Synthesis and styrene copolymerization of novel trisubstituted ethylenes: 5. Halogen ring-substituted 2-methoxyethyl phenylcyanoacrylates

Grace D. Lee, Mae I. Z. Madrid, Jullisa J. Maya, Andrew S. Nuelle, Nancy Padilla, Gia K. Pappas, Rechal K. Patel, Misael Villegas, Fernanda Aviles, Emily Schroeder, Farheen Shethwala, Jordan Villa, Sara M. Rocus, William S. Schjerven, and Gregory B. Kharas

DePaul University, Chemistry and Biochemistry Department, 1110 West Belden Avenue, Chicago, IL 60614-3214

Abstract

Novel trisubstituted ethylenes, halogen ring-substituted 2-methoxyethyl phenylcyanoacrylates, $RPhCH=C(CN)CO_2CH_2CH_2OCH_3$ (where R is 2-bromo, 3-bromo, 4-bromo, 2-chloro, 3-chloro, 4-chloro, 2-fluoro, 3-fluoro, 4-fluoro, 2-trifluoromethyl, 3-trifluoromethyl, 4-trifluoromethyl) were prepared and copolymerized with styrene. The ethylenes were synthesized by the piperidine catalyzed Knoevenagel condensation of ring-substituted benzaldehydes and 2-methoxyethyl cyanoacetate, and characterized by CHN analysis, IR, ^{1}H 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.

*Address correspondence to: Gregory B. Kharas, Chemistry and Biochemistry Department, DePaul University, Chicago, IL 60614-3214.

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 phenylcyanoacrylates, $R^1PhCH = C(CN)CO_2R^2$ (PCA) continue to attract attention as compounds with variety of applications [4-13]. 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].

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 [14]. 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 electrophylic 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 [15-17] 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 a number of halogen ring-substituted PCAs, such esters as methyl [18-19], ethyl [20], propyl [21], isopropyl [22], butyl [23], and isobutyl [24]. Our objectives in exploration of novel 2-methoxyethyl phenylcyanoacrylates (MEPA) were twofold: (1) to utilize Knoevenagel condensation for synthesis of MEPA 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 halogen ring-substituted 2-methoxyethyl phenylcyanoacrylates, $RPhCH=C(CN)CO_2CH_2CH_2OCH_3$, where R is 2-bromo, 3-bromo, 4-bromo, 2-chloro, 3-

chloro, 4-chloro, 2-fluoro, 3-fluoro, 4-fluoro, 2-trifluoromethyl, 3-trifluoromethyl, 4-trifluoromethyl, 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 [25].

2. Experimental

2.1. Materials

2-Bromo, 3-bromo, 4-bromo, 2-chloro, 3-chloro, 4-chloro, 2-fluoro, 3-fluoro, 4-fluoro, 2-trifluoromethyl, 3-trifluoromethyl, 4-trifluoromethyl-substituted benzaldehydes, 2-methoxyethyl cyanoacetate (≥98.0%), piperidine (99%), styrene (≥99%), 1,1'-azobis(cyclohexanecarbonitrile) (98%), (ABCN), and toluene (98%) supplied from Sigma-Aldrich Co., were used as received.

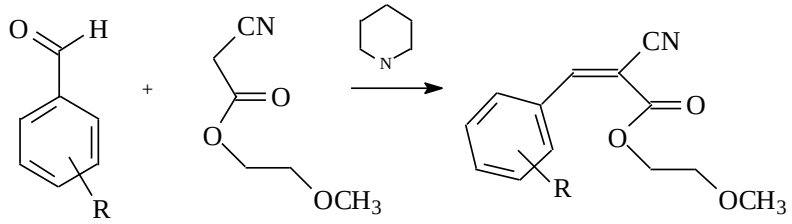
2.2. Instrumentation

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

3. Results and discussion

3.1. Synthesis and characterization of 2-methoxyethyl phenylcyanoacrylates

All MEPA compounds were synthesized by Knoevenagel condensation [26] of appropriate benzaldehydes with 2-methoxyethyl cyanoacetate, catalyzed by base, piperidine (Scheme 1).



Scheme 1. Synthesis of 2-methoxyethyl phenylcyanoacrylates, where R is 2-bromo, 3-bromo, 4-bromo, 2-chloro, 3-chloro, 4-chloro, 2-fluoro, 3-fluoro, 4-fluoro, 2-trifluoromethyl, 3-trifluoromethyl, 4-trifluoromethyl.

The preparation procedure was essentially the same for all the MEPA compounds. In a typical synthesis, equimolar amounts of 2-methoxyethyl 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, ^{1}H and ^{13}C NMR spectroscopies. No stereochemical analysis of the novel alkoxy ring-substituted MEPA was performed since no stereoisomers (*E* or/and *Z*) of known configuration were available.

3.1.1. *2-Methoxyethyl 2-bromophenylcyanoacrylate*

Yield: 82%; mp 56°C; ^{1}H NMR: δ8.3 (s, 1H, CH=), 8.2-7.4 (m, 4H, Ph), 4.5 (t, 2H, $OCOCH_2$), 3.7 (t, 2H, OCH_2), 3.4 (s, 3H, OCH_3); ^{13}C NMR: δ 163 (C=O), 154 (HC=), 136, 132, 129, 128, 127, 115 (Ph), 116 (CN), 106 (C=), 74 (OCH_2), 64 ($OCOCH_2$), 59 (OCH_3); IR: (cm^{-1}) 2992 (m, C-H), 2228 (m, CN), 1734 (s, C=O), 1585 (s, C=C), 1263 (s, C-O-CH_3), 708 (s, C-H out of plane). Anal. calcd. for $C_{13}H_{12}BrNO_3$: C, 50.34; H, 3.90; N, 4.52; Found: C, 48.14; H, 3.86; N, 4.54.

3.1.2. ***2-Methoxyethyl 3-bromophenylcyanoacrylate***

Yield: 95%; mp 56.2°C; ^{1}H NMR: δ8.2 (s, 1H, CH=), 8.1-7.3 (m, 4H, Ph), 4.5 (t, 2H, $OCOCH_2$), 3.7 (t, 2H, OCH_2), 3.4 (s, 3H, OCH_3); ^{13}C NMR: δ162 (C=O), 153 (HC=), 132, 131, 130 (Ph), 116 (CN), 100 (C=), 64 ($OCOCH_2$), 59 (OCH_3); IR: (cm^{-1}) 2982 (m, C-H), 2224 (m, CN), 1747 (s, C=O), 1609 (s, C=C), 1257 (s, C-O-CH_3), 781, 677 (s, C-H out of plane). Anal. calcd. for $C_{13}H_{12}BrNO_3$: C, 50.34; H, 3.90; N, 4.52; Found: C, 48.03; H, 3.63; N, 4.57.

3.1.3. ***2-Methoxyethyl 4-bromophenylcyanoacrylate***

Yield 73%; mp 42.4°C; ^{1}H NMR δ8.2 (s, 1H, CH=), 7.9-6.9 (m, 4H, Ph), 4.8 (t, 2H, $OCOCH_2$), 3.7 (t, 2H, OCH_2), 3.4 (s, 3H, OCH_3); ^{13}C NMR: δ 162 (C=O), 154 (HC=), 132, 131, 130 (Ph), 115 (CN), 103 (C=), 70 (OCH_2), 66 ($OCOCH_2$), 59 (OCH_3); IR: (cm^{-1}) 2928 (m, C-H), 2220 (m, CN), 1732 (s, C=O), 1603 (s, C=C), 1257 (s, C-O-CH_3), 791 (s, C-H out of plane). Anal. calcd. for $C_{13}H_{12}BrNO_3$: C, 50.34; H, 3.90; N, 4.52; Found: C, 48.09; H, 3.77; N, 4.19.

3.1.4. ***2-Methoxyethyl 2-chlorophenylcyanoacrylate***

Yield 82%; ^{1}H NMR δ8.2 (s, 1H, CH=), 7.9-7.3 (m, 4H, Ph), 4.3 (t, 2H, $OCOCH_2$), 3.7 (t, 2H, OCH_2), 3.4 (s, 3H, CH_3O); ^{13}C NMR δ 164 (C=O), 155 (HC=), 134, 133, 130, 129 (Ph), 115 (CN), 106 (C=), 70 (OCH_2), 66 ($OCOCH_2$), 59 (OCH_3); IR (cm^{-1}): 2884 (m, C-H), 2226 (m, CN), 1732 (s, C=O), 1609 (s, C=C), 1203 (s, C-O-CH_3), 862, 750 (s, C-H out of plane). Anal. Calcd. for $C_{13}H_{12}ClNO_3$: C, 58.77; H, 4.55; N, 5.27; Found: C, 54.77; H, 4.64; N, 5.17.

3.1.5. ***2-Methoxyethyl 3-chlorophenyl)phenylcyanoacrylate***

Yield 72%; mp 58.1°C; ^{1}H NMR δ8.2 (s, 1H, CH=), 7.9-7.3 (m, 4H, Ph), 4.8 (t, 2H, $OCOCH_2$), 3.7 (t, 2H, OCH_2), 3.4 (s, 3H, CH_3O); ^{13}C NMR δ 162 (C=O), 153 (HC=), 137, 135, 134, 130, 129 (Ph), 115 (CN), 105 (C=), 70 (OCH_2), 66 ($OCOCH_2$), 59 (OCH_3); IR (cm^{-1}): 2945 (m, C-H), 2226 (m, CN), 1717 (s, C=O), 1609 (s, C=C), 1271 (s, C-O-CH_3), 851, 787 (s, C-H out of plane). Anal. Calcd. for $C_{13}H_{12}ClNO_3$: C, 58.77; H, 4.55; N, 5.27; Found: C, 55.63; H, 4.51; N, 5.40.

3.1.6. ***2-Methoxyethyl 4-chlorophenoxy)phenylcyanoacrylate***

Yield 87%; mp 86.9°C; ^{1}H NMR δ8.2 (s, 1H, CH=), 8.1-7.3 (m, 4H, Ph), 4.8 (t, 2H, $OCOCH_2$), 3.7 (t, 2H, OCH_2), 3.4 (s, 3H, CH_3O); ^{13}C NMR δ162 (C=O), 154 (HC=), 140, 132, 131, 130, 129 (Ph), 115 (CN), 103 (C=), 70 (OCH_2), 66 ($OCOCH_2$), 59 (OCH_3); IR (cm^{-1}): 2899 (m, C-H), 2222 (m, CN), 1724 (s, C=O), 1612 (s, C=C), 1290 (s, C-O-CH_3), 829, 760 (s, C-H out of plane). Anal. Calcd. for $C_{13}H_{12}ClNO_3$: C, 58.77; H, 4.55; N, 5.27; Found: C, 56.06; H, 4.63; N, 5.60.

3.1.7. ***2-Methoxyethyl 2-fluorophenylcyanoacrylate***

Yield 84; ^{1}H NMR δ8.6 (s, 1H, CH=), 8.4-7.0 (m, 4H, Ph), 4.5 (t, 2H, $OCOCH_2$), 3.7 (t, 2H, OCH_2), 3.4 (s, 3H, CH_3O); ^{13}C NMR δ163 (C=O), 154 (HC=), 146, 135, 129, 125, 120 (Ph), 117 (CN), 105 (C=), 70 (OCH_2), 65 ($OCOCH_2$), 59 (OCH_3); IR (cm^{-1}): 2934 (m, C-H), 2228 (m, CN), 1742 (s, C=O), 1610 (s, C=C), 1236 (s, C-O-CH_3), 804 (s, C-H out of plane). Anal. Calcd. for $C_{13}H_{12}FNO_3$: C, 62.65; H, 4.85; N, 5.62; Found: C, 63.42; H, 4.61; N, 5.49.

3.1.8. ***2-Methoxyethyl 3-fluorophenylcyanoacrylates***

Yield 78%; ^{1}H NMR δ8.2 (s, 1H, CH=), 7.8-7.0 (m, 4H, Ph), 4.5 (t, 2H, $OCOCH_2$), 3.7 (t, 2H, OCH_2), 3.4 (s, 3H, CH_3O); ^{13}C NMR δ163 (C=O), 153 (HC=), 133, 132, 127, 122, 120, 117 (Ph), 116 (CN), 104 (C=), 70 (OCH_2), 65 ($OCOCH_2$), 59 (OCH_3); IR (cm^{-1}): 2935 (m, C-H), 2224 (m, CN), 1734 (s, C=O), 1614 (s, C=C), 1227 (s, C-O-CH_3), 872, 762 (s, C-H out of plane). Anal. Calcd. for $C_{13}H_{12}FNO_3$: C, 62.65; H, 4.85; N, 5.62; Found: C, 58.15; H, 4.75; N, 5.55.

3.1.9. ***2-Methoxyethyl 4-fluorophenylcyanoacrylate***

Yield 77%; ^{1}H NMR δ8.2 (s, 1H, CH=), 8.1-7.1 (m, 4H, Ph), 4.5 (t, 2H, $OCOCH_2$), 3.7 (t, 2H, OCH_2), 3.5 (s, 3H, CH_3O); ^{13}C NMR δ164 (C=O), 154 (HC=), 133, 129, 116 (Ph), 115 (CN), 102 (C=), 70 (OCH_2), 65 ($OCOCH_2$), 62 (OCH_3); IR (cm^{-1}): 2966 (m, C-H), 2224 (m, CN), 1720 (s, C=O), 1597 (s, C=C), 1240 (s, C-O-CH_3), 841 (s, C-H out of plane). Anal. Calcd. for $C_{13}H_{12}FNO_3$: C, 62.65; H, 4.85; N, 5.62; Found: C, 60.33; H, 4.96; N, 5.85.

3.1.10. ***2-Methoxyethyl 2-trifluoromethylphenylcyanoacrylates***

Yield 91%; ^{1}H NMR δ8.1 (s, 1H, CH=), 7.9-7.6 (m, 4H, Ph), 4.3 (t, 2H, $OCOCH_2$), 3.6 (t, 2H, OCH_2), 3.4 (s, 3H, CH_3O); ^{13}C NMR δ164 (C=O), 152 (HC=), 133, 132, 131, 126 (Ph), 114 (CN), 125 (CF_3), 120 (C=), 70 (OCH_2), 64 ($OCOCH_2$), 59 (OCH_3); IR (cm^{-1}): 2935 (m, C-H), 2231 (m, CN), 1749 (s, C=O), 1601 (s, C=C), 1296 (s, C-O-CH_3), 819, 771 (s, C-H out of plane). Anal. Calcd. for $C_{14}H_{12}F_3NO_3$: C, 56.19; H, 4.04; N, 4.68; Found: C, 52.98; H, 4.42; N, 4.44.

3.1.11. ***2-Methoxyethyl 3-trifluoromethylphenylcyanoacrylates***

Yield 81%; ^{1}H NMR δ8.3 (s, 1H, CH=), 8.2-7.5 (m, 4H, Ph), 4.5 (t, 2H, $OCOCH_2$), 3.7 (t, 2H, OCH_2), 3.4 (s, 3H, CH_3O); ^{13}C NMR δ163 (C=O), 153 (HC=), 137, 133, 132, 124 (Ph), 125 (CF_3), 116 (CN), 105 (C=), 69 (OCH_2), 64 ($OCOCH_2$), 59 (OCH_3); IR (cm^{-1}): 2914 (m, C-H), 2235 (m, CN), 1718 (s, C=O), 1609 (s, C=C), 1227 (s, C-O-CH_3), 866, 806, 762 (s, C-H out of plane). Anal. Calcd. for $C_{14}H_{12}F_3NO_3$: C, 56.19; H, 4.04; N, 4.68; Found: C, 52.98; H, 4.42; N, 4.44.

3.1.12. ***2-Methoxyethyl 4-trifluoromethylphenylcyanoacrylates***

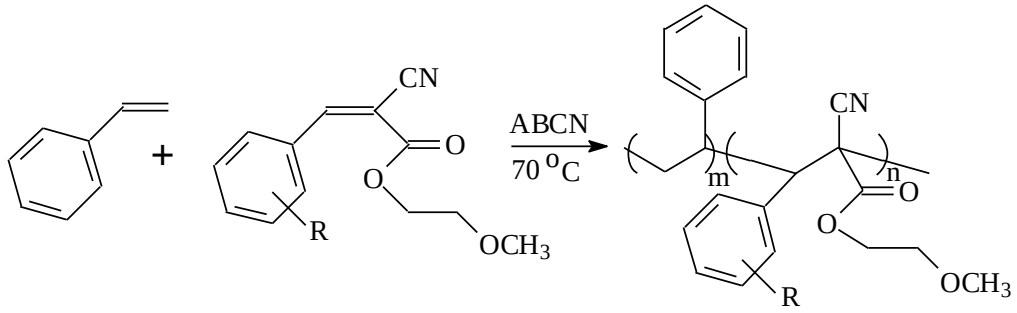
Yield 74%; mp 78.6°C; ^{1}H NMR δ8.3 (s, 1H, CH=), 8.2-7.7 (m, 4H, Ph), 4.5 (t, 2H, $OCOCH_2$), 3.7 (t, 2H, OCH_2), 3.5 (s, 3H, CH_3O); ^{13}C NMR δ162 (C=O), 153 (HC=), 134, 133, 131 (Ph), 126 (CF_3), 115 (CN), 106 (C=), 70 (OCH_2), 66 ($OCOCH_2$), 59 (OCH_3); IR (cm^{-1}): 2955 (m, C-H), 2228 (m, CN), 1726 (s, C=O), 1616 (s, C=C), 1121 (s, C-O-CH_3), 849, 764, 608 (s, C-H out of plane). Anal. Calcd. for $C_{14}H_{12}F_3NO_3$: C, 56.19; H, 4.04; N, 4.68; Found: C, 51.29; H, 3.86; N, 4.84.

3.2. *Homopolymerization*

An attempted homopolymerization of the MEPA 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 [14]. Homopolymerization of styrene (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 – MEPA copolymers*

Copolymers of the ST and the MEPA compounds, P(ST-co-MEPA) were prepared in 25-mL glass screw cap vials at ST/MEPA = 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 70ºC. 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 MEPA monomers). The novel synthesized MEPA 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 halogen ring-substituted 2-methoxyethyl phenylcyanoacrylates, RPhCH = $C(CN)CO_2CH_2CH_2OCH_3$, where R is 2-bromo, 3-bromo, 4-bromo, 2-chloro, 3-chloro, 4-chloro, 2-fluoro, 3-fluoro, 4-fluoro, 2-trifluoromethyl, 3-trifluoromethyl, 4-trifluoromethyl.

Table 1. Copolymerization of Styrene and 2-Methoxyethyl phenylcyanoacrylates.

R	Yield[a] (wt%)	N (wt%)	ST in copol. (mol%)	MEPA in copol. (mol%)
2-Bromo	11.2	2.32	73.8	26.2
3-Bromo	14.3	2.51	70.4	29.6
4-Bromo	12.3	2.36	73.1	26.9
2-Chloro	16.7	2.56	73.0	27.0
3-Chloro	15.2	2.64	71.8	28.2
4-Chloro	12.3	2.55	73.2	26.8
2-Fluoro	14.4	2.63	73.1	26.9
3-Fluoro	12.9	2.64	73.0	27.0
4-Fluoro	14.5	2.58	73.8	26.2
2-Trifluoromethyl	12.6	1.75	82.8	17.2
3-Trifluoromethyl	13.5	2.12	77.7	22.3
4-Trifluoromethyl	14.4	2.25	75.7	24.3

Nitrogen elemental analysis showed that between 17.2 and 29.6 mol% of MEPA is present in the copolymers prepared at ST/MEPA = 3 (mol), which is indicative of

relatively high reactivity of the MEPA monomers towards ST radical which is typical of phenoxy ring-substituted phenylcyanoacrylates [18-24]. Since MEPA monomers do not homopolymerize, the most likely structure of the copolymers would be isolated MEPA 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 ring-substituted 2-methoxyethyl phenylcyanoacrylates, $RPhCH=C(CN)CO_2CH_2CH_2OCH_3$ (where R is 2-bromo, 3-bromo, 4-bromo, 2-chloro, 3-chloro, 4-chloro, 2-fluoro, 3-fluoro, 4-fluoro, 2-trifluoromethyl, 3-trifluoromethyl, 4-trifluoromethyl) were prepared and copolymerized with styrene.

Acknowledgments

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