

Synthesis and styrene copolymerization of novel trisubstituted ethylenes:

9. Halogen, methyl, methoxy and nitro ring-substituted octyl phenylcyanoacrylates

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Abstract

Novel trisubstituted ethylenes, halogen, methyl, methoxy and nitro ring-substituted octyl phenylcyanoacrylates, $RPhCH=C(CN)CO_2CH_2(CH_2)_6CH_3$ (where R is 2-chloro-6-fluoro, 3-chloro-4-fluoro, 2-chloro-5-nitro, 4-chloro-3-nitro, 5-chloro-2-nitro, 5-iodo-2-methoxy, 2,4,5-trimethyl, 2,4,6-trimethyl, pentamethyl, 2,3-dimethyl-4-methoxy, 2,5-dimethyl-4-methoxy, 2,4-dimethoxy-3-methyl) were prepared and copolymerized with styrene. The ethylenes were synthesized by the piperidine catalyzed Knoevenagel condensation of ring-substituted benzaldehydes and octyl cyanoacetate, and characterized by CHN analysis, IR, 1H and ^{13}C NMR. All the ethylenes were copolymerized with styrene in solution with

radical initiation (ABCN) at 70°C. The compositions of the copolymers were calculated from nitrogen analysis.

1. Introduction

Cyanoacrylates is family of vinyl monomers renowned for their high reactivity, instant adhesive properties, and wide-ranging applications [1–3]. Trisubstituted ethylenes (TSE), ring-functionalized (R^1) alkyl (R^2) phenylcyanoacrylates, $R^1\text{PhCH} = \text{C}(\text{CN})\text{CO}_2R^2$ (PCA) continue to attract attention as compounds with variety of applications [4–11]. Thus, methoxy ring-substituted methyl phenylcyanoacrylate, MPCA was used in synthesis of pyridotriazines and triazolopyridines [4]. Dimethylamino ring-substituted MPCA was examined among other cyanovinylheteroaromatics in relation to organic nonlinear optics [5]. There are a number of applications of ethyl phenylcyanoacrylate, EPCA and its ring-substituted derivatives which include studies of catalysis [6] and potential antimicrobial and antioxidant agents [7]. 2,4-Dimethoxyphenyl EPCA was used in design, synthesis and study of anticancer activity of novel benzothiazole analogues [8], in synthesis of thiazacridine derivatives as anticancer agents against breast and hematopoietic neoplastic cells [9] and in DABCO-catalyzed Knoevenagel condensation using hydroxy ionic liquid as a promoter [10]. This EPCA was involved in catalysis study of N,N' -dialkylimidazolium dimethyl phosphates [11], in synthesis and study of antimicrobial activity of some cyanoacrylates [12], as well as in synthesis of antiproliferative active 2-aminobenzimidazole derivatives [13]. Methoxyphenyl octyl cyanoacrylate was synthesized and evaluated for UV-filter activity [14].

In regards to polymerization reactivity, previous studies showed that PCAs as all TSE monomers containing double bond substituents larger than fluorine have very low reactivity in radical homopolymerization due to polar and steric reasons [15]. Although steric difficulties preclude homopolymerization of such monomers, their copolymerization with a monosubstituted alkenes makes it possible to overcome these steric problems. Thus, copolymerization of electrophilic TSE monomers having double bonds substituted with halo, cyano, and carbonyl groups and electron-rich monosubstituted ethylenes such as styrene, N-vinylcarbazole, and vinyl acetate [16-18] show a tendency toward the formation of alternating copolymers - thus suggesting a way of functionalization of commercial polymers via introduction of isolated monomer units in copolymers. Earlier we have reported synthesis and styrene copolymerization of a number of halogen, methyl, methoxy and nitro ring-substituted methyl [19-21], ethyl [22], propyl [23, 24], isopropyl [25, 26], butyl [27], isobutyl [29, 30], and 2-methoxyethyl [31, 32] PCAs.

Our objectives in exploration of novel octyl phenylcyanoacrylates (OPCA) were twofold: (1) to utilize Knoevenagel condensation for synthesis of OPCA compounds with a variety of potentially reactive functional groups and (2) to explore feasibility of radical copolymerization with a commercial monomer styrene.

Thus, in continuation of our investigation of novel TSE compounds we have prepared octyl dichloro and difluoro ring-substituted cyanoacrylates, $RPhCH=C(CN)CO_2CH_2(CH_2)_6CH_3$, where R is 2-chloro-6-fluoro, 3-chloro-4-fluoro, 2-chloro-5-nitro, 4-chloro-3-nitro, 5-chloro-2-nitro, 5-iodo-2-methoxy, 2,4,5-trimethyl, 2,4,6-trimethyl, pentamethyl, 2,3-dimethyl-4-methoxy, 2,5-dimethyl-4-methoxy, 2,4-dimethoxy-

3-methyl, and explored the feasibility of their copolymerization with styrene. To the best of our knowledge there have been no reports on either synthesis of these compounds, nor their copolymerization with styrene [33].

2. Experimental

2.1. Materials

2-Chloro-6-fluoro, 3-chloro-4-fluoro, 2-chloro-5-nitro, 4-chloro-3-nitro, 5-chloro-2-nitro, 5-iodo-2-methoxy, 2,4,5-trimethyl, 2,4,6-trimethyl, pentamethyl, 2,3-dimethyl-4-methoxy, 2,5-dimethyl-4-methoxy, 2,4-dimethoxy-3-methylbenzaldehydes, octyl cyanoacetate ($\geq 98.0\%$), piperidine (99%), styrene ($\geq 99\%$), 1,1'-azobis(cyclohexanecarbonitrile) (98%), (ABCN), and toluene (98%) supplied from Sigma-Aldrich Co., were used as received.

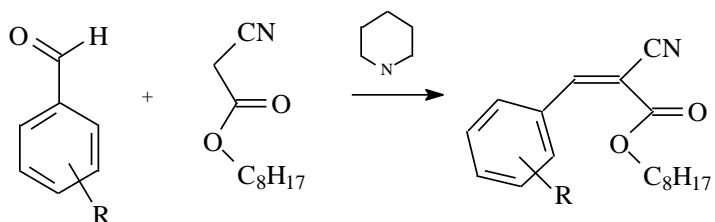
2.2. Instrumentation

Infrared spectra of the OPCA compounds and polymers (NaCl plates) were determined with an ABB FTLA 2000 FT-IR spectrometer. The melting points of the OPCA compounds were measured with TA (Thermal Analysis, Inc.) Model Q10 differential scanning calorimeter (DSC). ^1H and ^{13}C NMR spectra were obtained on 10-25% (w/v) OPCA solutions in CDCl_3 at ambient temperature using Avance 300 MHz spectrometer. CHN-elemental analyses of OPCA compounds and nitrogen analysis of the copolymers were performed by Midwest Microlab, LLC (IN).

3. Results and discussion

3.1. Synthesis and characterization of octyl phenylcyanoacrylates

All octyl phenylcyanoacrylates (OPCA) compounds were synthesized by Knoevenagel condensation [34] of appropriate benzaldehydes with octyl cyanoacetate, catalyzed by base, piperidine (Scheme 1).



Scheme 1. Synthesis of octyl phenylcyanoacrylates where R is 2-chloro-6-fluoro, 3-chloro-4-fluoro, 2-chloro-5-nitro, 4-chloro-3-nitro, 5-chloro-2-nitro, 5-iodo-2-methoxy, 2,4,5-trimethyl, 2,4,6-trimethyl, pentamethyl, 2,3-dimethyl-4-methoxy, 2,5-dimethyl-4-methoxy, 2,4-dimethoxy-3-methyl.

The preparation procedure was essentially the same for all the monomers. In a typical synthesis, equimolar amounts of octyl cyanoacetate and an appropriate benzaldehyde were mixed in equimolar ratio in a 20 mL vial. A few drops of piperidine were added with stirring. The product of the reaction was isolated by filtration and purified by crystallization from 2-propanol. The condensation reaction proceeded smoothly, yielding products, which were purified by conventional techniques. The compounds were characterized by IR, ^1H and ^{13}C NMR spectroscopies. No stereochemical analysis of the novel oxy ring-substituted OPCA was performed since no stereoisomers (*E* or/and *Z*) of known configuration were available.

3.1.1. Octyl 2-chloro-6-fluorophenylcyanoacrylate

Yield 91%; mp $^1\text{H NMR } \delta$ 8.3 (s, 1H, CH=), 7.7-7.0 (m, 3H, Ph), 4.3 (t, 2H, CO_2CH_2), 1.8 (q, 2H, OCH_2CH_2), 1.6-1.5 (m, 6H, $\text{OCH}_2\text{CH}_2(\text{CH}_2)_3$), 1.4-1.2 (m, 4H, $\text{O}(\text{CH}_2)_5(\text{CH}_2)_2$), 0.9 (t, 3H, CH_3); $^{13}\text{C NMR } \delta$ 162 (C=O), 149 (HC=), 161, 137-112 (Ph), 116 (CN), 112 (C=), 68 (OCH_2), 32 ($\text{O}(\text{CH}_2)_5\text{CH}_2$), 29 ($\text{O}(\text{CH}_2)_3(\text{CH}_2)_2$), 28 (OCH_2CH_2), 26 ($\text{O}(\text{CH}_2)_2\text{CH}_2$), 23 (CH_2CH_3), 14 (CH_3); IR (cm^{-1}): 2929 (m, C-H), 2234 (m, CN), 1742 (s, C=O), 1624 (s, C=C), 1264 (s, C-O- CH_3), 764 (s, C-H out of plane).
 Anal. Calcd. for $\text{C}_{18}\text{H}_{21}\text{ClFNO}_2$: C, 64.00; H, 6.27; N, 4.15; Found: C, 63.06; H, 6.37; N, 4.08.

3.1.2. Octyl 3-chloro-4-fluorophenylcyanoacrylate.

Yield 81%; mp 91.0°C ; $^1\text{H NMR } \delta$ 8.2 (s, 1H, CH=), 8.1-7.2 (m, 3H, Ph), 4.3 (t, 2H, CO_2CH_2), 1.8-1.7 (q, 2H, OCH_2CH_2), 1.6-1.5 (m, 6H, $\text{OCH}_2\text{CH}_2(\text{CH}_2)_3$), 1.4-1.2 (m, 4H, $\text{O}(\text{CH}_2)_5(\text{CH}_2)_2$), 0.9 (t, 3H, CH_3); $^{13}\text{C NMR } \delta$ 163 (C=O), 152 (HC=), 162, 142, 138, 132, 129, 126 (Ph), 116, (CN), 103 (C=), 68 (OCH_2), 32 ($\text{O}(\text{CH}_2)_5\text{CH}_2$), 29 ($\text{O}(\text{CH}_2)_3(\text{CH}_2)_2$), 28 (OCH_2CH_2), 26 ($\text{O}(\text{CH}_2)_2\text{CH}_2$), 23 (CH_2CH_3), 14 (CH_3); IR (cm^{-1}): 2929 (m, C-H), 2225 (m, CN), 1717 (s, C=O), 1594 (C=C), 1278 (s, C-O- CH_3), 836 (s, C-H out of plane). Anal. Calcd. for $\text{C}_{18}\text{H}_{21}\text{ClFNO}_2$: C, 64.00; H, 6.27; N, 4.15; Found: C, 60.96; H, 6.26; N, 4.67.

3.1.3. Octyl 2-chloro-5-nitrophenylcyanoacrylate.

Yield 82%; $^1\text{H NMR } \delta$ 9.0 (s, 1H, CH=), 8.7-7.6 (m, 3H, Ph), 4.3 (t, 2H, CO_2CH_2), 1.9-1.7 (q, 2H, OCH_2CH_2), 1.5-1.3 (m, 6H, $\text{OCH}_2\text{CH}_2(\text{CH}_2)_3$), 1.4-1.2 (m, 4H,

O(CH₂)₅(CH₂)₂, 0.9 (t, 3H, CH₃); ¹³C NMR δ 162 (C=O), 150 (HC=), 147, 143, 132-125 (Ph), 116 (CN), 110 (C=), 67 (OCH₂), 32 (O(CH₂)₅CH₂), 29 (O(CH₂)₃(CH₂)₂), 28 (OCH₂CH₂), 26 (O(CH₂)₂CH₂), 23 (CH₂CH₃), 13 (CH₃); IR (cm⁻¹): 2928 (m, C-H), 2230 (m, CN), 1736 (s, C=O), 1608 (C=C), 1265 (s, C-O-CH₃), 760 (s, C-H out of plane).
 Anal. Calcd. for C₁₈H₂₁ClN₂O₄: C, 59.26; H, 5.80; N, 7.68; Found: C, 59.50; H, 6.05; N, 7.75.

3.1.4. Octyl 4-chloro-3-nitrophenylcyanoacrylate.

Yield 82%; mp 91.6°C; ¹H NMR δ 8.4 (s, 1H, CH=), 8.3-7.7 (m, 3H, Ph), 4.3 (t, 2H, CO₂CH₂), 1.9-1.7 (q, 2H, OCH₂CH₂), 1.5-1.3 (m, 6H, OCH₂CH₂(CH₂)₃), 1.4-1.2 (m, 4H, O(CH₂)₅(CH₂)₂), 0.9 (t, 3H, CH₃); ¹³C NMR δ 161 (C=O), 150 (HC=), 148-124 (Ph), 116 (CN), 110 (C=), 68 (OCH₂), 32 (O(CH₂)₅CH₂), 29 (O(CH₂)₃(CH₂)₂), 28 (OCH₂CH₂), 26 (O(CH₂)₂CH₂), 23 (CH₂CH₃), 13 (CH₃); IR (cm⁻¹): 2956 (m, C-H), 2231 (m, CN), 1716 (s, C=O), 1542 (C=C), 1278 (s, C-O-CH₃), 785 (s, C-H out of plane). Anal. Calcd. for C₁₈H₂₁ClN₂O₄: C, 59.26; H, 5.80; N, 7.68; Found: C, 59.25; H, 5.86; N, 7.72.

3.1.5. Octyl 5-chloro-2-nitrophenylcyanoacrylate.

Yield 72%; mp 71.1°C; ¹H NMR δ 8.7 (s, 1H, CH=), 8.3-7.2 (m, 3H, Ph), 4.4 (t, 2H, CO₂CH₂), 1.8-1.7 (q, 2H, OCH₂CH₂), 1.5-1.4 (m, 6H, OCH₂CH₂(CH₂)₃), 1.4-1.2 (m, 4H, O(CH₂)₅(CH₂)₂), 0.9 (t, 3H, CH₃); ¹³C NMR δ 162 (C=O), 152 (HC=), 142-127 (Ph), 115 (CN), 100 (C=), 68 (OCH₂), 32 (O(CH₂)₅CH₂), 29.3 (O(CH₂)₃(CH₂)₂), 28.5 (OCH₂CH₂), 26 (O(CH₂)₂CH₂), 23 (CH₂CH₃), 14 (CH₃); IR (cm⁻¹): 2959 (m, C-H), 2232 (m, CN),

1733 (s, C=O), 1528 (s, C=C), 1265 (s, C-O-CH₃), 848 (s, C-H out of plane). Anal.

Calcd. for C₁₈H₂₁ClN₂O₄: C, 59.26; H, 5.80; N, 7.68; Found: C, 59.78; H, 6.24; N, 7.87.

3.1.6. Octyl 5-iodo-2-methoxyphenylcyanoacrylate.

Yield 89%; mp 77.0°C; ¹H NMR δ 8.6 (s, 1H, CH=), 8.5-6.7 (m, 3H, Ph), 4.3 (t, 2H, CO₂CH₂), 3.9 (s, 3H, PhOCH₃), 2.1-1.7 (q, 2H, OCH₂CH₂), 1.5-1.4 (m, 6H, OCH₂CH₂(CH₂)₃), 1.4-1.2 (m, 4H, O(CH₂)₅(CH₂)₂), 0.9 (t, 3H, CH₃); ¹³C NMR δ 162 (C=O), 149 (HC=), 143, 138, 123, 115 (Ph), 117 (CN), 104 (C=), 68 (OCH₂), 56 (PhOCH₃), 33 (O(CH₂)₅CH₂), 29.3 (O(CH₂)₃(CH₂)₂), 28.5 (OCH₂CH₂), 26 (O(CH₂)₂CH₂), 23 (CH₂CH₃), 14 (CH₃); IR (cm⁻¹): 2924 (m, C-H), 2222 (m, CN), 1717 (s, C=O), 1587 (s, C=C), 1254 (s, C-O-CH₃), 868 (s, C-H out of plane). Anal. Calcd. for C₁₉H₂₄INO₃: C, 51.71; H, 5.48; N, 3.17; Found: C, 53.47; H, 5.92; N, 3.35.

3.1.7. Octyl 2,4,5-trimethylphenylcyanoacrylate.

Yield 87%; mp 36.3°C; ¹H NMR δ 8.5 (s, 1H, CH=), 8.0, 7.0 (m, 2H, Ph), 4.3 (t, 2H, CO₂CH₂), 2.3 (s, 9H, PhCH₃), 1.8-1.7 (q, 2H, OCH₂CH₂), 1.5-1.4 (m, 6H, OCH₂CH₂(CH₂)₃), 1.4-1.2 (m, 4H, O(CH₂)₅(CH₂)₂), 0.9 (t, 3H, CH₃); ¹³C NMR δ 163 (C=O), 150 (HC=), 143-118 (Ph), 117 (CN), 110 (C=), 66 (OCH₂), 32 (O(CH₂)₅CH₂), 29.3 (O(CH₂)₃(CH₂)₂), 28.5 (OCH₂CH₂), 26 (O(CH₂)₂CH₂), 23 (CH₂CH₃), 20 (PhCH₃), 13 (CH₃); IR (cm⁻¹): 2928 (m, C-H), 2223 (m, CN), 1726 (s, C=O), 1611 (s, C=C), 1263 (s, C-O-CH₃), 760 (s, C-H out of plane). Anal. Calcd. for C₂₁H₂₉NO₂: C, 77.02; H, 8.93; N, 4.28; Found: C, 56.18; H, 7.24; N, 4.48.

3.1.8. Octyl 2,4,6-trimethylphenylcyanoacrylate.

Yield 79%; $^1\text{H NMR}$ δ 8.5 (s, 1H, CH=), 6.9 (m, 3H, Ph), 4.3 (t, 2H, CO₂CH₂), 2.3 (s, 9H, PhCH₃), 1.8-1.7 (q, 2H, OCH₂CH₂), 1.5-1.4 (m, 6H, OCH₂CH₂(CH₂)₃), 1.4-1.2 (m, 4H, O(CH₂)₅(CH₂)₂), 0.9 (t, 3H, CH₃); $^{13}\text{C NMR}$ δ 163 (C=O), 150 (HC=), 143-117 (Ph), 116 (CN), 110 (C=), 67 (OCH₂), 32 (O(CH₂)₅CH₂), 29.3 (O(CH₂)₃(CH₂)₂), 28.5 (OCH₂CH₂), 26 (O(CH₂)₂CH₂), 23 (CH₂CH₃), 20 (PhCH₃), 13 (CH₃); IR (cm⁻¹): 2931 (m, C-H), 2229 (m, CN), 1737 (s, C=O), 1614 (s, C=C), 1263 (s, C-O-CH₃), 783 (s, C-H out of plane). Anal. Calcd. for C₂₁H₂₉NO₂: C, 77.02; H, 8.93; N, 4.28; Found: C, 74.43; H, 8.82; N, 4.48.

3.1.9. Octyl pentamethylphenylcyanoacrylate.

Yield 87%; mp 71.3°C; $^1\text{H NMR}$ δ 8.7 (s, 1H, CH=), 4.3 (t, 2H, CO₂CH₂), 2.3 (s, 15H, PhCH₃), 1.8-1.7 (q, 2H, OCH₂CH₂), 1.5-1.4 (m, 6H, OCH₂CH₂(CH₂)₃), 1.4-1.2 (m, 4H, O(CH₂)₅(CH₂)₂), 0.9 (t, 3H, CH₃); $^{13}\text{C NMR}$ δ 162 (C=O), 160 (HC=), 138-112 (Ph), 116 (CN), 100 (C=), 67 (OCH₂), 32 (O(CH₂)₅CH₂), 29.3 (O(CH₂)₃(CH₂)₂), 28.5 (OCH₂CH₂), 26 (O(CH₂)₂CH₂), 23 (CH₂CH₃), 16.4 (PhCH₃), 13 (CH₃); IR (cm⁻¹): 2928 (m, C-H), 2231 (m, CN), 1728 (s, C=O), 1616 (s, C=C), 1276 (s, C-O-CH₃), 786 (s, C-H out of plane). Anal. Calcd. for C₂₃H₃₃NO₂: C, 77.70; H, 9.39; N, 3.94; Found: C, 75.91; H, 9.22; N, 4.25.

3.1.10. Octyl 2,3-dimethyl-4-methoxyphenylcyanoacrylate.

Yield 92%; mp 71.4°C; $^1\text{H NMR}$ δ 8.6 (s, 1H, CH=), 8.1, 6.8 (m, 2H, Ph), 4.3 (t, 2H, CO₂CH₂), 3.9 (s, 3H, PhOCH₃), 2.3, 2.2 (s, 6H, PhCH₃), 1.7-1.8 (q, 2H, OCH₂CH₂), 1.6-1.5 (m, 6H, OCH₂CH₂(CH₂)₃), 1.4-1.2 (m, 4H, O(CH₂)₅(CH₂)₂), 0.9 (t, 3H, CH₃); ^{13}C

NMR δ 163 (C=O), 153 (HC=), 162, 140-108 (Ph), 116 (CN), 101 (C=), 68 (OCH₂), 56 (PhOCH₃), 32 (O(CH₂)₅CH₂), 29 (O(CH₂)₃(CH₂)₂), 28 (OCH₂CH₂), 26 (O(CH₂)₂CH₂), 23 (CH₂CH₃), 13 (CH₃), 12 (PhCH₃); IR (cm⁻¹): 2933 (m, C-H), 2221 (m, CN), 1719 (s, C=O), 1581 (s, C=C), 1284 (s, C-O-CH₃), 737 (s, C-H out of plane). Anal. Calcd. for C₂₁H₂₉NO₃: C, 73.44; H, 8.51; N, 4.08; Found: C, 71.83; H, 7.96; N, 4.90.

3.1.11. Octyl 2,5-dimethyl-4-methoxyphenylcyanoacrylate.

Yield 91%; mp 83.1°C; ¹H NMR δ 8.5 (s, 1H, CH=), 8.2, 6.7 (m, 2H, Ph), 4.3 (t, 2H, CO₂CH₂), 3.9 (s, 3H, PhOCH₃), 2.4, 2.3 (s, 6H, PhCH₃), 1.7-1.8 (q, 2H, OCH₂CH₂), 1.6-1.5 (m, 6H, OCH₂CH₂(CH₂)₃), 1.4-1.2 (m, 4H, O(CH₂)₅(CH₂)₂), 0.9 (t, 3H, CH₃); ¹³C NMR δ 163 (C=O), 153 (HC=), 162, 140-108 (Ph), 117 (CN), 101 (C=), 68 (OCH₂), 56 (PhOCH₃), 32 (O(CH₂)₅CH₂), 29 (O(CH₂)₃(CH₂)₂), 28 (OCH₂CH₂), 26 (O(CH₂)₂CH₂), 23 (CH₂CH₃), 13 (CH₃), 12 (PhCH₃); IR (cm⁻¹): 2922 (m, C-H), 2215 (m, CN), 1717 (s, C=O), 1573 (s, C=C), 1271 (s, C-O-CH₃), 869 (s, C-H out of plane). Anal. Calcd. for C₂₁H₂₉NO₃: C, 73.44; H, 8.51; N, 4.08; Found: C, 73.91; H, 9.00; N, 4.32.

3.1.12. Octyl 2,4-dimethoxy-3-methylphenylcyanoacrylate.

Yield 87%; mp 58.8°C; ¹H NMR δ 8.6 (s, 1H, CH=), 8.5, 6.7 (m, 2H, Ph), 4.3 (t, 2H, CO₂CH₂), 3.9, 3.8 (s, 6H, PhOCH₃), 2.2 (s, 3H, PhCH₃), 1.7-1.8 (q, 2H, OCH₂CH₂), 1.6-1.5 (m, 6H, OCH₂CH₂(CH₂)₃), 1.4-1.2 (m, 4H, O(CH₂)₅(CH₂)₂), 0.9 (t, 3H, CH₃); ¹³C NMR δ 163 (C=O), 152 (HC=), 162, 142-112 (Ph), 117 (CN), 100 (C=), 68 (OCH₂), 56 (PhOCH₃), 32 (O(CH₂)₅CH₂), 29 (O(CH₂)₃(CH₂)₂), 28 (OCH₂CH₂), 26 (O(CH₂)₂CH₂), 23 (CH₂CH₃), 15 (CH₃), 14 (PhCH₃); IR (cm⁻¹): 2929 (m, C-H), 2219 (m, CN), 1717 (s,

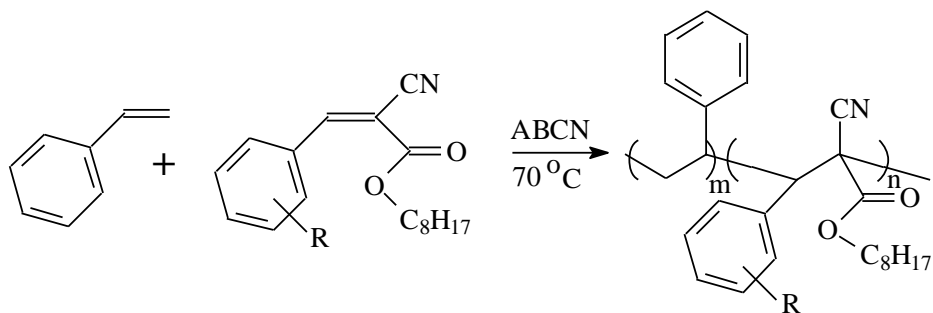
C=O), 1587 (s, C=C), 1243 (s, C-O-CH₃), 750 (s, C-H out of plane). Anal. Calcd. for C₂₁H₂₉NO₄: C, 70.17; H, 8.13; N, 3.90; Found: C, 68.47; H, 8.13; N, 4.48.

3.2. Homopolymerization

An attempted homopolymerization of the OPCA compounds in the presence of ABCN did not produce any polymer as indicated by the lack of a precipitate in methanol. The inability of the monomers to polymerize is associated with steric difficulties encountered in homopolymerization of 1,1- and 1,2-disubstituted ethylenes [15]. Homopolymerization of ST under conditions identical to those in copolymerization experiments yielded 18.3% of polystyrene, when polymerized for 30 min.

3.3. Synthesis and characterization of styrene – OPCA copolymers

Copolymers of the ST and the OPCA compounds, P(ST-co-OPCA) were prepared in 25-mL glass screw cap vials at ST/ OPCA = 3 (mol) the monomer feed using 0.12 mol/L of ABCN at an overall monomer concentration 2.44 mol/L in 10 mL of toluene. The copolymerization was conducted at 70°C. After a predetermined time, the mixture was cooled to room temperature, and precipitated dropwise in methanol. The composition of the copolymers was determined based on the nitrogen content (cyano group in OPCA). The novel synthesized OPCA compounds copolymerized readily with ST under free-radical conditions (Scheme 2) forming white flaky precipitates when their solutions were poured into methanol. The conversion of the copolymers was kept between 10 and 20% to minimize compositional drift (Table 1).



Scheme 2. Copolymerization of ST and the octyl phenylcyanoacrylates, where R is 2-chloro-6-fluoro, 3-chloro-4-fluoro, 2-chloro-5-nitro, 4-chloro-3-nitro, 5-chloro-2-nitro, 5-iodo-2-methoxy, 2,4,5-trimethyl, 2,4,6-trimethyl, pentamethyl, 2,3-dimethyl-4-methoxy, 2,5-dimethyl-4-methoxy, 2,4-dimethoxy-3-methyl.

Table 1. Copolymerization of styrene and octyl phenylcyanoacrylates.

R	Yield ^a (wt%)	N (wt%)	ST in copol. (mol%)	OPCA in copol. (mol%)
2-Chloro-6-fluoro	14.1	2.36	71.0	29.0
3-Chloro-4-fluoro	11.3	1.86	79.9	20.1
2-Chloro-5-nitro	10.5	4.74	68.5	31.5
4-Chloro-3-nitro	13.1	5.2	62.5	37.5
5-Chloro-2-nitro	10.2	4.96	65.7	34.3
5-Iodo-2-methoxy	16.4	2.16	66.6	33.4
2,4,5-Trimethyl	12.2	2.68	65.1	34.9
2,4,6-Trimethyl	12.7	1.44	70.3	29.7
Pentamethyl	11.1	1.92	78.2	21.8
2,3-Dimethyl-4-methoxy	12.4	2.26	72.7	27.3
2,5-Dimethyl-4-methoxy	16.7	2.51	67.4	32.6
2,4-Dimethoxy-3-methyl	14.1	2.47	66.6	33.4

Nitrogen elemental analysis showed that between 20.1 and 37.5 mol% of OPCA is present in the copolymers prepared at ST/OPCA = 3 (mol), which is indicative of

relatively high reactivity of the OPCA monomers towards ST radical which is typical of ring-substituted OPCA [18-26]. Since OPCA monomers do not homopolymerize, the most likely structure of the copolymers would be isolated OPCA monomer units alternating with short ST sequences (Scheme 2).

The copolymers prepared in the present work are all soluble in ethyl acetate, THF, DMF and CHCl_3 and insoluble in methanol, ethyl ether, and petroleum ether.

4 Conclusions

Novel trisubstituted ethylenes, halogen, methyl, methoxy and nitro octyl phenylcyanoacrylates, $\text{RPhCH}=\text{C}(\text{CN})\text{CO}_2\text{CH}_2(\text{CH}_2)_6\text{CH}_3$ (where R is 2-chloro-6-fluoro, 3-chloro-4-fluoro, 2-chloro-5-nitro, 4-chloro-3-nitro, 5-chloro-2-nitro, 5-iodo-2-methoxy, 2,4,5-trimethyl, 2,4,6-trimethyl, pentamethyl, 2,3-dimethyl-4-methoxy, 2,5-dimethyl-4-methoxy, 2,4-dimethoxy-3-methyl) were prepared and copolymerized with styrene.

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References

- [1] Klemarczyk, P.; Guthrie, J. Advances in anaerobic and cyanoacrylate adhesives. In *Advances in Structural Adhesive Bonding*, 1st ed.; Dillard, D., Ed.; Woodhead Publishing Limited: Cambridge, UK, 2010; pp. 96–131, ISBN 978-1-84569-435-7.
- [2] Shantha, K.L.; Thennarasu, S.; Krishnamurti, N. Developments and applications of cyanoacrylate adhesives. *J. Adhes. Sci. Technol.* 1989, 3, 237–260.

- [3] J.M. Korde and B. Kandasubramanian, Biocompatible alkyl cyanoacrylates and their derivatives as bio-adhesives, *Biomaterials Science*, 10.1039/C8BM00312B, 6, 7, (1691-1711), (2018).
- [4] Zaki MEA, Fathalla OA, Swelam SA, Aly HF (2004) Synthesis of pyrido[2,1-c][1,2,4]triazine, 1,2,4-triazolo[4,3-a]pyridine and 2-(pyrazolyl)nicotinonitrile and their effect on *Biomphalaria alexandrina* snail enzymes. *Acta Poloniae Pharmaceutica* 61: 55-64.
- [5] Matsuoka M, Takao M, Kitao T, Fujiwara T, Nakatsu K (1990) Cyanovinylheteroaromatics for Organic Nonlinear Optics. *Molecular Crystals and Liquid Crystals*, 182A: 71-79.
- [6] Burate PA, Javle BR, Desale PH, Kinage AK (2019) Amino acid amide based ionic liquid as an efficient organo-catalyst for solvent-free Knoevenagel condensation at room temperature. *Catalysis Letters* 149(9): 2368-2375.
- [7] Medyouni R, Hamdi N, Ben Said R, Al-Ayed AS, Zagrouba F (2013) Clean procedure and DFT study for the synthesis of 2-amino-3-ethoxycarbonyl-4-(aryl)-4H-pyrano-[3,2-c]-chromene-5-ones derivatives: A novel class of potential antimicrobial and antioxidant agents. *Journal of Chemistry* 2013: 1-4.
- [8] Hassan AY, Sarg MT, Hussein EM (2019) Design, synthesis and anticancer activity of novel benzothiazole analogues. *Journal of Heterocyclic Chemistry* 56(4): 1437-1457.

- [9] Moacyr JB, De Melo R, Wanessa LB, De Sena, RO, De Moura, Iris TT et al. (2017). Synthesis and anticancer evaluation of thiazacridine derivatives reveals new selective molecules to hematopoietic neoplastic cells. *Combinatorial Chemistry & High Throughput Screening* 20(8): 713.
- [10] Meng D, Qiao Y, Wang X, Wen W, Zhao S (2018) DABCO-catalyzed Knoevenagel condensation of aldehydes with ethyl cyanoacetate using hydroxy ionic liquid as a promoter. *RSC Advances* 8(53): 30180-30185.
- [11] Brica S, Freimane L, Kulikovska L, Zicmanis A (2017) N,N'-dialkylimidazolium dimethyl phosphates - promising media and catalysts at the same time for condensation reactions. *Chemical Science International Journal* 19(4): 1-9.
- [12] Bhuiyan M, Mosharef H, Rahman KM, Alam MA, Mahmud M (2013) Microwave assisted Knoevenagel condensation: synthesis and antimicrobial activities of some α -cyanoacrylates. *Pakistan Journal of Scientific and Industrial Research, Series A: Physical Sciences* 56(3): 131-137.
- [13] Nowicka A, Liskiewicz H, Nawrocka WP, Wietrzyk J, Kempinska K, Drys A (2014) Synthesis and antiproliferative activity in vitro of new 2-aminobenzimidazole derivatives. Reaction of 2-arylideneaminobenzimidazole with selected nitriles containing active methylene group. *Central European Journal of Chemistry* 12(10): 1047-1055.
- [14] Synthesis and evaluation of octocrylene-inspired compounds for UV-filter activity. Polonini, Hudson C.; Lopes, Rosangela S.; Beatriz, Adilson; Gomes, Roberto S.;

- Silva, Adriano O.; de Lima, Ricardo V.; Nunes, Glaucia A.; Brandao, Marcos Antonio F.; Raposo, Nadia R. B.; de Lima, Denis P. *Quimica Nova* (2014), 37(6), 1004-1009.
- [15] Odian, G. *Principles of Polymerization*, 4th Ed., Wiley-Interscience: New York, 2004.
- [16] Hall, H. K., Jr.; Padias, A. B. *J. Polym. Sci. Part A: Polym. Chem.* **2004**, 42, 2845-2858.
- [17] Hall, H. K. Jr.; Ykman, P. *Macromolecules*. 1977, 10, 464.
- [18] Kharas, G. B. *Trisubstituted Ethylene Copolymers. In Polymeric Materials Encyclopedia*, Salamone, J.C., (Ed.) CRC Press: Boca Raton, FL, 11, 8405, 1996.
- [19] Novel Copolymers of Styrene. 16. Halogen Ring-Disubstituted Methyl 2-Cyano-3-Phenyl-2-Propenoates. G.B. Kharas, S.E. Chavez, H. Browning, J. Sepe, M.E. Romanelli, M. Susnis, G. Choquegonzales, K. Fuentes, R. Treneva, and C. Murphy. *J. Macromol. Sci.* A51(10) 751-755 (2014).
- [20] Novel Copolymers of Styrene and Alkyl and Alkoxy Ring-trisubstituted Methyl 2-cyano-3-phenyl-2-propenoates. G.B. Kharas, M.J. Lazzarotto, K.A. Ledin, M.M. Mulvaney, J. R. Nazarof, J.E. Pineda, L.A.M. Tomas, R. Teets, and K. Watson. *J. Macromol. Sci.*, 43 (8) 1127-1133 (2006).
- [21] Novel Copolymers of Trisubstituted Ethylenes and Styrene – 5. Ring-disubstituted Methyl 2-Cyano-3-phenyl-2-propenoates. K.Kim, M. Morales, M.J. Scully, C.D. Seitz,

- A.-M. Sikora, A.M. Spaulding, R.Sudman, A.C. Sullivan, G.B. Kharas, K.Watson. *Designed Monomers and Polymers*, 2, 333-341 (1999).
- [22] Novel Copolymers of Styrene. 8. Haloalkyl Ring-substituted Ethyl 2-Cyano-3-phenyl-2-propenoates. G.B. Kharas, B.M. Fitzpatrick, M.C. Francis, C. Gallardo, J.L. Gehle, G.M. Giovannini, M.E. Giovannini, J.K. Jerzewski, S.L. LaFary, L.N. Lessor, D.E. Macias. *J. Macromol. Sci. A50* (4) 370-374 (2013).
- [23] Synthesis and styrene copolymerization of novel trisubstituted ethylenes: 11. Halogen ring-substituted propyl 2-cyano-3-phenyl-2-propenoates. K.E. Humanski, S.D. Patterson, P.J. Pecorin, M.M. Perfitt, J. Romero, W.R. Sassack, S.M. Sweeney, C.O. Talwar, D.A. Tolentino, M.E. Wilson, W.S. Schjerven & G.B. Kharas. *J. Macromol. Sci. A55*:10, 709-717, DOI: 10.1080/10601325.2018.1526639 (2018).
- [24] Synthesis and radical copolymerization of novel propyl cyanoacrylate monomers. Knight, J.D., L. Arellano, K.O. Conger, E. Crespo, J.E. Hollembeak, N.M. Jazdzewski, A.A. Pater, D.H. Possley, K.N. Rivera, C. Saucedo, J.E. Spitz, T.L. Vacala, N.W. Woo, W.S. Schjerven, G.B. Kharas, *Polym. Bull.* 77, 1433-1448 (2020) DOI: 10.1007/s00289-019-02810-2
- [25] Synthesis and styrene copolymerization of novel chloro and fluoro ring-disubstituted isopropyl cyanophenylacrylates. C.R. Savittieri, A.A. Shinde, Sara M. Rocus, W.S. Schjerven, G.B. Kharas. *ChemRxiv* (23.12.2019).
<https://doi.org/10.26434/chemrxiv.11401347.v1>

- [26] Synthesis and styrene copolymerization of novel methoxy and methyl ring-trisubstituted isopropyl cyanophenylacrylates. J.J. Ludtke, S.M. Rocus, W.S. Schjerven, G.B. Kharas. *Intern. J. Chem. Stud.* 3 (4) 48-51 (2019).
- [27] Novel Copolymers of Styrene. 12. Halogen Ring-Disubstituted Butyl 2-Cyano-3-Phenyl-2-Propenoates. G.B. Kharas, S.M. Rocus, H.E. Aynessazian, Z.L. Christy-Aronson, I.C. Chaoui-Boudrane, R.M. Lange, J.C. Richardson, B.S. Sukhera, S.T. Tamrakar, and C.A. Vanjo. *J. Macromol. Sci. A53* (6) 335-339 (2016).
- [28] . Novel Copolymers of Styrene. 13. Alkyl and Alkoxy Ring-Trisubstituted Butyl 2-Cyano-3-Phenyl-2-Propenoates. G.B. Kharas, Y. Gao, A.M. Clara, V.J. Curtis, R. Da Silva Bechara Soares, B. Dugan, C.E. Duncan, E.R. Gluzman, N. Gomez, M.Y. Kawarski, and D.M. Kestin. *J. Macromol. Sci. A53*(7) 389-393 (2016).
- [29] Synthesis and styrene copolymerization of novel fluoro and chloro ring-disubstituted isobutyl phenylcyanoacrylates. Christopher D. Ahlers, Aisha A. Ahmed, Umamah Alam, Alima A. Sajwani, Megan V. Salloum, Makayla A. Schneider, Heysel M. Serra, Richard C. Tanawath, Gabriella L. Triolo, Marisol Velazquez, Sara M. Rocus, William S. Schjerven, Gregory B. Kharas. *ChemRxiv* (06.10.2020)
<https://doi.org/10.26434/chemrxiv.11401347.v9>
- [30] Synthesis and styrene copolymerization of methyl and methoxy tri, tetra, penta ring-substituted isobutyl phenylcyanoacrylates. Monique L.P. Lotto, Yasmeen Lowe, Raza Malik, Raisa A. Munshi, Udit Persaud, Grace Rajaramsiva, Maximillian A. Ramirez, Claire P. Rossi, Sara M. Rocus, William S. Schjerven and Gregory B. Kharas. *ChemRxiv* (23.10.2020) <https://doi.org/10.26434/chemrxiv.11336852.v2>

- [31] Synthesis and styrene copolymerization of novel trisubstituted ethylenes: 9. Ring-disubstituted 2-methoxyethyl 2-cyano-3-phenyl-2-propenoates. Ehab Abdelhamid, Hussein Abourahma, Julia Bellino, Joshua S.M. Bowser, Lourdes De Anda, Richard E. DeMaria, Erika Galeczka, Madeline Martin, Abdulrafey Nasir, Alexis Pawlak, Ashley Pezza, Rachel Quade, Anna Schell, Valerie Tafoya, Bhavi D. Vashi, Sabah I. Vikaruddin, Sophia L. Zygowski, Sara M. Rocus, William S. Schjerven, and Gregory B. Kharas. ChemRxiv. Preprint. (10.02.2021).
<https://doi.org/10.26434/chemrxiv.13262660.v9>
- [32] Synthesis and styrene copolymerization of novel trisubstituted ethylenes: 10. Methyl and methoxy ring-trisubstituted phenylcyanoacrylates. Mariah A. Byk, Althia J. Coyoc, Mariah S. Flowers, Werhawet Gebremeskel, Bogdan Gontar, Jose Gonzalez Jr, Patrick J. Hartrich, Anna C. Howell, Sara M. Rocus, William S. Schjerven, and Gregory B. Kharas. ChemRxiv. Preprint. (15.02.2021).
<https://doi.org/10.26434/chemrxiv.13262660.v10>
- [33] SciFinder; Chemical Abstracts Service: Columbus, OH; <https://scifinder.cas.org> (accessed March 16, 2021).
- [34] Smith, M. B.; March, J. *Addition to Carbon-Hetero Multiple Bonds*, In March's Advanced Organic Chemistry, J. Wiley & Sons: New York, Ch.16, 1225, **2001**.