%}$[b] (°C)	Char[c] (%)	$T_{5\%}$[b] (°C)	Char[c] (%)
C-BIS-A1[d]	197	446	0.42	466	55.0
C-BIS-A2[d]	221	458	0.36	476	53.9
C-BIS-A3[d]	237	467	0.70	482	50.8

[a] Inflection in baseline on DSC thermogram obtained in N_2 with a heating rate of 10 °C/min.
[b] Temperature at which 5% weight loss occurred on TGA thermogram obtained with a heating rate of 10 °C/min.
[c] Char yield at 800 °C.
[d] Powdered samples held at 300 °C for 30 min, then at 350 °C for 30 min.

a simple four-step sequence starting from commercially available 6-bromopicolinic acid has resulted in the same compound, which was confirmed by ^{1}H and ^{13}C NMR, FT-IR, melting point and elemental analysis. In terms of the number of synthesis steps involved, the one-step biological route has a clear advantage over the chemical route. Both types of PEPCA were used to successfully prepare its thermosetting bis(benzylester) and bis(amide) derivatives. Thus, PEPCA has been demonstrated to possess good thermal properties for use as an endcapping agent for phenylethynyl-terminated thermosetting polymers for various aerospace applications. Moreover, our work illustrates the feasibility of incorporating the use of building blocks produced via biologically processes [22] in the design and synthesis of high performance polymers.

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