Synthesis and styrene copolymerization of novel mono, di, and tri ring-substituted tert-butyl phenylcyanoacrylates

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Abstract

Novel ring-substituted tert-butyl phenylcyanoacrylates, $RPhCH=C(CN)CO_2C(CH_3)_3$, where R is 4-phenoxy, 3-iodo, 2,4-dimethoxy, 3,4-dimethoxy, 4-ethoxy-3-methoxy, 4-fluoro-3-methoxy, 4-hydoxy-3,5-dimethyl, 2,3,4-trimethoxy, 2,4,5-trimethoxy, were prepared and copolymerized with styrene. The acrylates were synthesized by the piperidine catalyzed Knoevenagel condensation of ring-substituted benzaldehydes and tret-butyl cyanoacetate, and characterized by CHN analysis, IR, ^{1}H and ^{13}C NMR. All the acrylates were copolymerized with styrene in solution with radical initiation at 70°C. The compositions of the copolymers were calculated from nitrogen analysis.

Introduction

4-Phenoxyphenyl decyl phenylcyanoacrylate (PCA) and its derivatives are reported as antimicrobials which prevent bacterial adhesion to surfaces [1]. 2,4-Diethoxyphenyl ethyl PCA is involved in synthesis of (arylmethylene)cyanothioacetamides in a Michael reaction [2]. 2,4-Dimethoxyphenyl propyl PCA [3], 2,5-dimethoxyphenyl isobutyl PCA [4], 2,4-dimethoxyphenyl butyl PCA [5], 2,4-dimethoxyphenyl isopropyl PCA [6] were synthesized and copolymerized with styrene. (*2E*)-3,4-Dimethoxyphenyl t-butyl PCA was involved in conjugate addition of perfluoroarenes to α,β-unsaturated carbonyls enabled by an alkoxide-hydrosilane system [7] and in preparation of acylaminobenzamide derivatives for the treatment of diseases caused by the supermultiplication of vascular intimal cells [8]. 4-Ethoxy-3-methoxyphenyl butyl [9] and isopropyl, as well as 4-hydroxy-3,5-dimethylphenyl isopropyl [10], and 4-fluoro-3-methoxyphenyl isobutyl [11] PCAs were prepared and copolymerized with vinyl benzene. Synthesis and styrene copolymerization was reported for 2,3,4-trimethoxyphenyl isobutyl PCA [12]. 2,4,5-Trimethoxy functionalized styrene was reported as bioactive component of the bark of Duguetia panamensis [13]. It also was mentioned in study of pachypophyllin and pachypostaudins A and B - three bisnorlignans from Pachypodanthium staudtii [14] and in study of anti-inflammatory and antinociceptive activities of a phenylpropanoid-enriched fraction of Duguetia furfuracea [15].

In this work we have prepared novel ring-substituted tert-butyl phenylcyanoacrylates, $RPhCH=C(CN)CO_2C(CH_3)_3$, where R is 4-phenoxy, 3-iodo, 2,4-dimethoxy, 3,4-dimethoxy, 4-ethoxy-3-methoxy, 4-fluoro-3-methoxy, 4-hydoxy-3,5-dimethyl, 2,3,4-trimethoxy, 2,4,5-trimethoxy, 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 [16].

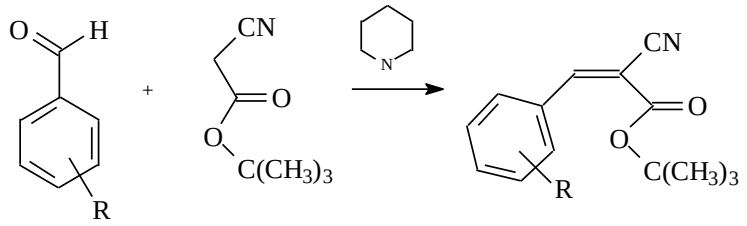
2. Experimental

4-Phenoxy, 3-iodo, 2,4-dimethoxy, 3,4-dimethoxy, 4-ethoxy-3-methoxy, 4-fluoro-3-methoxy, 4-hydoxy-3,5-dimethyl, 2,3,4-trimethoxy, 2,4,5-trimethoxybenzaldehyde, tert-butyl 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. Instrumentation was reported in [17].

3. Results and discussion

3.1. Synthesis and characterization of tert-butyl phenylcyanoacrylates

All tert-butyl phenylcyanoacrylates (TBCA) compounds were synthesized by Knoevenagel condensation [18] of appropriate benzaldehydes with tert-butyl cyanoacetate, catalyzed piperidine (Scheme 1).



Scheme 1. Synthesis of tert-butyl phenylcyanoacrylates where R is 4-phenoxy, 3-iodo, 2,4-dimethoxy, 3,4-dimethoxy, 4-ethoxy-3-methoxy, 4-fluoro-3-methoxy, 4-hydoxy-3,5-dimethyl, 2,3,4-trimethoxy, 2,4,5-trimethoxy.

The preparation procedure was essentially the same for all the monomers. In a typical synthesis, equimolar amounts of tert-butyl 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 compounds were characterized by IR, ^{1}H and ^{13}C NMR, and elemental analysis. No stereochemical analysis of the novel compounds was performed since no stereoisomers (*E* or/and *Z*) of known configuration were available.

3.1.1. Tert-butyl 4-phenoxyphenylcyanoacrylate

Yield 77%; mp 99.7°C; ^{1}H NMR δ 8.0 (s, 1H, CH=), 7.9-6.9 (m, 9H, Ph), 1.5 (s, 9H, CH_3); ^{13}C NMR δ 162 (C=O), 153 (HC=), 156, 133, 130, 126, 125, 120, 119 (Ph), 116 (CN), 102 (C=), 84 (OC), 28 (CH_3); IR (cm^{-1}): 2984 (m, C-H), 2224 (m, CN), 1745 (s, C=O), 1595 (s, C=C), 1269 (s, C-O-CH_3), 842 (s, C-H out of plane). Anal. Calcd. for $C_{20}H_{19}NO_3$: C, 74.75; H, 5.96; N, 4.36; Found: C, 73.44; H, 5.48; N, 4.47.

3.1.2. Tert-butyl 3-iodo-phenylcyanoacrylate

Yield 92%; ^{1}H NMR δ8.2 (s, 1H, CH=), 8.0-6.9 (m, 4H, Ph), 1.6 (s, 9H, CH_3); ^{13}C NMR δ161 (C=O), 152 (HC=), 142, 140, 134, 131, 129 (Ph), 115 (CN), 106 (C=), 84 (OC), 28 (CH_3); IR (cm^{-1}): 2955 (m, C-H), 2239 (m, CN), 1744 (s, C=O), 1610 (s, C=C), 1194 (s, C-O-CH_3), 859 (s, C-H out of plane). Anal. Calcd. for $C_{14}H_{14}INO_2$: C, 47.34; H, 3.97; N, 3.94; Found: C, 47.97; H, 4.10; N, 4.49.

3.1.3. Tert-butyl 2,4-dimethoxyphenylcyanoacrylate

Yield 98%; mp 108.7°C; ^{1}H NMR δ8.6 (s, 1H, CH=), 8.4-6.3 (m, 3H, Ph), 3.9 (s, 6H, CH_3O), 1.6 (s, 9H, CH_3); ^{13}C NMR δ166 (C=O), 148 (HC=), 163, 161, 131, 114, 106, 100 (Ph), 117 (CN), 98 (C=), 85 (OC), 56 (CH_3O), 28 (CH_3); IR (cm^{-1}): 2999 (m, C-H), 2224 (m, CN), 1734 (s, C=O), 1597 (s, C=C), 1290 (s, C-O-CH_3), 782 (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, 61.59; H, 5.21; N, 6.63.

3.1.4. Tert-butyl 3,4-dimethoxyphenylcyanoacrylate

Yield 98%; ^{1}H NMR δ8.1 (s, 1H, CH=), 7.8-6.8 (m, 3H, Ph), 3.9 (s, 6H, CH_3O), 1.6 (s, 9H, CH_3); ^{13}C NMR δ162 (C=O), 149 (HC=), 153, 128, 112, 111 (Ph), 117 (CN), 101 (C=), 83 (OC), 56 (CH_3O), 28 (CH_3); IR (cm^{-1}): 2974 (m, C-H), 2241 (m, CN), 1704 (s, C=O), 1614 (s, C=C), 1250 (s, C-O-CH_3), 779 (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, 64.27; H, 6.50; N, 5.23.

3.1.5. Tert-butyl 4-ethoxy-3-methoxyphenylcyanoacrylate

Yield 90%; mp 94.1°C; ^{1}H NMR δ8.0 (s, 1H, CH=), 7.9-6.7 (m, 3H, Ph), 4.1 (q, 2H, OCH_2), 3.9 (s, 3H, CH_3O), 1.6 (s, 9H, CH_3), 1.4 (t, 3H, $OCH_2C\underline{H}_3$); ^{13}C NMR δ162 (C=O), 153 (HC=), 153, 149, 127, 125, 112 (Ph), 117 (CN), 101 (C=), 83 (OC), 64 (CH_2), 56 (CH_3O), 28 (CH_3), 14 ($CH_2\underline{C}H_3$); IR (cm^{-1}): 2987 (m, C-H), 2245 (m, CN), 1712 (s, C=O), 1641 (s, C=C), 1257 (s, C-O-CH_3), 829 (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, 61.08; H, 5.98; N, 4.60.

3.1.6. Tert-butyl 4-fluoro-3-methoxyphenylcyanoacrylate

Yield 92%; ^{1}H NMR δ8.1 (s, 1H, CH=), 7.9-7.0 (m, 3H, Ph), 3.9 (s, 3H, CH_3O), 1.6 (s, 9H, CH_3); ^{13}C NMR δ161 (C=O), 153 (HC=), 152, 128, 126, 115 (Ph), 117 (CN), 114 (C=), 84 (OC), 56 (CH_3O), 28 (CH_3); IR (cm^{-1}): 2978 (m, C-H), 2239 (m, CN), 1714 (s, C=O), 1612 (s, C=C), 1264 (s, C-O-CH_3), 812 (s, C-H out of plane). Anal. Calcd. for $C_{15}H_{16}FNO_3$: C, 64.97; H, 5.82; N, 5.05; Found: C, 63.92; H, 5.66; N, 6.17.

3.1.7. *Tert-butyl 4-hydroxy-3,5-dimethylphenylcyanoacrylate*

Yield 96%; mp 145.5°C; ^{1}H NMR δ8.0 (s, 1H, CH=), 7.7 (d, 2H, Ph), 5.2 (s, 1H, OH), 2.3 (d, 6H, $PhCH_3$), 1.6 (s, 9H, CH_3); ^{13}C NMR δ162, (C=O), 154 (HC=), 156, 132, 124 (Ph), 116 (CN), 101 (C=), 83 (OC), 28 (CH_3), 16 ($PhCH_3$); IR (cm^{-1}): 3420 (s, OH), 2932 (m, C-H), 2232 (m, CN), 1724 (s, C=O), 1622 (s, C=C), 1284 (s, C-O-C), 889 (s, C-H out of plane). Anal. Calcd. for $C_{16}H_{19}NO_3$: C, 70.31; H, 7.01; N, 5.12; Found: C, 69.36; H, 6.39; N, 5.10.

3.1.8. Tert-butyl 2,3,4-trimethoxyphenylcyanoacrylate

Yield 98%; ^{1}H NMR δ 8.5 (s, 1H, CH=), 8.2, 6.8 (d, 2H, Ph), 4.0 (s, 9H, CH_3OPh), 1.6 (s, 9H, CH_3); ^{13}C NMR δ 162 (C=O), 155 (HC=), 158, 148, 142, 125, 119 (Ph), 117 (CN), 102 (C=), 83 (OC), 62, 61, 56 (CH_3OPh), 28 ($OCCH_3$); IR (cm^{-1}): 2984 (m, C-H), 2245 (m, CN), 1743 (s, C=O), 1528 (s, C=C), 1236 (s, C-O-CH_3), 784 (s, C-H out of plane). Anal. Calcd. for $C_{17}H_{21}NO_5$: C, 63.94; H, 6.63; N, 4.39; Found: C, 63.53; H, 6.16; N, 4.95.

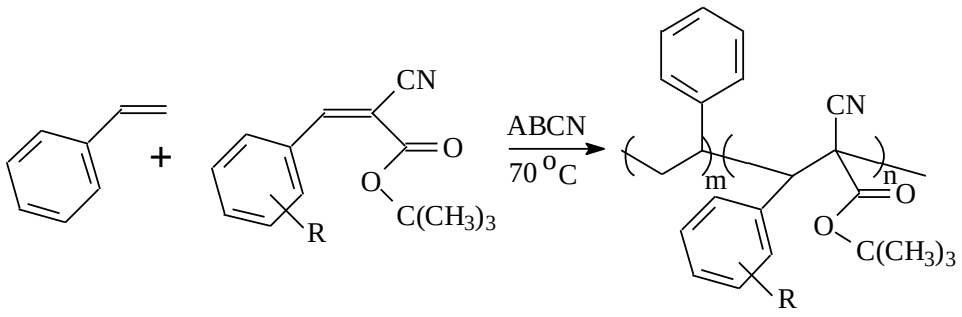
3.1.9. Tert-butyl 2,4,5-trimethoxyphenylcyanoacrylate

Yield 96%; mp 140°C; ^{1}H NMR δ 8.6 (s, 1H, CH=), 8.0, 6.5 (d, 2H, Ph), 4.0 (s, 9H, CH_3OPh), 1.6 (s, 9H, CH_3); ^{13}C NMR δ 162 (C=O), 156 (HC=), 155, 147, 143, 112, 110 (Ph), 117 (CN), 99 (C=), 83 (OC), 56 (CH_3OPh), 28 ($OCCH_3$); IR (cm^{-1}): 2982 (m, C-H), 2240 (m, CN), 1740 (s, C=O), 1522 (s, C=C), 1239 (s, C-O-CH_3), 788 (s, C-H out of plane). Anal. Calcd. for $C_{17}H_{21}NO_5$: C, 63.94; H, 6.63; N, 4.39; Found: C, 61.33; H, 5.95; N, 4.52.

3.2. ***Synthesis and characterization of styrene – TBCA copolymers***

Copolymers of the ST and the TBCA compounds, P(ST-co-TBCA) were prepared in 25-mL glass screw cap vials at ST/ TBCA = 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 TBCA).

The novel synthesized TBCA 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 tert-butyl phenylcyanoacrylates, where R is 4-phenoxy, 3-iodo, 2,4-dimethoxy, 3,4-dimethoxy, 4-ethoxy-3-methoxy, 4-fluoro-3-methoxy, 4-hydoxy-3,5-dimethyl, 2,3,4-trimethoxy, 2,4,5-trimethoxy.

Table 1. Copolymerization of styrene and tert-butyl phenylcyanoacrylates.

R	Yield[a] (wt%)	N (wt%)	ST in copol. (mol%)	TBCA in copol. (mol%)
4-Phenoxy	12.3	2.23	74.7	25.3
3-Iodo	14.6	2.35	69.8	30.2
2,4-Dimethoxy	13.7	1.70	83.7	16.3
3,4-Dimethoxy	13.1	2.05	79.1	20.9
4-Ethoxy-3-methoxy	15.1	1.78	82.3	17.7
4-Fluoro-3-methoxy	16.2	2.64	70.9	29.1
4-Hydoxy-3,5-dimethyl	11.2	1.77	83.3	16.7
2,3,4-Trimethoxy	13.3	2.06	79.6	20.4
2,4,5-Trimethoxy	10.5	1.64	83.7	16.3

Nitrogen elemental analysis showed that between 16.3 and 30.2 mol% of TBCA is present in the copolymers prepared at ST/ TBCA = 3 (mol), which is indicative of relatively high reactivity of the TBCA monomers towards ST radical which is typical of alkoxy ring-substituted TBCA. Since TBCA monomers do not homopolymerize, the most likely structure of the copolymers would be isolated TBCA 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, tert-butyl phenylcyanoacrylates, $RPhCH=C(CN)CO_2C(CH_3)_3$ (where R is 4-phenoxy, 3-iodo, 2,4-dimethoxy, 3,4-dimethoxy, 4-ethoxy-3-methoxy, 4-fluoro-3-methoxy, 4-hydoxy-3,5-dimethyl, 2,3,4-trimethoxy, 2,4,5-trimethoxy) were prepared and copolymerized with styrene.

Acknowledgments

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