

# Strecker 3-Component Reaction for Post-Polymerization Modification of Pendant Aldehyde Functional Polymers

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**Abstract:** Aldehydes have always been useful building blocks in organic chemistry due to their high and diverse reactivity. They also offer easy access to various other functionalities and allow reactions to be performed under mild conditions. This distinguished versatility has allowed aldehyde-bearing polymers to be a good platform for post-polymerization modification reactions to prepare functional polymers. This study exploited the Strecker 3-component reaction to obtain polymers with  $\alpha$ -aminonitrile groups at the side chain for the first time. For this purpose, firstly, an aldehyde-functional polymer was synthesized from 4-formylphenyl methacrylate through free radical polymerization and then modified with amine compounds in the presence of trimethylsilyl cyanide and a catalytic amount of *p*-toluenesulfonic acid at room temperature. The spectroscopic analyses confirmed the successful synthesis of corresponding  $\alpha$ -aminonitriles.

**Keywords:** Post-polymerization modification, Strecker 3-component reaction, aldehyde-functional polymers

## Aldehit Yan Fonksiyonlu Polimerlerin Post-Polimerleşme Modifikasyonu için Strecker 3-Bileşenli Reaksiyonu

**Özet:** Aldehitler yüksek ve çeşitli reaktiviteleri nedeniyle organik kimyada her zaman yararlı yapı taşları olmuştur. Ayrıca, çeşitli diğer fonksiyonel gruplara kolay erişim sağlarlar ve reaksiyonların ılımlı koşullar altında gerçekleştirilmesine olanak tanırırlar. Bu seçkin çok yönlülük, aldehit taşıyan polimerlerin fonksiyonel polimerlerin hazırlanması amacıyla polimerizasyon sonrası modifikasyon reaksiyonları için iyi bir platform olmasına olanak sağlamıştır. Bu çalışma, ilk kez yan zincirde  $\alpha$ -aminonitril gruplarına sahip polimerler elde etmek için Strecker 3-bileşenli reaksiyonundan yararlanmıştır. Bu amaçla öncelikle 4-formilfenil metakrilattan serbest radikal polimerizasyonu yoluyla aldehit fonksiyonlu bir polimer sentezlenmiş ve daha sonra oda sıcaklığında trimetilsilil siyanür ve katalitik miktarda *p*-toluensülfonik asit varlığında amin bileşikleriyle modifiye edilmiştir. Spektroskopik analizler, ilgili  $\alpha$ -aminonitrillerin başarılı sentezini doğrulamıştır.

**Anahtar Kelimeler:** Polimerizasyon sonrası modifikasyon, Strecker 3-bileşenli reaksiyon, aldehit fonksiyonlu polimerler

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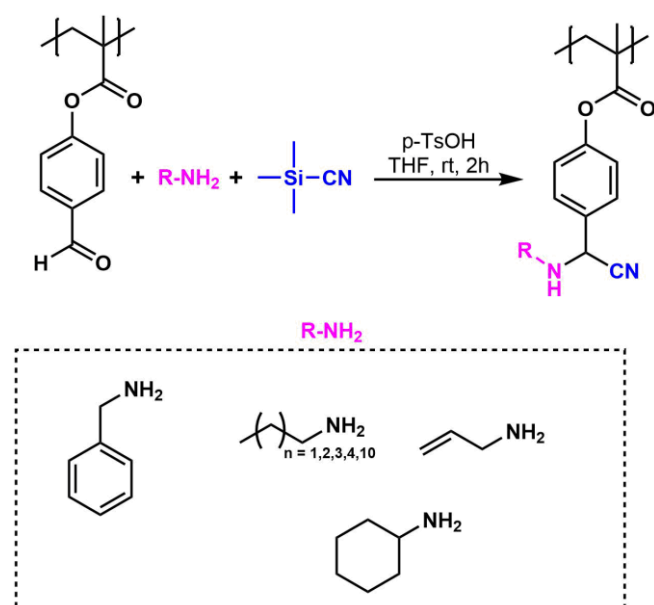
### 1. Introduction

Post-polymerization modification (PPM) is a crucial method in polymer chemistry, and it is significant for the synthesis of specifically designed functional polymers that could not be easily synthesized from corresponding functional monomers due to the possibility of losing the desired functionality under conventional polymerization conditions. "Click" reactions such as copper-catalyzed azide-alkyne cycloaddition (CuAAC) reaction, Diels-Alder reaction, thiol-yne/ene reactions, and multicomponent reactions (MCRs) are frequently used PPM tools (Geng et al., 2021; Blasco et al., 2017; Günay et al., 2013). Among them, MCRs are notably important in providing an atom-economic, fast, efficient, and less-waste-producing synthetic road, which makes them a good candidate for a "greener" chemistry approach (Zhi et al., 2019; Cioc

et al., 2014). Strecker 3-component reaction (S-3CR), introduced by Strecker (1850), is one of the oldest and most commonly studied MCRs where an aldehyde or a ketone, an amine, and a cyanide source are reacted to give  $\alpha$ -aminonitriles which are an exceptionally important class of molecules not only because they are medicinally important but also because they can easily be converted to other biologically relevant molecules such as  $\alpha$ -aminoacids,  $\alpha$ -aminoalcohols,  $\alpha$ -aminoketones/aldehydes, 1,2-diamines, and heterocyclic compounds (Kouznetsov & Galvis, 2018). In the classical S-3CR, aldehyde, amine, and highly toxic HCN or metal salts of cyanide are used in aqueous media. Over the years, many modifications have been made to S-3CR. Several less toxic cyanating agent alternatives such as trimethylsilyl cyanide

(TMSCN) (Liu et al., 2023; Shen et al., 2009), diethylphosphorocyanidate ((EtO)<sub>2</sub>P(O)CN) (Harusawa & Shioiri, 2016), tributyltin cyanide (Bu<sub>3</sub>SnCN) (Ishitani et al., 1998), diethylaluminum cyanide (Et<sub>2</sub>AlCN) (Nakamura et al., 2004), and acetone cyanohydrin (ACH, CN(OH)CMe<sub>2</sub>) (Sipos & Jablonkai, 2009) have been reported in the literature. TMSCN has several advantages, such as its good solubility in organic solvents, relatively safer nature, and better performance as a cyanating agent for imines under mild conditions (Xi et al., 2023). Also, it is known that many catalysts, from simple Bronsted acids such as *p*-toluenesulfonic acid (*p*-TsOH) (Reddy & Raghu, 2008) to Lewis acids like InCl<sub>3</sub> (Ranu et al., 2002) to complex macromolecular materials (Maleki et al., 2016), can catalyze S-3CR using TMSCN. Due to its inherent reactivity, the aldehyde group gives many valuable reactions easily under mild conditions ranging from imine/oxime/hydrazone formation to aldol reactions and MCRs and is frequently used in polymer chemistry for the synthesis of new types of polymers (Suesmatsu et al., 1983; Kreye et al., 2011; Kusumoto et al., 2013; Tunca, 2018; Negrell et al., 2018).

Pendant aldehyde functional polymers can be synthesized from the polymerization of aldehyde-functional monomers such as 4-vinylbenzaldehyde (Gao & Lam, 2008; Jackson et al., 2011) or 4-formylphenyl methacrylate (4FPM) (García-Acosta et al., 2007; Ravi Sankar et al., 2008; Kim et al., 2012) and can be used as PPM platforms. In a recent study (Akar et al., 2022), our group demonstrated that aldehyde-functional polymers can be easily modified via the reductive etherification reaction using alcohol or thiol nucleophiles in the presence of chlorodimethylsilane to obtain alkoxy- or thioether-/thioacetal-pendant polymers with high yields at room temperature. In this study, we aimed to further demonstrate the versatility of the aldehyde-functional polymers via S-3CR for the first time, using a range of amines, TMSCN, and *p*-TsOH catalyst to obtain polymers with  $\alpha$ -aminonitrile moiety at the side chain. Scheme 1 depicts the general strategy followed in this study.



Scheme 1. General representation for the PPM of the aldehyde-functional polymer via S-3CR.

## 2. Experimental Part

### 2.1 Materials

4-Hydroxybenzaldehyde (98%, Sigma-Aldrich), methacryloyl chloride (97%, Sigma-Aldrich), triethylamine ( $\geq 99.5$ , Sigma-Aldrich), azobis(cyclohexanecarbonitrile) (ABCN, 98%, Sigma-Aldrich), benzylamine (99%, Sigma-Aldrich), trimethylsilyl cyanide (TMSCN, 98%, Sigma-Aldrich), allylamine (98%, Sigma-Aldrich),

propylamine ( $\geq 99\%$ , Sigma-Aldrich), butylamine (99.5%, Sigma-Aldrich), pentylamine (99%, Fisher Scientific), hexylamine ( $\geq 99.0\%$  Merck), dodecylamine ( $\geq 99\%$ , Sigma-Aldrich), cyclohexylamine ( $\geq 99.5\%$ , Sigma-Aldrich), *p*-toluenesulfonic acid monohydrate (*p*TsOH, 97%, Alfa Aesar), InCl<sub>3</sub> (98%, Sigma-Aldrich), trifluoroacetic acid (TFA, 99%, Sigma-Aldrich), hydrochloric acid (HCl, 37%, Sigma-Aldrich), sulfuric acid (H<sub>2</sub>SO<sub>4</sub>, 98%, Sigma-Aldrich), triflic acid (TfOH,  $\geq 99\%$ , Sigma-Aldrich) were used as received. Tetrahydrofuran (THF,  $\geq 99.9\%$ , Sigma-Aldrich), 1,4-dioxane ( $\geq 99.5\%$ , Sigma-Aldrich), chloroform (CHCl<sub>3</sub>,  $\geq 99\%$ , Sigma-Aldrich), dimethyl sulfoxide (DMSO,  $\geq 99.7\%$ , Sigma-Aldrich), acetonitrile (CH<sub>3</sub>CN, 99.8%, Sigma-Aldrich), and toluene (99.8%, Sigma-Aldrich) were anhydrous and were of HPLC quality, and used without further purification. Methanol, hexane and diethyl ether were of reagent grade and used without further purification.

### 2.2. Instrumentation

<sup>1</sup>H NMR (500 MHz) and <sup>13</sup>C NMR (125 MHz) spectra were recorded using an Agilent VNMR5 500 instrument in CDCl<sub>3</sub>. Gel permeation chromatography (GPC) measurements were carried out with an Agilent Instrument (series 1100) using a refractive index detector loaded with Waters Styragel columns (HR 5E, HR 4E, HR 3, HR 2, 4.6 mm internal diameter, 300 mm length, packed with 5  $\mu$ m particles). The effective molecular weight ranges of the columns are 2000–4,000,000, 50–100,000, 500–30,000, and 500–20,000 g/mol, respectively. THF was used as an eluent at a flow rate of 0.3 mL/min at 30 °C, and 2,6-di-*tert*-butyl-4-methylphenol was used as an internal standard. The weight-average molecular weight (*M<sub>w</sub>*) and dispersity (*Đ*) of the polymers were calculated based on narrow linear polystyrene (PS) standards (Polymer Laboratories) ranging between 2300 and 3,050,000 g/mol. FT-IR spectra were recorded on an Agilent Technologies Cary 630 FT-IR instrument over the range of 4000–400 cm<sup>-1</sup>.

### 2.3. Synthetic Procedures

#### 2.3.1. Synthesis of aldehyde-functional polymer (P0)

4-Formylphenyl methacrylate (4FPM) (6.58 g, 34.6 mmol) was added to a 50 mL Schlenk flask and dissolved in 33 mL of DMSO. Next, ABCN (0.42 g, 1.73 mmol) was added to this solution, and the reaction mixture was degassed by three freeze-pump-thaw cycles, left in a vacuum, and the mixture was allowed to stir at 80 °C for 14 h. After the specified time, the reaction mixture was cooled to room temperature, precipitated into 300 mL diethyl ether, and decanted. The dissolution-precipitation (CHCl<sub>3</sub>-diethyl ether) process was repeated two times. The obtained polymer was finally dried in a vacuum oven for 24 h to give the P0 as a white powder (yield = 4.6 g, 70%). <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  9.96 (s, 1H, CH=O), 7.81-7.24 (m, 4H, ArH), 2.26 - 1.42 (m, 5H, main backbone). <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  190.68, 174.64, 154.92, 134.29, 131.25, 121.73, 45.95, 20.33, 18.35.

#### 2.3.2. General procedure for PPM of P0 via Strecker reaction

P0 (50 mg, 0.26 mmol based on repeating unit, 1 eq) was added to a 10 mL round-bottom flask and dissolved in 1 mL of THF. To this solution were added amine (0.52 mmol, 2 eq), TMSCN (0.39 mmol, 1.5 eq), and *p*-TsOH (0.026 mmol, 0.1 eq) in the given order. The mixture was then stirred at room temperature for 2 h. After that, the reaction mixture was directly precipitated into 20 mL of methanol or diethyl ether or diethyl ether:hexane (1:1, v:v) mixture, and the solvent was decanted. The dissolution-precipitation (CHCl<sub>3</sub>-methanol or CHCl<sub>3</sub>-diethyl ether or CHCl<sub>3</sub>-diethyl ether:hexane (1:1, v:v)) process was repeated two times. Finally, the obtained polymer was dried in a vacuum oven at room temperature overnight.

#### 2.3.3. Synthesis of P1

General procedure was followed. Benzylamine (57.4  $\mu$ L, 0.52 mmol), TMSCN (49.3  $\mu$ L, 0.39 mmol), and *p*-TsOH (5 mg, 0.026 mmol) were used. The mixture was precipitated into 20 mL of methanol to give P1 as a white solid (yield = 24 mg, 30%). <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  8.30 (s, 1H, CH=N), 7.44 - 7.06 (m, 9H, ArH), 4.67 (m, 1H, CHCN), 3.97 - 3.86 (d, 2H, NCH<sub>2</sub>Ph), 2.31 - 1.27 (m, 5H, main

backbone).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  174.58, 150.75, 137.98, 128.67, 127.69, 121.58, 118.53, 52.73, 51.20, 45.94.

### 2.3.4. Synthesis of P2

General procedure was followed. Propylamine (43.2  $\mu\text{L}$ , 0.52 mmol), TMSCN (49.3  $\mu\text{L}$ , 0.39 mmol), and *p*-TsOH (5 mg, 0.026 mmol) were used. The mixture was precipitated into 20 mL of methanol to give P2 as a white solid (yield = 38 mg, 57%).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  9.94 (s, 1H,  $\text{CH}=\text{O}$ ), 8.25 (s, 1H,  $\text{CH}=\text{N}$ ), 7.46 (s, 2H, *ArH*), 7.09 (s, 2H, *ArH*), 4.80 (m, 1H,  $\text{CHCN}$ ), 3.57 (s, 2H,  $\text{CH}=\text{NCH}_2$ ), 2.78-2.68 (m, 2H,  $\text{CH}(\text{CN})\text{NHCH}_2$ ), 1.53-1.41 (m, 7H  $\text{NCH}_2\text{CH}_2\text{CH}_3$  and main backbone), 0.95-0.84 (m, 3H,  $\text{NCH}_2\text{CH}_2\text{CH}_3$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  175.29, 159.59, 150.76, 132.90, 129.02, 125.81, 121.71, 118.87, 63.39, 53.90, 49.28, 45.74, 22.79, 11.66.

### 2.3.5. Synthesis of P3

General procedure was followed. Butylamine (52  $\mu\text{L}$ , 0.52 mmol), TMSCN (49.3  $\mu\text{L}$ , 0.39 mmol), and *p*-TsOH (5 mg, 0.026 mmol) were used. The mixture was precipitated into 20 mL of diethyl ether/hexane (1:1, v:v) to give P3 as a white solid (yield = 30 mg, 42%).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  8.25 (s, 1H,  $\text{CH}=\text{N}$ ), 7.46 (m, 2H, *ArH*), 7.08 (m, 2H, *ArH*), 4.79 (m, 1H,  $\text{CHCN}$ ), 2.82 - 2.71 (d, 2H,  $\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ), 2.36 (s, 2H,  $\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ), 1.56 - 1.39 (m, 8H,  $\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$  and main backbone), 0.92 (m, 3H,  $\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  175.12, 159.46, 150.71, 129.00, 128.53, 125.85, 121.52, 118.90, 61.39, 53.92, 47.19, 39.73, 31.68, 29.86, 20.28, 13.92.

### 2.3.6. Synthesis of P4

The general procedure was followed. Pentylamine (61  $\mu\text{L}$ , 0.52 mmol), TMSCN (49.3  $\mu\text{L}$ , 0.39 mmol), and *p*-TsOH (5 mg, 0.026 mmol) were used. The mixture was precipitated into 20 mL of ether to give P4 as a white solid (yield = 20 mg, 27%).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  8.25 (s, 1H,  $\text{CH}=\text{N}$ ), 7.46 (s, 2H, *ArH*), 7.08 (s, 2H, *ArH*), 4.79 (m, 1H,  $\text{CHCN}$ ), 3.60 (m, 2H,  $\text{CH}=\text{NCH}_2$ ), 2.83-2.71 (m, 2H,  $\text{CH}(\text{CN})\text{NCH}_2$ ), 1.52-1.33 (m, 11H,  $\text{NCH}_2(\text{CH}_2)_3\text{CH}_3$  and main backbone), 0.89 (m, 3H,  $\text{NCH}_2(\text{CH}_2)_3\text{CH}_3$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  150.62, 128.97, 128.59, 121.54, 118.96, 61.76, 53.92, 47.61, 29.29, 22.49, 14.03.

### 2.3.7. Synthesis of P5

The general procedure was followed. Hexylamine (69.5  $\mu\text{L}$ , 0.52 mmol), TMSCN (49.3  $\mu\text{L}$ , 0.39 mmol), and *p*-TsOH (5 mg, 0.026 mmol) were used. The mixture was precipitated into 20 mL of diethyl ether/hexane (1:1, v:v) to give P5 as a white solid (yield = 36 mg, 46%).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  8.25 (s, 1H,  $\text{CH}=\text{N}$ ), 7.46 (s, 2H, *ArH*), 7.08 (s, 2H, *ArH*), 4.79 (m, 1H,  $\text{CHCN}$ ), 3.59 (m, 2H,  $\text{CH}=\text{NCH}_2$ ), 2.83 - 2.71 (d, 2H,  $\text{CH}(\text{CN})\text{NHCH}_2$ ), 1.52 - 1.29 (m, 13H,  $\text{NCH}_2(\text{CH}_2)_4\text{CH}_3$  and main backbone), 0.88 (m, 3H,  $\text{NCH}_2(\text{CH}_2)_4\text{CH}_3$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  175.25, 159.72, 150.81, 133.12, 128.38, 125.85, 121.55, 118.86, 61.78, 53.93, 47.68, 31.63, 29.59, 26.82, 22.58, 14.05.

### 2.3.8. Synthesis of P6

The general procedure was followed. Dodecylamine (121  $\mu\text{L}$ , 0.52 mmol), TMSCN (49.3  $\mu\text{L}$ , 0.39 mmol), and *p*-TsOH (5 mg, 0.026 mmol) were used. The mixture was precipitated into 20 mL of methanol to give P6 as a white solid (yield = 28 mg, 29%).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  9.98 (s, 1H,  $\text{HC}=\text{O}$ ), 8.24 (s, 1H,  $\text{CH}=\text{N}$ ), 7.45 (m, 2H, *ArH*), 7.07 (m, 2H, *ArH*), 4.78 (m, 1H,  $\text{CHCN}$ ), 3.60 (s, 2H,  $\text{CH}=\text{NCH}_2$ ), 2.84 - 2.71 (m, 2H,  $\text{CH}(\text{CN})\text{NHCH}_2$ ), 1.69 - 1.26 (m, 25H,  $\text{NCH}_2(\text{CH}_2)_{10}\text{CH}_3$  and main backbone), 0.88 (s, 3H,  $\text{NCH}_2(\text{CH}_2)_{10}\text{CH}_3$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  175.49, 159.79, 150.77, 133.04, 128.55, 121.69, 61.82, 53.96, 47.80, 31.92, 29.66, 27.22, 22.69, 14.14.

### 2.3.9. Synthesis of P7

The general procedure was followed. Allylamine (39.4  $\mu\text{L}$ , 0.52 mmol), TMSCN (49.3  $\mu\text{L}$ , 0.39 mmol), and *p*-TsOH (5 mg, 0.026 mmol) were used. The mixture was precipitated into 20 mL of diethyl ether to give P7 as a whitish-yellow solid (yield = 33 mg, 50%).  $^1\text{H}$

NMR ( $\text{CDCl}_3$ )  $\delta$  9.97 (s, 1H,  $\text{HC}=\text{O}$ ), 8.28 (s, 1H,  $\text{CH}=\text{N}$ ), 7.46 (s, 2H, *ArH*), 7.07 (s, 2H, *ArH*), 5.86 (s, 1H,  $\text{NCH}_2\text{CH}=\text{CH}_2$ ), 5.33-5.19 (m, 2H,  $\text{NCH}_2\text{CH}=\text{CH}_2$ ), 4.80 (m, 1H,  $\text{CHCN}$ ), 4.25 (m, 2H,  $\text{CH}=\text{NCH}_2\text{CH}=\text{CH}_2$ ), 3.39 (m, 2H,  $\text{CH}(\text{CN})\text{NHCH}_2\text{CH}=\text{CH}_2$ ), 1.52 - 1.41 (m, 5H, main backbone).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  175.42, 160.68, 150.76, 140.81, 134.69, 129.02, 125.91, 120.92, 117.98, 52.81, 49.91, 46.04, 41.99, 30.92, 21.33.

### 2.3.10. Synthesis of P8

The general procedure was followed. Cyclohexylamine (60  $\mu\text{L}$ , 0.52 mmol), TMSCN (49.3  $\mu\text{L}$ , 0.39 mmol), and *p*-TsOH (5 mg, 0.026 mmol) were used. The mixture was precipitated into 20 mL of methanol to give P8 as a white solid (yield = 19 mg, 26%).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  9.98 (s, 1H,  $\text{HC}=\text{O}$ ), 8.27 (s, 1H,  $\text{CH}=\text{N}$ ), 7.65 (m, 2H, *ArH*), 7.06 (m, 2H, *ArH*), 4.83 (s, 1H,  $\text{CHCN}$ ), 3.20 (s, 1H,  $\text{CH}=\text{NCH}$ ), 2.84 (s, 1H,  $\text{CH}(\text{CN})\text{NHCH}$ ), 1.98 - 1.26 (m, 15H,  $\text{CH}_2$  of cyclohexyl ring and main backbone).  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  175.18, 165.38, 152.02, 134.58, 129.31, 129.25, 121.16, 119.23, 69.90, 54.88, 51.01, 45.88, 34.36, 33.79, 31.92, 24.78.

## 3. Results and Discussion

The aldehyde-functionalized polymer was synthesized from 4-formylphenyl methacrylate (4FPM) monomer according to previously published study by our group (Akar et al., 2022). Briefly, 4-hydroxybenzaldehyde was reacted with methacryloyl chloride to obtain 4FPM, and the resulting monomer (i.e., 4FPM) was then polymerized via free radical polymerization (FRP) using the initiator 1,1-azobis(cyclohexanecarbonitrile) (ABCN) in DMSO at 80  $^\circ\text{C}$  for 14 h. The obtained polymer (P0) showed a high molecular weight ( $M_w = 100$  kDa) with a broad polydispersity ( $\text{PDI} = 2.33$ ), which can be expected due to the nature of the FRP. As shown in Fig. 2A, aldehyde proton ( $\text{HC}=\text{O}$ ) and aromatic protons of P0 were detected at 9.96 and 7.81 - 7.24 ppm, respectively. Also, in the FT-IR spectrum of P0 given in Fig. 2C, the aldehyde  $\text{C}=\text{O}$  stretching peak was observed at 1698  $\text{cm}^{-1}$ , while the ester carbonyl peak was detected at 1750  $\text{cm}^{-1}$ . These results confirmed that P0 was synthesized successfully. After the preparation of the aldehyde-functional polymer, a series of experiments were conducted to determine the optimum conditions for PPM of P0 via S-3CR. To this end, P0 was reacted with benzylamine (BA), trimethylsilyl cyanide (TMSCN), and *p*-toluenesulfonic acid (*p*-TsOH) in THF at room temperature for 2 h at different BA/TMSCN/*p*-TsOH mole ratios (Fig. 1 and Table 1).

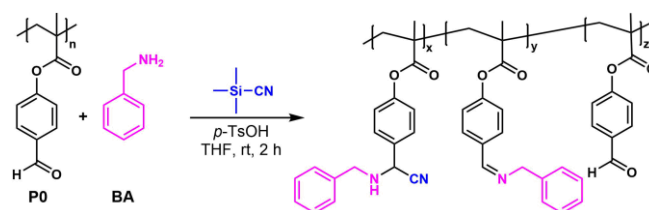


Fig. 1. Model reaction between P0 and BA and the resulting product distribution.

The conversion of aldehyde to the corresponding  $\alpha$ -aminonitrile ( $\alpha$ -AN) and imine products was calculated by comparing the integral ratios of benzylic methylene protons ( $\text{NCH}_2\text{Ph}$ ) with the methine proton next to the cyano group ( $\text{CHCN}$ ) and to the imine proton ( $\text{CH}=\text{N}$ ) using  $^1\text{H}$  NMR.



**Table 1** Optimization studies of the reactants<sup>a</sup>

| Run | BA (eq) <sup>b</sup> | TMSCN (eq) <sup>b</sup> | <i>p</i> -TsOH (eq) <sup>b</sup> | <i>x/y/z</i> <sup>c</sup> |
|-----|----------------------|-------------------------|----------------------------------|---------------------------|
| 1   | 1.1                  | 1.1                     | 0.1                              | 0.70/0.20/0.10            |
| 2   | 1.5                  | 1.1                     | 0.1                              | 0.85/0.10/0.05            |
| 3   | 2                    | 1.1                     | 0.1                              | 0.90/0.10/0               |
| 4   | 2                    | 1.5                     | 0.1                              | 0.97/0.03/0               |
| 5   | 2                    | 2                       | 0.1                              | 0.96/0.04/0               |
| 6   | 2                    | 1.5                     | 0.2                              | 0.97/0.03/0               |
| 7   | 2                    | 1.5                     | 0.05                             | 0.90/0.10/0               |

<sup>a</sup>The reactions were carried out in 1 mL of THF at room temperature for 2 h. <sup>b</sup>Per repeating unit of P0. <sup>c</sup>Determined by <sup>1</sup>H NMR.

First, using equal moles of BA and TMSCN (1.1 eq each) per aldehyde unit of P0 in the presence of 0.1 eq of *p*-TsOH as catalyst resulted in the formation of α-AN with 70% conversion and imine with 20% conversion while leaving 10% unreacted aldehyde (Table 1, run 1). Increment of BA to 1.5 eq while keeping TMSCN and *p*-TsOH constant led to the formation of 85% α-AN and 10% imine, and 5% aldehyde remained unreacted (Table 1, run 2). Further increase of BA to 2 eq resulted in full consumption of the aldehyde; 90% of α-AN and 10% of imine were obtained at the end of the reaction (Table 1, run 3). Moreover, increasing TMSCN to 1.5 eq while keeping BA at 2 eq afforded near quantitative conversion (97%) of aldehyde to α-AN with only 3% imine product (Table 1, run 4). Similar α-AN conversion (96%) was obtained when increasing TMSCN to 2 eq (Table 1, run 5). These results indicate that the optimum equivalents of BA and TMSCN per aldehyde are 2/1.5 (BA/TMSCN). We also examined the effect of the acid catalyst equivalent on conversion. Increasing the acid equivalent to 0.2 eq using the optimum equivalents of the reactants given above led to the same α-AN conversion (97%) obtained in the 0.1 eq case (Table 1, run 6); however, lowering *p*-TsOH to 0.05 eq caused a slight decrease in the conversion (90%) (Table 1, run 7). Thus, the ideal mole ratio of BA/TMSCN/*p*-TsOH per aldehyde was found to be 2/1.5/0.1.

The effect of different acid catalysts on S-3CR was next examined using the optimum mole ratios of the reactants. It was found that *p*-TsOH still gave the best results (Table 2, run 1) with 97% α-AN formation, followed by trifluoroacetic acid (TFA), which led to the formation of α-AN with 62% conversion and imine product with 26% conversion, the remaining 12% was unreacted aldehyde (Table 2, run 2). Utilizing other acid catalysts, namely triflic acid (TfOH), InCl<sub>3</sub>, HCl, and H<sub>2</sub>SO<sub>4</sub>, resulted in insoluble polymers that could not be characterized (Table 2, runs 3-6).

**Table 2** Effect of different catalysts on Strecker reaction<sup>a</sup>

| Run | Catalyst                       | Efficiency (%) <sup>b</sup> |
|-----|--------------------------------|-----------------------------|
| 1   | <i>p</i> -TsOH                 | 97/3/0                      |
| 2   | TFA                            | 62/26/12                    |
| 3   | TfOH                           | - <sup>c</sup>              |
| 4   | InCl <sub>3</sub>              | - <sup>c</sup>              |
| 5   | HCl                            | - <sup>c</sup>              |
| 6   | H <sub>2</sub> SO <sub>4</sub> | - <sup>c</sup>              |

<sup>a</sup>Reactions were carried out using BA/TMSCN/catalyst at a mole ratio of 2/1.5/0.1 per repeating unit of P0 in 1 mL of THF at room temperature for 2 h. <sup>b</sup>Mole ratios of α-aminonitrile/imine/aldehyde segments in the resulting polymer were determined by <sup>1</sup>H NMR. <sup>c</sup>Insoluble polymer was obtained.

Finally, the effect of different solvents on the reaction was examined. As can be seen in Table 3, THF was still the best

solvent with 97% α-AN formation (Table 3, run 1), followed by another cyclic ether-type solvent 1,4-dioxane which showed slightly lower efficiency with 95% α-AN and 5% imine product (Table 3, run 2). Using a relatively less polar halogenated solvent CHCl<sub>3</sub> resulted in only 40% α-AN formation along with 28% imine product and 32% unreacted aldehyde (Table 3, run 3). Other solvents, namely CH<sub>3</sub>CN and toluene, gave insoluble polymers which could not be characterized (Table 3, runs 4-5).

**Table 3** Effect of different solvents on Strecker reaction<sup>a</sup>

| Run | Solvent            | Efficiency (%) <sup>b</sup> |
|-----|--------------------|-----------------------------|
| 1   | THF                | 97/3/0                      |
| 2   | 1,4-dioxane        | 95/5/0                      |
| 3   | CHCl <sub>3</sub>  | 40/28/32                    |
| 4   | CH <sub>3</sub> CN | - <sup>c</sup>              |
| 5   | Toluene            | - <sup>c</sup>              |

<sup>a</sup>Reactions were carried out using BA/TMSCN/*p*-TsOH at a mole ratio of 2/1.5/0.1 per repeating unit of P0 in 1 mL of solvent at room temperature for 2 h. <sup>b</sup>Mole ratios of α-aminonitrile/imine/aldehyde segments in the resulting polymer were determined by <sup>1</sup>H NMR. <sup>c</sup>Insoluble polymer was obtained.

Given all these results, it was found that the optimum mole ratio of reactants for PPM reactions *via* S-3CR was found to be 2/1.5/0.1 (BA/TMSCN/*p*-TsOH) per repeating unit of P0 in THF at room temperature for 2 h.

The <sup>1</sup>H NMR spectrum of the modified polymer (P1) (Table 1, run 4) is given in Fig. 2B. Complete disappearance of HC=O peak at 9.96 ppm confirms the quantitative conversion of aldehyde to corresponding α-AN and imine products. Benzylic methylene protons were detected at 3.86 - 3.97 ppm. Comparison of CHCN and CH=N protons at 4.67 and 8.30 ppm, respectively, gave a ratio of 0.97/0.03, which indicated the formation of α-AN with 97% efficiency with only 3% imine product. Notably, aromatic protons of the parent polymer shifted upfield after the reaction and were observed at 7.06 - 7.44 ppm overlapped with aromatic protons of the formed α-AN and imine products. The structure of P1 was further confirmed by the FT-IR spectrum given in Fig. 2C. Aldehyde C=O stretching peak at 1698 cm<sup>-1</sup> disappeared while a broad peak at 3300 cm<sup>-1</sup> assignable to the formed NH group was observed. The molecular weight (*M<sub>w</sub>*) of P1 was also measured by GPC and found to be higher than P0 as expected, precisely 200 kDa, and its *Đ* was 2.64.

The proposed strategy was also extended to a range of amine compounds, from short and long-chain aliphatic amines to allylamine and cyclohexylamine. The results of the amine scope are collected in Table 4.

**Table 4** Amine scope of the reaction<sup>a</sup>

| Polymer | Amine           | <i>M<sub>w</sub></i> (kDa) <sup>b</sup> / <i>Đ</i> <sup>b</sup> | Efficiency (%) <sup>c</sup> |
|---------|-----------------|-----------------------------------------------------------------|-----------------------------|
| P0      |                 | 100.0/2.33                                                      | -                           |
| P1      | benzylamine     | 200.0/2.64                                                      | 97/3/0                      |
| P2      | propylamine     | 150.8/4.37                                                      | 90/8/2                      |
| P3      | butylamine      | 170.7/3.03                                                      | 90/10/0                     |
| P4      | pentylamine     | 220.4/2.19                                                      | 90/10/0                     |
| P5      | hexylamine      | 130.9/2.24                                                      | 90/10/0                     |
| P6      | dodecylamine    | 190.8/3.19                                                      | 75/18/7                     |
| P7      | allylamine      | 180.9/4.23                                                      | 85/6/9                      |
| P8      | cyclohexylamine | 160.3/3.36                                                      | 27/66/7                     |

<sup>a</sup>Reactions were carried out using amine/TMSCN/*p*-TsOH at a mole

ratio of 2/1.5/0.1 per repeating unit of P0 in 1 mL of THF at room temperature for 2 h. <sup>b</sup>Determined by GPC calibrated based on linear PS standards in THF. <sup>c</sup>Mole ratios of  $\alpha$ -aminonitrile/imine/aldehyde segments in the resulting polymer were determined by <sup>1</sup>H NMR.

For all amine compounds, the  $M_w$  of the modified polymer was higher than P0, and  $\alpha$ -AN efficiency was between 27% and 97%. When aliphatic amines with shorter alkyl chains were used, the conversion of aldehyde to  $\alpha$ -AN was 90% (Table 4, entries 2-5), while dodecylamine gave 75% efficiency for  $\alpha$ -AN formation (Table 4, entry 6). Allylamine

also showed good efficiency with 85%  $\alpha$ -AN and 6% imine products (Table 4, entry 7). Lastly, in the case of cyclohexylamine, the predominant product was imine with 66% efficiency, while only 27%  $\alpha$ -AN was obtained, and 7% of aldehyde remained unreacted (Table 4, entry 8), which can be attributed to the steric hindrance of the bulky cyclohexyl group. <sup>1</sup>H NMR spectra of selected modified polymers are given in Fig. 3, showing distinct signals related to their chemical structure and thus confirming the attachment of these groups to P0.

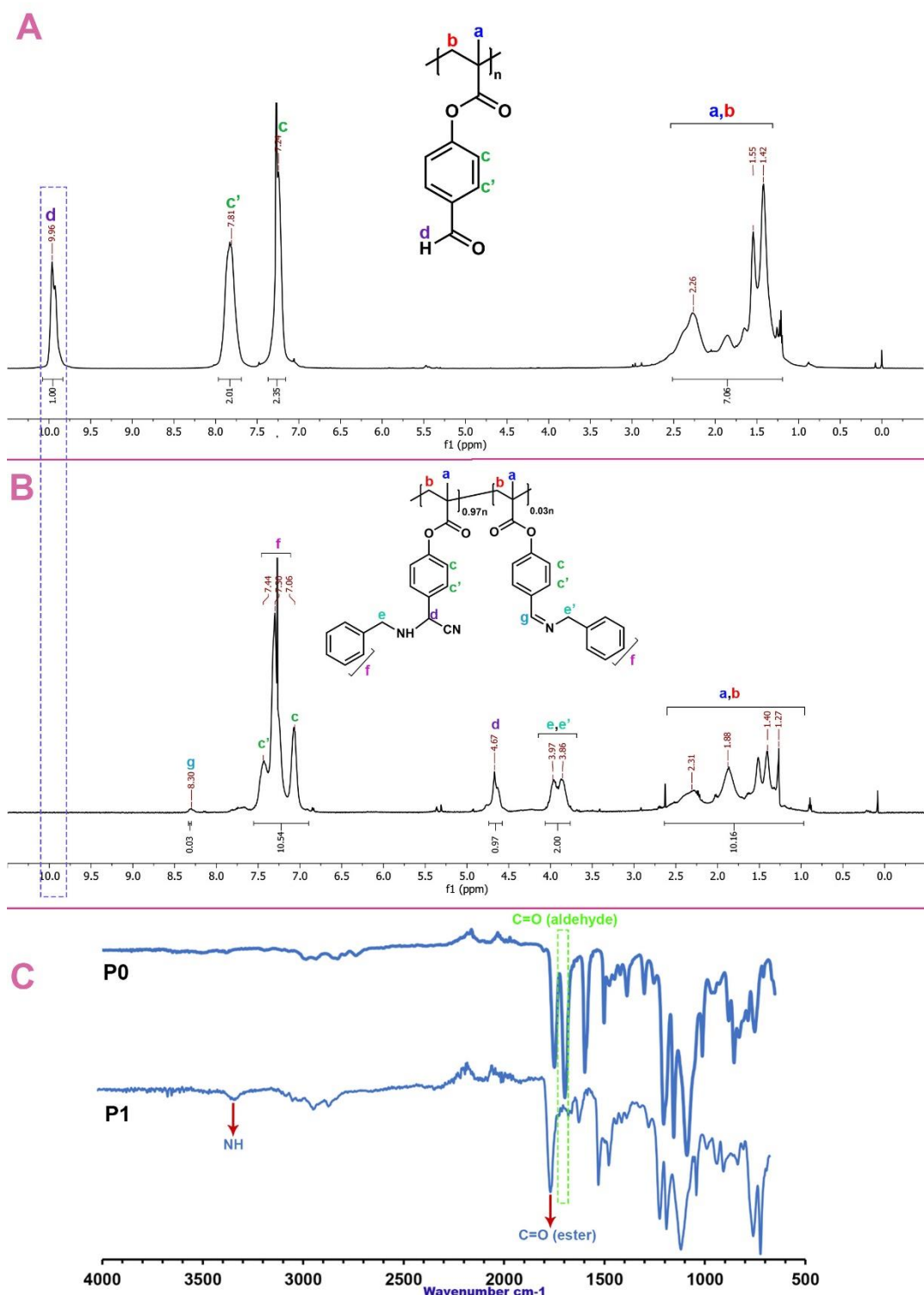


Fig. 2. <sup>1</sup>H NMR (A and B) and FT-IR spectra (C) of P0 and P1.

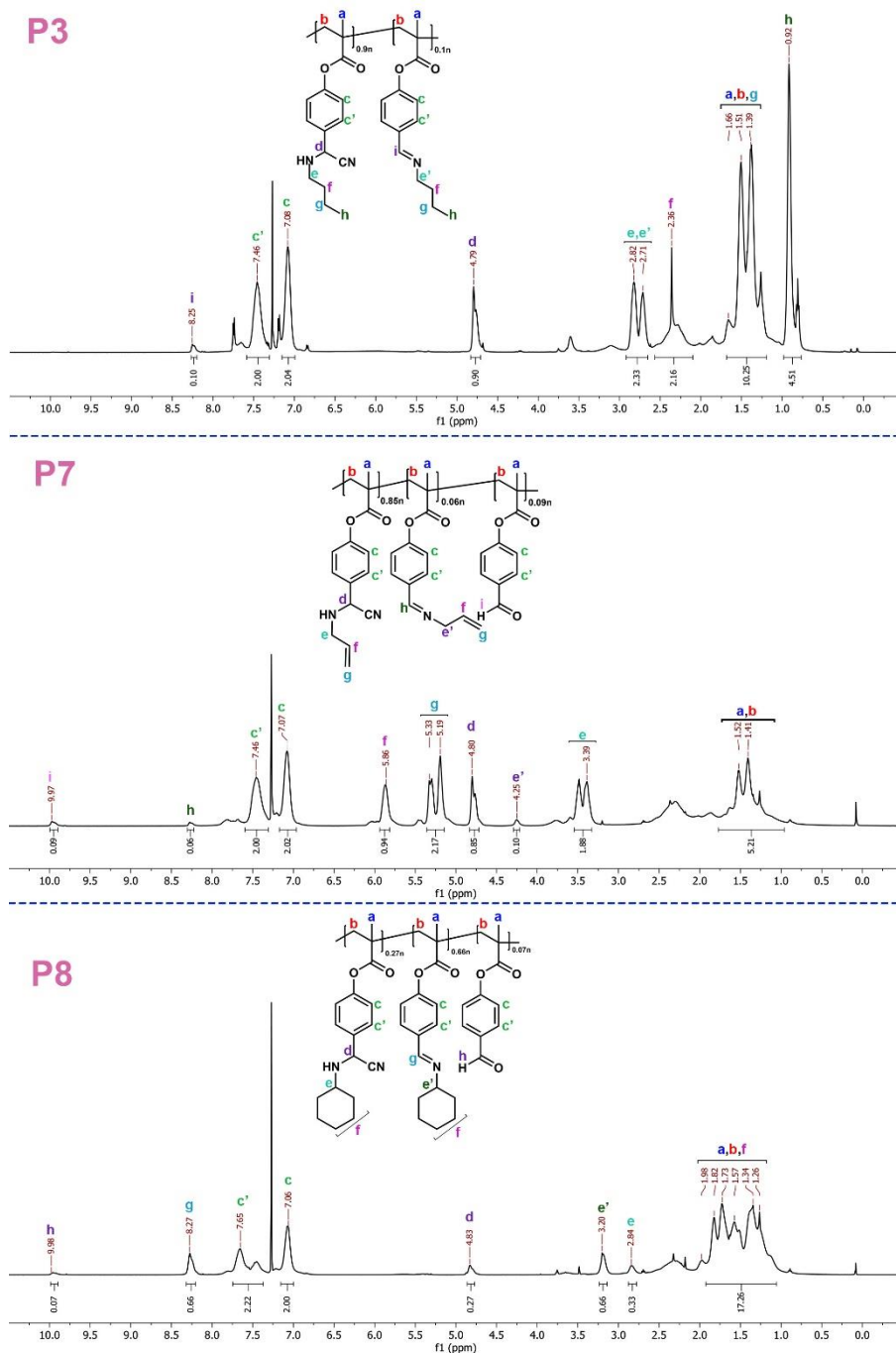


Fig. 3.  $^1\text{H}$  NMR spectra of P3, P7 and P8.

## 4. Conclusion

In summary, the versatility of aldehydes was successfully extended for the first time to the Strecker 3-component reaction (S-3CR) for PPM of aldehyde-functional polymers using different amine compounds and trimethylsilyl cyanide. It was found that pendant aldehyde can be converted to  $\alpha$ -aminonitrile with moderate to near quantitative efficiencies, as confirmed by various spectroscopic analyses. Given the growing interest in MCRs, it is believed the proposed strategy might be a good candidate to study in this field as it offers operationally simple reaction conditions. Overall, this study may pave a new way for PPM in the polymer literature.

## Author Contributions

The authors contributed equally to this work.

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