Synthesis and styrene copolymerization of novel phenoxy and benzyloxy ring-substituted tert-butyl phenylcyanoacrylates

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Abstract

Novel phenoxy and benzyloxy ring-substituted tert-butyl phenylcyanoacrylates, RPhCH=C(CN)$CO_2C(CH_3)_3$ (where R is 3-phenoxy, 3-(4-chlorophenoxy), 3-(4-methoxyphenoxy), 3-(4-methylphenoxy), 2-benzyloxy, 3-benzyloxy) 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 ethylenes were copolymerized with styrene in solution with radical initiation at 70°C. The compositions of the copolymers were calculated from nitrogen analysis.

1. Introduction

Phenoxy ring-substituted phenylcyanoacrylates served as multipurpose screening compounds [1], as products of microwave-assisted Knoevenagel condensation of ethyl

cyanoacetate with aromatic aldehydes in aqueous triazine-based microporous network [2], in simple, efficient, and green method for synthesis of trisubstituted electrophilic alkenes using Lipase as a Biocatalyst [3], imidazolium chloride immobilized SBA-15 as a heterogenized organocatalyst for solvent free Knoevenagel condensation using microwave [4]. Preparation of ethyl 3-(4-benzyloxyphenyl)-2-cyanoacrylate was reported [5]. This cyanoacrylate was also described in synthesis, biological evaluation, and molecular modeling studies of arylidene-thiazolidinediones with potential hypoglycemic and hypolipidemic activities [6] as well as in its synthesis as analytically pure compounds in flow reactors [7, 8]. The use of electroosmotic flow as a pumping mechanism for semi-preparative scale continuous flow synthesis of this acrylate is reported in [9]. *Para*-benzyloxyphenyl-2-cyanoacrylate is mentioned in synthesis and biological activity studies of novel acridinylidene and benzylidene thiazolidinediones [10]. It is also reported in the preparation and reaction of enolates within micro reactors [11, 12]. Solid-supported continuous flow synthesis of this cyanoacrylate in microreactors using electroosmotic flow (EOF) was described [13-15]. Nucleophilic Michael addition of 2-thioxo-4-imidazolidinone to 3-aryl-2-cyanoacrylates followed by benzylation gave 5-arylidene-3-(4-bromobenzyl)-1-methyl-2-thioxo-4-imidazolidinones. All products were obtained as Z isomers [16]. This cyanoacrylate was involved in preparation of (alkoxybenzyl)pyrrolidinone derivatives as nootropics [17].

Earlier we have reported synthesis and styrene copolymerization of a number of phenoxy and benzyloxy ring-substituted methyl [18-20], ethyl [21], propyl [22, 23], isopropyl [24], butyl [25, 26], isobutyl [27], 2-methoxyethyl [28, 29], and octyl [30] phenylcyanoacrylates.

Thus, in continuation of our investigation of novel trisubstituted ethylene compounds we have prepared tert-butyl phenoxy and benzyloxy ring-substituted phenylcyanoacrylates (OPCA), $RPhCH=C(CN)CO_2C(CH_3)_3$, where R is 3-phenoxy, 3-(4-chlorophenoxy), 3-(4-methoxyphenoxy), 3-(4-methylphenoxy), 2-benzyloxy, 3-benzyloxy, 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 [31].

2. Experimental

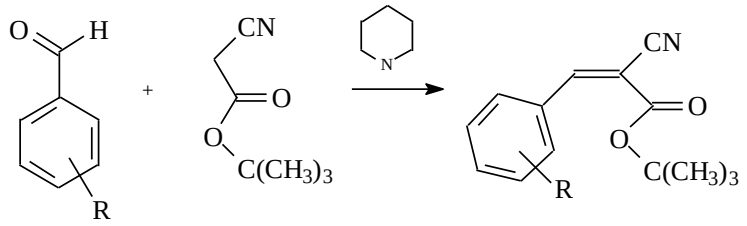
Materials

3-Phenoxy, 3-(4-chlorophenoxy), 3-(4-methoxyphenoxy), 3-(4-methylphenoxy), 2-benzyloxy, 3-benzyloxybenzaldehydes, 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.

3. Results and discussion

3.1. Synthesis and characterization of tert-butyl phenylcyanoacrylates

All tert-butyl phenylcyanoacrylates (OPCA) compounds were synthesized by Knoevenagel condensation [32] of appropriate benzaldehydes with tert-butyl cyanoacetate, catalyzed piperidine (Scheme 1).



Scheme 1. Synthesis of tert-butyl phenylcyanoacrylates where R is 3-phenoxy, 3-(4-chlorophenoxy), 3-(4-methoxyphenoxy), 3-(4-methylphenoxy), 2-benzyloxy, 3-benzyloxy.

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 3-phenoxyphenylcyanoacrylate***

Yield 86%; ^{1}H NMR δ 8.1 (s, 1H, CH=), 7.8-6.9 (m, 9H, Ph), 1.4 (s, 9H, CH_3); ^{13}C NMR δ 162 (C=O), 153 (HC=), 158, 157, 133, 130, 127, 118, 114 (Ph), 115 (CN), 104 (C=), 84 (OC), 28 (CH_3); IR (cm^{-1}): 2957 (m, C-H), 2224 (m, CN), 1725 (s, C=O), 1585 (s, C=C), 1237 (s, C-O-CH_3), 786 (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, 72.15; H, 6.26; N, 4.51.

3.1.2. ***Tert-butyl 3-(4-chlorophenoxy)phenylcyanoacrylate***.

Yield 76%; ^{1}H NMR δ 8.1 (s, 1H, CH=), 7.8-6.8 (m, 8H, Ph), 1.6 (s, 9H, CH_3); ^{13}C NMR δ 162 (C=O), 153 (HC=), 157, 156, 132, 133, 130, 128, 120, 114 (Ph), 116 (CN), 106 (C=), 85 (OC), 27 (CH_3); IR (cm^{-1}): 3100-2820 (m, C-H), 2223 (m, CN), 1724 (s, C=O), 1598 (C=C), 1199 (s, C-O-CH_3), 876 (s, C-H out of plane). Anal. Calcd. for $C_{20}H_{18}ClNO_3$: C, 67.51; H, 5.10; N, 3.94; Found: C, 66.68; H, 5.12; N, 3.17.

3.1.3. ***Tret-butyl 3-(4-methoxyphenoxy)phenylcyanoacrylate***.

Yield 89%; ^{1}H NMR δ 8.1 (s, 1H, CH=), 7.8-6.8 (m, 8H, Ph), 3.8 (s, 3H, $PhOCH_3$), 1.4 (t, 9H, CH_3); ^{13}C NMR δ 161 (C=O), 154 (HC=), 157, 152, 133, 121, 115, 114 (Ph), 116 (CN), 103 (C=), 55 ($PhOCH_3$), 27 (CH_3); IR (cm^{-1}): 2922 (m, C-H), 2222 (m, CN), 1714 (s, C=O), 1502 (C=C), 1283 (s, C-O-CH_3), 877 (s, C-H out of plane). Anal. Calcd. for $C_{21}H_{21}NO_4$: C, 71.78; H, 6.02; N, 3.99; Found: C, 67.96; H, 6.51; N, 4.94.

3.1.4. ***Tret-butyl 3-(4-methylphenoxy)phenylcyanoacrylate***.

Yield 79%; ^{1}H NMR δ 8.1 (s, 1H, CH=), 7.7-6.8 (m, 8H, Ph), 2.3 (s, 3H, $PhCH_3$), 1.4 (t, 3H, CH_3); ^{13}C NMR δ 161 (C=O), 154 (HC=), 158, 155, 133, 131, 130, 119 (Ph), 115 (CN), 105 (C=), 84 (OCO<u>C</u>), 28 $(CH_3)_3$, 21 ($PhCH_3$); IR (cm^{-1}): 2928 (m, C-H), 2226 (m, CN), 1724 (s, C=O), 1614 (s, C=C), 1234 (s, C-O-CH_3), 852 (s, C-H out of plane). Anal. Calcd. for $C_{21}H_{21}NO_3$: C, 75.20; H, 6.31; N, 4.18; Found: C, 78.64; H, 6.55; N, 3.27.

3.1.5. ***Tret-butyl 2-benzyloxyphenylcyanoacrylate***

Yield 74%; mp 88.3°C; ^{1}H NMR δ 8.8 (s, 1H, CH=), 8.4-6.8 (m, 9H, Ph), 5.1 (s, 2H, $PhCH_2$), 1.6 (t, 9H, $(CH_3)_3$); ^{13}C NMR δ 162 (C=O), 147 (HC=), 158, 137, 136, 131, 130, 129, 127, 122, 112 (Ph), 116 (CN), 104 (C=), 84 (OCO<u>C</u>), 71 ($PhCH_2$), 28 $(CH_3)_3$;

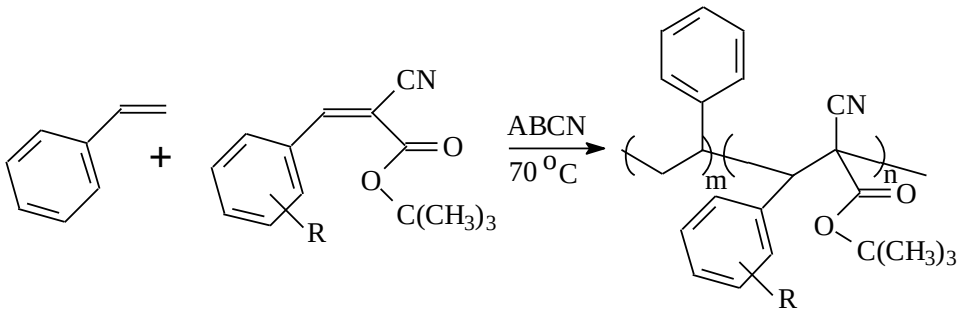
IR (cm^{-1}): 2928 (m, C-H), 2220 (m, CN), 1716 (s, C=O), 1602 (s, C=C), 1248 (s, C-O-CH_3), 751 (s, C-H out of plane). Anal. Calcd. for $C_{21}H_{21}NO_3$: C, 75.20; H, 6.31; N, 4.18; Found: C, 74.43; H, 6.01; N, 4.43.

3.1.6. ***Tert-butyl 3-benzyloxyphenylcyanoacrylate***

Yield 94%; mp 122.2°C; ^{1}H NMR δ8.1 (s, 1H, CH=), 7.7-7.0 (m, 9H, Ph), 5.1 (s, 2H, $PhCH_2$), 1.6 (s, 9H, $(CH_3)_3$); ^{13}C NMR δ161 (C=O), 154 (HC=), 159, 137, 132, 129, 128, 127, 113 (Ph), 116 (CN), 105 (C=), 84 (OC), 70 (OCH_2), 28 (CH_3); IR (cm^{-1}): 2964 (m, C-H), 2221 (m, CN), 1723 (s, C=O), 1592 (s, C=C), 1224 (s, C-O-CH_3), 853 (s, C-H out of plane). Anal. Calcd. for $C_{21}H_{21}NO_3$: C, 75.20; H, 6.31; N, 4.18; Found: C, 75.16; H, 6.53; N, 4.14.

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 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 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 tert-butyl phenylcyanoacrylates, where R is 3-phenoxy, 3-(4-chlorophenoxy), 3-(4-methoxyphenoxy), 3-(4-methylphenoxy), 2-benzyloxy, 3-benzyloxy.

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

R	Yield[a] (wt%)	N (wt%)	ST in copol. (mol%)	OPCA in copol. (mol%)
3-Phenoxy	12.5	3.01	58.1	41.9
3-(4-Chlorophenoxy)	12.2	2.48	66.7	33.3
3-(4-Methoxyphenoxy)	13.8	2.70	61.7	38.3
3-(4-Methylphenoxy)	12.4	2.83	60.6	39.4
2-Benzyloxy	17.1	3.00	85.2	14.8
3-Benzyloxy	14.2	2.50	88.3	11.7

Nitrogen elemental analysis showed that between 11.7 and 41.9 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 alkoxy 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, tert-butyl phenylcyanoacrylates, $RPhCH=C(CN)CO_2CH_2(CH_2)_6CH_3$ (where R is 3-phenoxy, 3-(4-chlorophenoxy), 3-(4-methoxyphenoxy), 3-(4-methylphenoxy), 2-benzyloxy, 3-benzyloxy) were prepared and copolymerized with styrene.

Acknowledgments

The authors are grateful to acknowledge that the project was partly supported by Chicago Society of Coating Technology.

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