Synthesis and styrene copolymerization of novel difluoro and chlorofluoro 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 and Gregory B. Kharas

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

ABSTRACT

Novel difluoro and chlorofluoro ring-disubstituted isobutyl phenylcyanoacrylates, $RPhCH=C(CN)CO_2CH_2CH(CH_3)_2$ (where R is 2,3-difluoro, 2,4-difluoro, 2,6-difluoro, 3,4-difluoro, 3,5-difluoro, 2-chloro-4-fluoro, 2-chloro-6-fluoro, 3-chloro-2-fluoro, 3-chloro-4-fluoro, 4-chloro-3-fluoro) were synthesized by the piperidine catalyzed Knoevenagel condensation of ring-disubstituted benzaldehydes and isobutyl cyanoacetate and characterized by CHN analysis, IR, ^{1}H and ^{13}C NMR. The acrylates were copolymerized with styrene in solution with radical initiation at 70°C. The compositions of the copolymers were calculated from nitrogen analysis.

*Contact: gkharas@depaul.edu

1. Introduction

2,6-Difluoro ring-disubstituted ethyl phenylcyanoacrylate was reported in base-catalyzed cyclocondensation of 2,6-dihalobenzaldehydes, ethyl cyanoacetate, and thiourea [1]. There are citations of difluorophenyl functional group organic reactions, i.e. 1-ethenyl-3,5-difluorobenzene: in nickel-catalyzed reductive cross-coupling of aryl bromides with vinyl acetate [2]; in the stabilized iminium catalyzed (*E*)-polyene cyclization [3]; in selective Rhodium-catalyzed hydroformylation of terminal arylalkynes and conjugated enynes to (poly)enals enabled by a π-acceptor biphosphoramidite ligand [4]; iron-catalysed asymmetric carboazidation of styrenes [5]; in radical asymmetric aminoazidation and diazidation of styrenes [6]; in palladium-catalyzed tandem C-C activation/cyclization induced by carbopalladation of functionalized nitriles for synthesis of benzo dipyrromethenes [7]; in preparation of triazole compounds that modulate HSP90 activity [8]; in solid-phase synthesis of miconazole analogs via an iodoetherification reaction [9]. 1-Chloro-4-ethenyl-2-fluoro-benzene was applied: in hexamethyldisilazane lithium (LiHMDS)-promoted hydroboration of alkynes and alkenes with pinacolborane [10]; in stereoselective gold(I)-catalyzed vinylcyclopropanation via generation of sulfur-substituted vinyl carbene equivalent [11]; in preparation of indazolyl pyridinones and related heterocycles as kinase inhibitors for the treatment of cancer [12]; in quantitation of ERK1/2 inhibitor cellular target occupancies with a reversible slow off-rate probe[13]; in iron-catalyzed carboamination of olefins: synthesis of amines and disubstituted β-amino acids [14]; in development of a practical synthesis of ERK inhibitor GDC-0994 [15, 16].

Earlier we have reported synthesis and styrene copolymerization a number of difluoro and chlorofluoro ring-disubstituted PCAs, such esters as methyl [17-19], ethyl [20], propyl [21-23], isopropyl [24-26], and butyl [27, 28].

In this work we have prepared difluoro and chlorofluoro ring-disubstituted isobutyl PCA, $RPhCH=C(CN)CO_2CH_2CH(CH_3)_2$, where R is 2,3-difluoro, 2,4-difluoro, 2,6-difluoro, 3,4-difluoro, 3,5-difluoro, 2-chloro-4-fluoro, 2-chloro-6-fluoro, 3-chloro-2-fluoro, 3-chloro-4-fluoro, 4-chloro-3-fluoro, and their copolymers with styrene. To the best of our knowledge, there have been no reports on either synthesis of these compounds, nor their copolymerization with styrene [29].

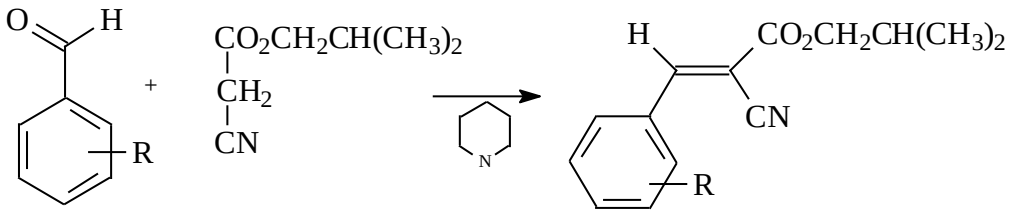
2. Experimental

2,3-Difluoro, 2,4-difluoro, 2,6-difluoro, 3,4-difluoro, 3,5-difluoro, 2-chloro-4-fluoro, 2-chloro-6-fluoro, 3-chloro-2-fluoro, 3-chloro-4-fluoro, 4-chloro-3-fluoro benzaldehydes, isobutyl cyanoacetate, piperidine, styrene, 1,1'-azobis(cyclohexanecarbonitrile) (ABCN), and toluene supplied from Sigma-Aldrich Co., were used as received. Instrumentation details are reported in [30].

3. Results and discussion

3.1. Synthesis and characterization of isobutyl phenylcyanoacrylates

All isobutyl phenylcyanoacrylates (IPCA) compounds were synthesized by Knoevenagel condensation [31] of appropriate benzaldehydes with isobutyl cyanoacetate, catalyzed by base, piperidine (Scheme 1).



Scheme 1. Synthesis of isobutyl R-phenylcyanoacrylates, where R is 2,3-difluoro, 2,4-difluoro, 2,6-difluoro, 3,4-difluoro, 3,5-difluoro, 2-chloro-4-fluoro, 2-chloro-6-fluoro, 3-chloro-2-fluoro, 3-chloro-4-fluoro, 4-chloro-3-fluoro.

The preparation procedure was essentially the same for all the monomers. In a typical synthesis, equimolar amounts of isobutyl 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 reactions was allowed to proceed 48 hrs at r.t. 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. Melting points of the compounds in crystalline state were measured by DSC. The compounds were characterized by IR, ^{1}H and ^{13}C NMR spectroscopies. No stereochemical analysis of the novel ring-substituted IPCA was performed since no stereoisomers (*E* or/and *Z*) of known configuration were available.

3.1.1. ***Isobutyl 2,3-difluorophenylcyanoacrylate***

Yield: 53.3%; ^{1}H NMR: δ 8.2 (s, 1H, CH=), 7.9-7.0 (m, 3H, Ph), 4.1 (d, 2H, CH_2), 2.0 (m, 1H, CH), 1.0 (d, 6H, CH_3); ^{13}C NMR: δ 162 (C=O), 152 (HC=), 151, 146, 144, 125,

124, 120 (Ph), 115 (CN), 106 (C=), 73 (CH_2), 28 (CH), 17 (CH_3); IR: (cm^{-1}) 2964 (m, C-H), 2225 (m, CN), 1732 (s, C=O), 1624 (s, C=C), 1250 (s, C-O-CH_3), 824, 743 (s, C-H out of plane). Anal. calcd. for $C_{14}H_{13}F_2NO_2$: C, 63.39; H, 4.94; N, 5.28; Found: C, 65.52; H, 5.45; N, 6.37.

3.1.2. ***Isobutyl 2,4-difluorophenylcyanoacrylate***

Yield 71.4%; mp 52.8°C; ^{1}H NMR: δ8.5 (s, 1H, CH=), 7.0 (m, 3H, Ph), 4.1 (d, 2H, CH_2), 2.1 (m, 1H, CH), 1.0 (d, 6H, CH_3); ^{13}C NMR: δ168 (C=O), 152 (HC=), 150, 144, 131 (Ph), 116 (CN), 105 (C=), 73 (CH_2), 28 (CH), 19 $(CH_3)_2$; IR: (cm^{-1}) 3132-2813 (m, C-H), 2225 (m, CN), 1722 (s, C=O), 1620 (s, C=C), 1287 (s, C-O-CH_3), 852 (s, C-H out of plane). Anal. calcd. for $C_{14}H_{13}F_2NO_2$: C, 63.39; H, 4.94; N, 5.28; Found: C, 63.11; H, 4.98; N, 5.24.

3.1.3. ***Isobutyl 2,6-difluorophenylcyanoacrylate***

Yield 88.2%; ^{1}H NMR: δ8.3 (s, 1H, CH=), 7.6-6.8 (m, 3H, Ph), 4.2 (d, 2H, CH_2), 2.1 (m, 1H, CH), 1.0 (d, 6H, CH_3); ^{13}C NMR: δ162 (C=O), 159 (HC=), 143, 134, 112, 111 (Ph), 115 (CN), 110 (C=), 73 (CH_2), 28 (CH), 19 $(CH_3)_2$; IR: (cm^{-1}) 2966 (m, C-H), 2232 (m, CN), 1732 (s, C=O), 1628 (s, C=C), 1259 (s, C-O-CH_3), 789, 764 (s, C-H out of plane). Anal. calcd. for $C_{14}H_{13}F_2NO_2$: C, 63.39; H, 4.94; N, 5.28; Found: C, 62.74; H, 5.30; N, 5.87.

3.1.4. ***Isobutyl 3,4-difluorophenylcyanoacrylate***

Yield 74%; mp 78.7°C; ^{1}H NMR δ8.2 (s, 1H, CH=), 8.0-7.0 (m, 3H, Ph), 4.1 (d, 2H, CH_2), 2.0 (m, 1H, CH), 1.0 (d, 6H, CH_3); ^{13}C NMR δ 163 (C=O), 155 (HC=), 149, 129,

127, 120, 118 (Ph), 115 (CN), 104 (C=), 73 (CH_2), 28 (CH), 19 (CH_3); IR (cm^{-1}): 2962 (m, C-H), 2232 (m, CN), 1720 (s, C=O), 1627 (s, C=C), 1269 (s, C-O-CH_3), 786, 759 (s, C-H out of plane). Anal. Calcd. for $C_{14}H_{13}F_2NO_2$: C, 63.39; H, 4.94; N, 5.28; Found: C, 61.46; H, 5.02; N, 5.19.

3.1.5. ***Isobutyl 3,5-difluorophenylcyanoacrylate***

Yield 85.5%; mp 73.3°C; ^{1}H NMR: δ8.2 (s, 1H, CH=), 7.2-5.9 (m, 3H, Ph), 4.1 (d, 2H, CH_2), 2.1 (m, 1H, CH), 1.0 (d, 6H, CH_3); ^{13}C NMR: δ163 (C=O), 152 (HC=), 148, 136, 132, 114 (Ph), 115 (CN), 104 (C=), 73 (CH_2), 28 (CH), 19 (CH_3); IR: (cm^{-1}) 2863 (m, C-H), 2256 (m, CN), 1747 (s, C=O), 1657 (s, C=C), 1256 (s, C-O-CH_3), 841, 752 (s, C-H out of plane). Anal. calcd. for $C_{14}H_{13}F_2NO_2$: C, 63.39; H, 4.94; N, 5.28; Found: C, 60.51; H, 5.21; N, 5.52.

3.1.6. ***Isobutyl 2-chloro-4-fluorophenylcyanoacrylate***

Yield 76.6%; mp 72.1°C; ^{1}H NMR: δ8.6 (s, 1H, CH=), 8.3-7.0 (s, 3H, Ph), 4.1 (d, 2H, CH_2), 2.1 (m, 1H, CH), 1.0 (d, 6H, CH_3); ^{13}C NMR: δ169 (C=O), 152 (HC=), 137, 132, 113, 111, 109 (Ph), 114 (CN), 105 (C=), 74 (CH_2), 28 (CH), 19 $(CH_3)_2$; IR: (cm^{-1}) 2962 (m, C-H), 2225 (m, CN), 1720 (s, C=O), 1591 (s, C=C), 1236 (s, C-O-CH_3), 823, 750 (s, C-H out of plane). Anal. calcd. for $C_{14}H_{13}ClFNO_2$: C, 59.69; H, 4.65; N, 4.97; Found: C, 59.60; H, 4.71; N, 5.06.

3.1.7**.** ***Isobutyl 2-chloro-6-fluorophenylcyanoacrylate***

Yield 82%; ^{1}H NMR δ8.2 (s, 1H, CH=), 7.6-6.9 (m, 3H, Ph), 4.1 (d, 2H, CH_2), 2.1 (m, 1H, CH), 0.9 (d, 6H, CH_3) ; ^{13}C NMR δ163 (C=O), 158 (HC=), 157, 146, 135, 133, 131,

129 (Ph), 115 (CN), 112 (C=), 73 (CH_2), 28 (CH), 19 $(CH_3)_2$; IR (cm^{-1}): 3521-2813 (m, C-H), 2244 (m, CN), 1744 (s, C=O), 1614 (s, C=C), 1228 (s, C-O-CH_3), 812, 752 (s, C-H out of plane). Anal. Calcd. for $C_{14}H_{13}ClFNO_2$: C, 59.69; H, 4.65; N, 4.97; Found: C, 58.26; H, 4.88; N, 5.09.

3.1.8. ***Isobutyl 3-chloro-2-fluorophenylcyanoacrylate***

Yield 46%; ^{1}H NMR δ8.5 (s, 1H, CH=), 8.2-7.2 (s, 3H, Ph), 4.1 (s, 2H, CH_2), 2.0 (m, 1H, CH), 1.0 (d, 6H, $(CH_3)_2$; ^{13}C NMR δ161 (C=O), 156 (HC=), 137, 131, 127, 125, 122 (Ph), 115 (CN), 107 (C=), 73 (CH_2), 28 (CH), 20 $(CH_3)_2$; IR (cm^{-1}): 2956 (m, C-H), 2229 (m, CN), 1734 (s, C=O), 1653 (s, C=C), 1288 (s, C-O-CH_3), 842, 752 (s, C-H out of plane). Anal. Calcd. for $C_{14}H_{13}ClFNO_2$: C, 59.69; H, 4.65; N, 4.97; Found: C, 59.56; H, 4.95; N, 5.16.

3.1.9. ***Isobutyl 3-chloro-4-fluorophenylcyanoacrylate***

Yield 96.6%; mp 124.3°C; ^{1}H NMR: δ8.1 (s, 1H, CH=), 8.0, 7.2 (m, 3H, Ph), 4.1 (d, 2H, CH_2), 2.1 (m, 1H, CH), 1.0 (d, 6H, CH_3); ^{13}C NMR: δ162 (C=O), 152 (HC=), 159, 134, 131, 129, 123, 118 (Ph), 115 (CN), 104 (C=), 73 (CH_2), 28 (CH), 19 $(CH_3)_2$; IR: (cm^{-1}) 2934 (m, C-H), 2228 (m, CN), 1715 (s, C=O), 1567 (s, C=C), 1223 (s, C-O-CH_3), 835, 756 (s, C-H out of plane). Anal. calcd. for $C_{14}H_{13}ClFNO_2$: C, 59.69; H, 4.65; N, 4.97; Found: C, 59.04; H, 4.60; N, 4.65.

3.1.10. ***Isobutyl 4-chloro-3-fluorophenylcyanoacrylate***

Yield 78%; mp 112.1°C; ^{1}H NMR δ8.2 (s, 1H, CH=), 8.0-7.4 (m, 3H, Ph), 4.1 (d, 2H, CH_2), 2.1 (m, 1H, CH), 0.9 (d, 6H, CH_3) ; ^{13}C NMR δ162 (C=O), 152 (HC=), 157, 128,

126, 118, 117, 116 (Ph), 115 (CN), 105 (C=), 73 (CH_2), 28 (CH), 19 $(CH_3)_2$; IR (cm^{-1}): 3519-2827 (m, C-H), 2228 (m, CN), 1717 (s, C=O), 1624 (s, C=C), 1228 (s, C-O-CH_3), 846 (s, C-H out of plane). Anal. Calcd. for $C_{14}H_{13}ClFNO_2$: C, 59.69; H, 4.65; N, 4.97; Found: C, 59.50; H, 4.64; N, 5.04.

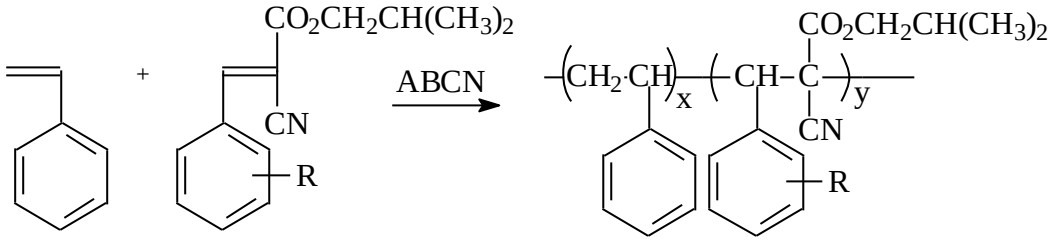
3.2. *Synthesis and characterization of styrene – IPCA copolymers*

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

Table 1. Copolymerization of isobutyl phenylcyanoacrylates with styrene.

R	Yield[a] (wt%)	N (wt%)	ST in copol. (mol%)	IPCA in copol. (mol%)
2,3-Difluoro	12.2	1.76	83.6	16.4
2,4-Difluoro	11.3	3.01	65.8	34.2
2,6-Difluoro	16.4	2.67	71.4	28.6
3,4-Difluoro	14.2	2.62	72.1	27.9
3,5-Difluoro	17.3	1.61	85.3	14.7
2-Chloro-4-fluoro	12.5	2.50	72.8	27.2
2-Chloro-6-fluoro	11.2	2.36	75.0	25.0
3-Chloro-2-fluoro	15.2	2.45	73.6	26.4
3-Chloro-4-fluoro	14.7	2.78	68.1	31.9
4-Chloro-3-fluoro	12.3	2.41	74.2	25.8

Nitrogen elemental analysis showed that between 14.7 and 34.2 mol% of IPCA is present in the copolymers, which is indicative of relatively high reactivity of the IPCA monomers towards ST radical which is typical of halogen ring-substituted different esters PCA [17-29]. Since IPCA monomers do not homopolymerize, the most likely structure of the copolymers would be isolated IPCA monomer (y = 1) units alternating with short ST sequences (x > 1) (Scheme 2).



Scheme 2. Copolymerization of ST and the ring-substituted isobutyl phenylcyanoacrylates, RPhCH = $C(CN)CO_2CH_2CH(CH_3)_2$, R = 2,3-difluoro, 2,4-difluoro, 2,6-difluoro, 3,4-difluoro, 3,5-difluoro, 2-chloro-4-fluoro, 2-chloro-6-fluoro, 3-chloro-2-fluoro, 3-chloro-4-fluoro, 4-chloro-3-fluoro.

.

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 difluoro and chlorofluoro ring-disubstituted isobutyl phenylcyanoacrylates, $RPhCH=C(CN)CO_2CH_2CH(CH_3)_2$ (where R is 2,3-difluoro, 2,4-difluoro, 2,6-difluoro, 3,4-difluoro, 3,5-difluoro, 2-chloro-4-fluoro, 2-chloro-6-fluoro, 3-chloro-2-fluoro, 3-chloro-4-fluoro, 4-chloro-3-fluoro) were synthesized and copolymerized with styrene. The compositions of the copolymers were calculated from nitrogen analysis.

Acknowledgments

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

References

1. Some observations on the base-catalyzed cyclocondensation of 2,6-dihalobenzaldehydes, ethyl cyanoacetate, and thiourea. By Al-Omar, Mohamed A.;

Al-Obaid, Abdul-Rahman M.; El-Brollosy, Nasser R.; El-Emam, Ali A. Synthetic Communications (2010), 40(10), 1530-1538.

2. Nickel-Catalyzed Reductive Cross-Coupling of Aryl Bromides with Vinyl Acetate in Dimethyl Isosorbide as a Sustainable Solvent. Su, Mincong; Huang, Xia; Lei, Chuanhu; Jin, Jian. Organic Letters (2022), Ahead of Print.
3. The stabilized iminium catalyzed (E)-polyene cyclization: trapping of non-activated terminating groups enabled by cation-π interactions. Warnica, Josephine M.; Gleason, James L. Canadian Journal of Chemistry (2021), Ahead of Print.
4. Selective Rhodium-Catalyzed Hydroformylation of Terminal Arylalkynes and Conjugated Enynes to (Poly)enals Enabled by a π-Acceptor Biphosphoramidite Ligand. Zhao, Jiangui; Zheng, Xueli; Tao, Shaokun; Zhu, Yuxin; Yi, Jiwei; Tang, Songbai; Li, Ruixiang; Chen, Hua; Fu, Haiyan; Yuan, Maolin. Organic Letters (2021), 23(15), 6067-6072.
5. Iron-catalysed asymmetric carboazidation of styrenes. Ge, Liang; Zhou, Huan; Chiou, Mong-Feng; Jiang, Heming; Jian, Wujun; Ye, Changqing; Li, Xiaoyan; Zhu, Xiaotao; Xiong, Haigen; Li, Yajun; et al. Nature Catalysis (2021), 4(1), 28-35.
6. Iron-Catalyzed Radical Asymmetric Aminoazidation and Diazidation of Styrenes. Lv, Daqi; Sun, Qiao; Zhou, Huan; Ge, Liang; Qu, Yanjie; Li, Taian; Ma, Xiaoxu; Li, Yajun; Bao, Hongli. Angewandte Chemie, International Edition (2021), 60(22), 12455-12460.
7. Palladium-Catalyzed Tandem C-C Activation/Cyclization Induced by Carbopalladation of Functionalized Nitriles: Synthesis of Benzo Dipyrromethenes.

Chen, Lepeng; Gong, Julin; Zhang, Yetong; Shao, Yinlin; Chen, Zhongyan; Li, Renhao; Chen, Jiuxi. Organic Letters (2020), 22(17), 6943-6947.

8. Preparation of triazole compounds that modulate HSP90 activity. Chae, Junghyun; Demko, Zachary; Ying, Weiwen; Du, Zhenjian; Foley, Kevin; James, David; Przewloka, Teresa; Song, Minghu; Zhang, Shijie; Ng, Howard P.; et al. PCT Int. Appl. (2007), WO 2007139955 A2 20071206.
9. A solid-phase synthesis of miconazole analogs via an iodoetherification reaction. Tortolani, David R.; Biller, Scott A. Tetrahedron Letters (1996), 37(32), 5687-5690.
10. Hexamethyldisilazane Lithium (LiHMDS)-Promoted Hydroboration of Alkynes and Alkenes with Pinacolborane. Liu, Jichao; Wu, Caiyan; Hu, Tinghui; Yang, Wei; Xie, Yaoyao; Shi, Yinyin; Liu, Qianrui; Shao, Yinlin; Zhang, Fangjun. Journal of Organic Chemistry (2022), Ahead of Print.
11. Stereoselective gold(I)-catalyzed vinylcyclopropanation via generation of sulfur-substituted vinyl carbene equivalent. Yuan, Tengrui; Ryckaert, Bram; Van Hecke, Kristof; Hullaert, Jan; Winne, Johan M. Angewandte Chemie, International Edition (2021), 60(8), 4070-4074.
12. Preparation of indazolyl pyridinones and related heterocycles as kinase inhibitors for the treatment of cancer and other diseases. Zhang, Jintao; Xu, Wen; Jian, Shanzhong; Li, Qun. PCT Int. Appl. (2019), WO 2019037640 A1 20190228.
13. Quantitation of ERK1/2 inhibitor cellular target occupancies with a reversible slow off-rate probe. Lebraud, Honorine; Surova, Olga; Courtin, Aurelie; O'Reilly, Marc;

Valenzano, Chiara R.; Nordlund, Par; Heightman, Tom D. Chemical Science (2018), 9(45), 8608-8618.

14. Iron-Catalyzed Carboamination of Olefins: Synthesis of Amines and Disubstituted β-Amino Acids. Qian, Bo; Chen, Shaowei; Wang, Ting; Zhang, Xinhao; Bao, Hongli. Journal of the American Chemical Society (2017), 139(37), 13076-13082.
15. Development of a Practical Synthesis of ERK Inhibitor GDC-0994. Linghu, Xin; Wong, Nicholas; Iding, Hans; Jost, Vera; Zhang, Haiming; Koenig, Stefan G.; Sowell, C. Gregory; Gosselin, Francis. Organic Process Research & Development (2017), 21(3), 387-398.
16. Discovery of Highly Potent, Selective, and Efficacious Small Molecule Inhibitors of ERK1/2. Ren, Li; Grina, Jonas; Moreno, David; Blake, James F.; Gaudino, John J.; Garrey, Rustam; Metcalf, Andrew T.; Burkard, Michael; Martinson, Matthew; Rasor, Kevin; et al. Journal of Medicinal Chemistry (2015), 58(4), 1976-1991.
17. Novel Copolymers of Trisubstituted Ethylenes with Styrene - 7. Halogen ring-disubstituted methyl 2-cyano-3-phenyl-2-propenoates. G.B. Kharas, K. Kim, K.C. Beinlich, S.B. Benington, S.K. Brennan, M. Morales, N.E. Ruano, D.Y. Won, E. Adibu, and K. Watson. Polym. Bull., 45, 351-357 (2000).
18. 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).

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. 7. Dihalogen Ring-substituted Ethyl 2-Cyano-3-phenyl-2-propenoates and Styrene. G.B. Kharas, A.A. Delgado, K. Aco, L.M. Cardenas, M.L. Lopez, A.D. Mazerat, P.D. Merageas, D.M. Perone, M.D. Pickering, C.S. Samuelson, C.L. Shelly. J. Macromol. Sci. A50 (4) 365-369 (2013).
21. Novel Copolymers of Styrene. 9. Chloro and Fluoro Ring-Disubstituted Propyl 2-Cyano-3-Phenyl-2-Propenoates. G.B. Kharas, W.S. Schjerven, F.A.S. Aldakheel, E.J. Crespo, Z.M. Gaskell, K.J.M. Jordan, J.D. Knight, A.R. Moses, and A.H.A. Niyazi. J. Macromol. Sci. A54(2) 67-70 (2017).
22. Synthesis and Radical Copolymerization of Novel Phenyl-Disubstituted Cyanoacrylates. C.R. Savittieri, S.M. Tinsley, A.J. Diehn, F. Hai, K.E. Humanski, E.J. Kempke, B.Y. Killam, J. Kozeny, E.W. Makhoul, M.C. Obert, A.C. Parisi, V.C. Parrilli, and G.B. Kharas. Acad. J Polym Sci. 2019; 2(5): 555597. DOI:10.19080/AJOP.2019.02.555597.
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 styrene copolymerization of novel ring-disubstituted isopropyl cyanoacrylates. P.M. Whelpley, S. Bajramovic, D.M. Bracamontes, G.A. Buechner, A.D. Eremin, E.J. Kowalczyk, D.D. Lender, R. McCann, W.S. Schjerven, G.B. Kharas. ChemRxiv (24.09.2019). https://doi.org/10.26434/chemrxiv.9891161.v1
25. Synthesis and Styrene Copolymerization of Novel Dihalogen Ring-Substituted Isopropyl Cyanophenylacrylates. S. Flieger, P.M. McCaw, S. Mouradkhanian, B. Pedroza, M.M. Peffley, R.L. Pride, P.R. Ramirez, M.S. Rogers, B. Romanov, M. Saleh, C. Soler, L.D. Warnick, and G.B. Kharas. ChemRxiv (19.12.2019). https://doi.org/10.26434/chemrxiv.11336852.v1
26. 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 (18.12.2019). https://doi.org/10.26434/chemrxiv.11401347.v1
27. Novel Copolymers of Styrene. 11. Fluoro Ring-substituted Butyl 2-Cyano-3-Phenyl-2-Propenoates. G.B. Kharas, W.S. Schjerven, L.M. Maurer, G.C. Mcgee, M.E. Mcgovern, L.E. Palaciaos, H.M. Pollard-Durodola, R.E. Riccio, and J. Weingard. J. Macromol. Sci. A53(5) 258-261 (2016).
28. 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).
29. SciFinder Structure Search March 6, 2022.

30. Synthesis and styrene copolymerization of novel alkyl ring-substituted isobutyl 2-cyano-3-phenyl-2-propenoates. Schjerven, William S.; Groy, Randi; Antonishina, Yekaterina S.; Black, Claire I.; Bolin, Madysen P.; Caniglia, John; Daroach, Deepak P.; Farooqui, Farah T.; Feiz, Yalda; Garcia, Sam; Gasparini, Gabriella; Kharas, Gregory B. Abstracts of Papers, 259th ACS National Meeting & Exposition, Philadelphia, PA, United States, March 22-26, (2020), POLY-0388.
31. 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).