Synthesis and styrene copolymerization of novel trisubstituted ethylenes:

2. Alkoxy ring-substituted 2-methoxyethyl phenylcyanoacrylates

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Abstract

Novel trisubstituted ethylenes, alkoxy ring-substituted 2-methoxyethyl phenylcyanoacrylates, $RPhCH=C(CN)CO_2CH_2CH_2OCH_3$ (where R is 2-methoxy, 3-methoxy, 4-methoxy, 2-ethoxy, 3-ethoxy, 4-ethoxy, 4-propoxy, 4-butoxy, 4-hexyloxy) 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, ^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.

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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 alkoxy ring-substituted PCAs, such esters as methyl [18], ethyl [19], propyl [20], isopropyl [21], and butyl [22].

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 alkoxy ring-substituted 2-methoxyethyl phenylcyanoacrylates, $RPhCH=C(CN)CO_2CH_2CH_2OCH_3$, where R is 2-methoxy, 3-methoxy, 4-methoxy, 2-ethoxy, 3-ethoxy, 4-ethoxy, 4-propoxy, 4-butoxy, 4-hexyloxy, 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 [23].

2. Experimental

2.1. Materials

2-Methoxy (≥97.5%), 3-methoxy (98%), 4-methoxy (98%), 2-ethoxy (98%), 3-ethoxy(95%), 4-ethoxy (96%), 4-propoxy (≥97%), 4-butoxy (95%), 4-hexyloxy (96%) 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 [24] of appropriate benzaldehydes with 2-methoxyethyl cyanoacetate, catalyzed by base, piperidine (Scheme 1).
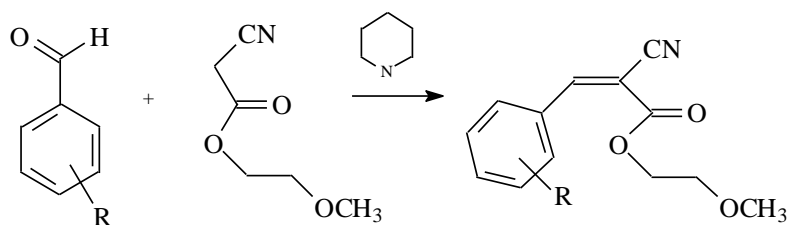
Scheme 1. Synthesis of 2-methoxyethyl phenylcyanoacrylates where R is 2-methoxy, 3-methoxy, 4-methoxy, 2-ethoxy, 3-ethoxy, 4-ethoxy, 4-propoxy, 4-butoxy, 4-hexyloxy.

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-methoxyphenylcyanoacrylate*

Yield: 93%; mp 61.8°C; ^{1}H NMR: δ 8.8 (s, 1H, CH=), 8.3, 7.6, 7.1, 6.9 (s, 4H, Ph), 4.5 (t, 2H, OCOCH$_2$), 3.9 (s, 3H, CH$_3$OPh), 3.7 (t, 2H, OCH$_2$), 3.4 (s, 3H, OCH$_3$);
^{13}C NMR: δ 163 (C=O), 150 (HC=), 135, 129, 128, 121 (Ph), 116 (CN), 103 (C=), 74 (OCH$_2$), 65 (OCOCH$_2$), 59 (OCH$_3$), 56 (PhOCH$_3$); IR: (cm^{-1}) 2891 (m, C-H), 2222 (m,

CN), 1728 (s, C=O), 1597 (s, C=C), 1263 (s, C-O-CH$_3$), 758 (s, C-H out of plane). Anal. calcd. for C$_{15}$H$_{16}$NO$_4$: C, 64.36; H, 5.79; N, 5.36; Found: C, 62.89; H, 5.65; N, 5.45.

3.1.2. *2-Methoxyethyl 3-methoxyphenylcyanoacrylate*

Yield 84%; ^{1}H NMR δ 8.2 (s, 1H, CH=), 7.7-6.9 (m, 4H, Ph), 4.5 (t, 2H, OCOCH$_2$), 3.9 (s, 3H, CH$_3$OPh), 3.7 (t, 2H, OCH$_2$), 3.4 (s, 3H, OCH$_3$); ^{13}C NMR: δ 163 (C=O), 156 (HC=), 134, 133, 130, 124, 121 (Ph), 116 (CN), 103 (C=), 74 (OCH$_2$), 66 (OCOCH$_2$), 59 (OCH$_3$), 56 (PhOCH$_3$); IR: (cm^{-1}) 2945 (m, C-H), 2215 (m, CN), 1730 (s, C=O), 1634 (s, C=C), 1242 (s, C-O-CH$_3$), 769 (s, C-H out of plane). Anal. calcd. for C$_{15}$H$_{16}$NO$_4$: C, 64.36; H, 5.79; N, 5.36; Found: C, 61.19; H, 5.85; N, 5.52.

3.1.3. *2-Methoxyethyl 4-methoxyphenylcyanoacrylate*

Yield 73%; ^{1}H NMR δ 8.2 (s, 1H, CH=), 8.1-6.8 (m, 4H, Ph), 4.5 (t, 2H, OCOCH$_2$), 3.9 (s, 3H, CH$_3$OPh), 3.7 (t, 2H, OCH$_2$), 3.4 (s, 3H, OCH$_3$); ^{13}C NMR: δ 163 (C=O), 154 (HC=), 149, 133, 132, 130, 125 (Ph), 116 (CN), 99 (C=), 74 (OCH$_2$), 66 (OCOCH$_2$), 57 (OCH$_3$), 56 (PhOCH$_3$); IR: (cm^{-1}) 2949 (m, C-H), 2210 (m, CN), 1715 (s, C=O), 1624 (s, C=C), 1263 (s, C-O-CH$_3$), 841, 814, 762 (s, C-H out of plane). Anal. calcd. for C$_{15}$H$_{16}$NO$_4$: C, 64.36; H, 5.79; N, 5.36; Found: C, 63.19; H, 5.82; N, 5.43.

3.1.4. *2-Methoxyethyl 2-ethoxyphenylcyanoacrylate*

Yield 74%; ^{1}H NMR δ 8.8 (s, 1H, CH=), 8.6-6.7 (m, 4H, Ph), 4.4 (t, 2H, OCOCH$_2$), 4.1 (q, 2H, CH$_2$OPh), 3.7 (t, 2H, OCH$_2$), 3.4 (s, 3H, CH$_3$O), 1.3 (s, 3H, CH$_2$C<u>H</u>$_3$); ^{13}C NMR δ 163 (C=O), 150 (HC=), 145, 130, 129, 121, 112 (Ph), 115 (CN), 102 (C=), 70 (OCH$_2$), 64 (CH$_3$<u>C</u>H$_2$O), 64 (OCOCH$_2$), 59 (OCH$_3$), 15 (<u>C</u>H$_3$CH$_2$O); IR (cm^{-1}): 2984 (m, C-H),

2222 (m, CN), 1728 (s, C=O), 1597 (s, C=C), 1261 (s, C-O-CH$_3$), 754 (s, C-H out of plane). Anal. Calcd. for C$_{15}$H$_{17}$NO$_4$: C, 65.44; H, 6.22; N, 5.09; Found: C, 63.09; H, 6.52; N, 5.34.

3.1.5. *2-Methoxyethyl 3-ethoxyphenylcyanoacrylate*

Yield 79%; ^{1}H NMR δ 8.1 (s, 1H, CH=), 7.6 – 6.7 (m, 4H, Ph), 4.2 (t, 2H, OCOCH$_2$), 4.1 (q, 2H, CH$_2$OPh), 3.6 (t, 2H, OCH$_2$), 3.4 (s, 3H, CH$_3$O), 1.4 (s, 3H, CH$_2$C$\underline{H}_3$); ^{13}C NMR δ 164 (C=O), 149 (HC=), 141, 131, 130, 122, 21, 115 (Ph), 116 (CN), 101 (C=), 70 (OCH$_2$), 64 (CH$_3$$\underline{C}H_2$O), 63 (OCOCH$_2$), 59 (OCH$_3$), 14 ($\underline{C}H_3CH_2$O); IR (cm^{-1}): 2957 (m, C-H), 2224 (m, CN), 1730 (s, C=O), 1568 (s, C=C), 1267 (s, C-O-CH$_3$), 772 (s, C-H out of plane). Anal. Calcd. for C$_{15}$H$_{17}$NO$_4$: C, 65.44; H, 6.22; N, 5.09; Found: C, 63.11; H, 6.80; N, 5.23.

3.1.6. *2-Methoxyethyl 4-ethoxyphenylcyanoacrylate*

Yield 92%; ^{1}H NMR δ 8.2 (s, 1H, CH=), 8.0-6.7 (m, 4H, Ph), 4.4 (t, 2H, OCOCH$_2$), 4.1 (q, 2H, CH$_2$OPh), 3.7 (t, 2H, OCH$_2$), 3.4 (s, 3H, CH$_3$O), 1.3 (s, 3H, CH$_2$C$\underline{H}_3$); ^{13}C NMR δ 165 (C=O), 151 (HC=), 134, 132, 131, 130, 115 (Ph), 116 (CN), 99 (C=), 70 (OCH$_2$), 65 (CH$_3$$\underline{C}H_2$O), 64 (OCOCH$_2$), 59 (OCH$_3$), 15 ($\underline{C}H_3CH_2$O); IR (cm^{-1}): 2995 (m, C-H), 2220 (m, CN), 1726 (s, C=O), 1587 (s, C=C), 1267 (s, C-O-CH$_3$), 838 (s, C-H out of plane). Anal. Calcd. for C$_{15}$H$_{17}$NO$_4$: C, 65.44; H, 6.22; N, 5.09; Found: C, 62.97; H, 6.43; N, 5.99.

3.1.7. *2-Methoxyethyl 4-propoxyphenylcyanoacrylate*

Yield 74%; mp 78.4°C; ^{1}H NMR δ 8.2 (s, 1H, CH=), 8.0, 6.9 (m, 4H, Ph), 4.4 (t, 2H, OCOCH$_2$), 4.0 (t, 2H, CH$_3$CH$_2$C$\underline{H}_2$O), 3.7 (t, 2H, CH$_2$O), 3.4 (s, 3H, OCH$_3$), 1.8 (m, 2H, CH$_3$C$\underline{H}_2$CH$_2$O), 1.0 (t, 3H, C$\underline{H}_3$CH$_2$CH$_2$); ^{13}C NMR δ 163 (C=O), 155 (HC=), 134, 132, 125, 115, 114 (Ph), 116 (CN), 99 (C=), 70 (CH$_3$CH$_2$C$\underline{H}_2$O), 69 (OCH$_2$), 64 (OCOCH$_2$), 58 (OCH$_3$), 23 (CH$_3$C$\underline{H}_2$CH$_2$O), 10 (CH$_3$); IR (cm^{-1}): 3031-2815 (m, C-H), 2220 (m, CN), 1722 (s, C=O), 1564 (C=C), 1287 (s, C-O-CH$_3$), 837 (s, C-H out of plane). Anal. Calcd. for C$_{16}$H$_{19}$NO$_4$: C, 66.42; H, 6.62; N, 4.84; Found: C, 67.86; H, 6.94; N, 4.92.

3.1.8. *2-Methoxyethyl 4-butoxyphenylcyanoacrylates*

Yield 73; ^{1}H NMR δ 8.2 (s, 1H, CH=), 7.9, 6.9 (s, 4H, Ph), 4.4 (t, 2H, OCOCH$_2$), 4.0 (t, 2H, C$_3$H$_7$C$\underline{H}_2$O), 3.7 (t, 2H, OCH$_2$), 3.4 (s, 3H, OCH$_3$), 1.8 (m, 2H, C$_2$H$_5$C$\underline{H}_2$CH$_2$O), 1.5 (m, 2H, CH$_3$C$\underline{H}_2$CH$_2$CH$_2$O), 1.0 (t, 3H, C$\underline{H}_3$CH$_2$CH$_2$CH$_2$O); ^{13}C NMR δ 164 (C=O), 155 (HC=), 134, 133, 124, 120, 115, 114 (Ph), 116 (CN), 99 (C=), 70 (OCH$_2$), 68 (C$_3$H$_7$C$\underline{H}_2$O), 64 (OCOCH$_2$), 31 (C$_2$H$_5$C$\underline{H}_2$CH$_2$O), 19 (CH$_3$C$\underline{H}_2$CH$_2$CH$_2$O), 14 (C$\underline{H}_3$CH$_2$CH$_2$CH$_2$O); IR (cm^{-1}): 3937 (m, C-H), 2222 (m, CN), 1726 (s, C=O), 1587 (C=C), 1263 (s, C-O-CH$_3$), 970 (s, C-H out of plane). Anal. Calcd. for C$_{17}$H$_{21}$NO$_4$: C, 67.31; H, 6.98; N, 4.62; Found: C, 65.48; H, 7.06; N, 4.85.

3.1.9. *2-Methoxyethyl 4-hexyloxyphenylcyanoacrylate*

Yield 72.0%; ^{1}H NMR δ 8.2 (s, 1H, CH=), 8.0, 6.9 (s, 4H, Ph), 4.5 (t, 2H, OCOCH$_2$), 4.0 (m, 2H, C$_5$H$_{11}$CH$_2$), 3.6 (t, 2H, CH$_2$O), 3.4 (s, 3H, OCH$_3$), 1.8 (m, 2H, C$\underline{H}_2$CH$_2$O), 1.6 (m, 2H, C$\underline{H}_2$CH$_2$CH$_2$O), 1.4 (m, 4H, C$\underline{H}_2$CH$_2$CH$_2$CH$_2$O & C$\underline{H}_2$CH$_2$CH$_2$CH$_2$CH$_2$O), 0.9

(d, 3H, CH$_3$); ^{13}C NMR δ 164 (C=O), 155 (HC=), 134, 125, 124 (Ph), 116 (CN), 99

(C=), 70 (OCH$_2$), 68 (C$_5$H$_{11}$CH$_2$O), 64 (OCOCH$_2$), 58 (OCH$_3$), 32 (CH$_2$CH$_2$CH$_2$CH$_2$O),

29 (CH$_2$CH$_2$O), 25 (CH$_2$CH$_2$CH$_2$O), 22 (CH$_3$CH$_2$), 14 (CH$_3$CH$_2$); IR (cm^{-1}): 3068 (m, C-

H), 2215 (m, CN), 1728 (s, C=O), 1587 (C=C), 1266 (s, C-O-CH$_3$), 724 (s, C-H out of

plane). Anal. Calcd. for C$_{19}$H$_{25}$NO$_4$: C, 68.86; H, 7.60; N, 4.23; Found: C, 16.19; H, 7.93;

N, 4.33.

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).
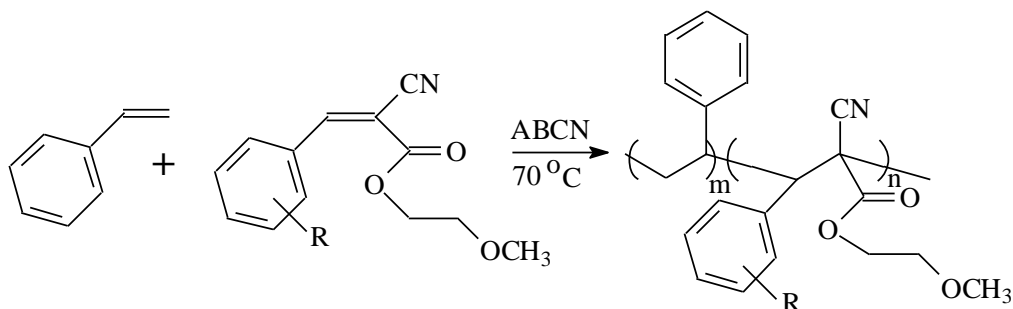
Scheme 2. Copolymerization of ST and alkoxy ring-substituted 2-methoxyethyl

phenylcyanoacrylates, $RPhCH = C(CN)CO_2CH_2CH_2OCH_3$. R is 2-methoxy, 3-methoxy, 4-

methoxy, 2-ethoxy, 3-ethoxy, 4-ethoxy, 4-propoxy, 4-butoxy, 4-hexyloxy.

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

R	Yield[a] (wt%)	N (wt%)	ST in copol. (mol%)	MEPA in copol. (mol%)
2-methoxy	14.2	2.78	70.0	30.0
3-methoxy	12.3	2.02	80.6	19.4
4-methoxy	11.2	2.22	78.0	22.0
2-Ethoxy	14.9	2.43	74.3	25.7
3-Ethoxy	13.6	2.66	70.7	29.3
4-Ethoxy	13.4	2.19	77.8	22.2
4-Propoxy	11.2	1.99	79.9	20.1
4-Butoxy	12.6	2.28	74.9	25.1
4-Hexyloxy	13.5	2.09	76.5	23.5

Nitrogen elemental analysis showed that between 19.4 and 30.0 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 alkoxy ring-substituted phenylcyanoacrylates [18-22]. 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, alkoxy ring-substituted 2-methoxyethyl phenylcyanoacrylates, RPhCH=C(CN)CO$_2$CH$_2$CH$_2$OCH$_3$ (where R is 2-methoxy, 3-methoxy, 4-methoxy, 2-ethoxy, 3-ethoxy, 4-ethoxy, 4-propoxy, 4-butoxy, 4-hexyloxy) were prepared and copolymerized with styrene.

Acknowledgments

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