Propiolate–Olefin–Olefin Three-component Annulation mediated by the Addition of Stannyl Radicals

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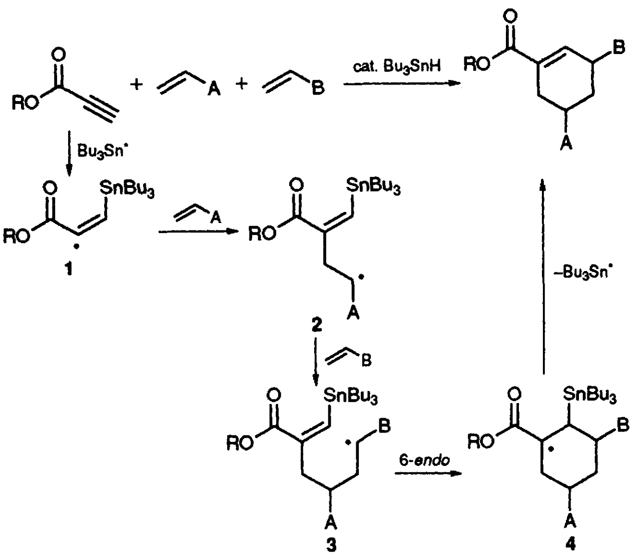
Cyclohexenecarboxylates are formed from ethyl propiolate and two different kinds of olefins *via* consecutive radical addition reactions initiated by the addition of stannyl radicals to the propiolate triple bonds.

Recently, we reported novel radical-based annulation reactions with one equivalent of ethyl propiolate and two equivalents of alkenes mediated by the addition of stannyl radicals to the propiolate triple bonds.[1] The intermediate α-ethoxycarbonyl-β-stannylvinyl radical **1** is moderately nucleophilic, and only electron-deficient olefins participated in the annulation process. Close inspection of the proposed mechanism for this type of annulation reaction (A = B = electron-withdrawing group, Scheme 1) reveals that the second radical intermediate **2** should be relatively electrophilic and more likely to react with electron-rich olefins (A = electron-withdrawing group, B = electron-donating group).[2] We now report the realisation of this triple component annulation strategy, which allows easy access to substituted cyclohexenecarboxylate derivatives.

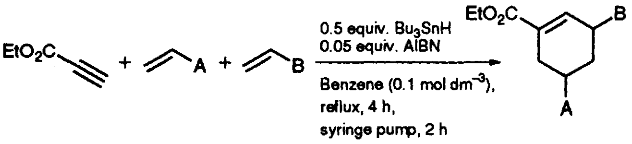
Ethyl propiolate and two different olefins (2–10 equiv.) were dissolved in benzene (0.1 mol dm^{-3}) and the solution was heated under reflux. Tributylstannane (0.5 equiv.) solution in benzene containing azoisobutyronitrile, AIBN, (0.05 equiv.) was added *via* a syringe pump over 2 h and the mixture was heated for a further 2 h before the usual work-up. The results of the reactions are summarized in Table 1. The annulation reactions utilizing butyl vinyl ether and acrylate–methacrylate afforded relatively low yields of the AB-type cyclohexenecarboxylates (mixture of isomers)† accompanied by comparable amounts of AA-type byproducts (entries 1, 2). Employment of styrene increased the yields of AB-type products considerably (entries 3, 4, 5)‡ and a BB-type cyclohexenecarboxylate (ethyl 3,5-diphenylcyclohexenecarboxylate) was isolated as the major byproduct in each case. More interestingly, incorporation of any two of the three different styrene derivatives (pentafluorostyrene, styrene and 3,4-dimethoxystyrene) was possible, and AB-type cyclohexenecarboxylates were obtained (entries 6, 7, 8).§ Methyl acrylate and pentafluorostyrene reacted with ethyl propiolate affording AB-type cyclohexenecarboxylates¶ accompanied by comparable amount of AA-type by-products (entry 9).

These radical reactions are reminiscent of the ionic Michael–Michael–Michael ring closure annulations[3] and complement them in the sense that various styrene derivatives can be used as effective radical acceptors. As the majority of annulation products were isolated as diastereoisomeric and regioisomeric mixtures and purification of individual isomers was not practical, it appeared that more useful products would be obtained by oxidative aromatization. In the event, reaction of several cyclohexenecarboxylates with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone, DDQ, (5 equiv.) in hot chloro-



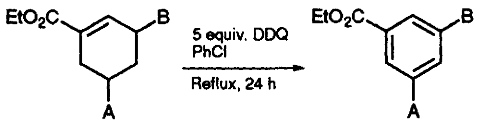
Scheme 1

Table 1



Entry	$CH_2=CH$–A	$CH_2=CH$–B	Yield (%)
1	$CH_2=CHCO_2Me$[a]	$CH_2=CHOBu$[c]	41
2	$CH_2=C(CH_3)CO_2Me$[a]	$CH_2=CHOBu$[c]	21
3	$CH_2=CHCO_2Me$[a]	$CH_2=CHPh$[c]	62
4	$CH_2=C(CH_3)CO_2Me$[a]	$CH_2=CHPh$[c]	54
5	$CH_2=CHCN$[a]	$CH_2=CHPh$[c]	48
6	$CH_2=CHPh$[b]	$CH_2=CHC_6H_3(OMe)_2$[d]	22
7	$CH_2=CHC_6F_5$[b]	$CH_2=CHPh$[d]	41
8	$CH_2=CHC_6F_5$[b]	$CH_2=CHC_6H_3(OMe)_2$[d]	37
9	$CH_2=CHCO_2Me$[a]	$CH_2=CHC_6F_5$[e]	30

[a] 5 equiv. [b] 2 equiv. [c] 10 equiv. [d] 2.5 equiv. [e] 6 equiv.



A = CO$_2$Me, B = OBu 62%
A = CO$_2$Me, B = Ph 56%
A = C$_6$F$_5$, B = Ph 59%
A = CO$_2$Me, B = C$_6$F$_5$ 59%

Scheme 2

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† Products were obtained after careful column chromatographic separation, but GC-MS analysis revealed presence of four AB-type isomers (*ca.* 5:2:2:1) from entry 1 and two AB-type isomers (*ca.* 1:4) from entry 2. Mass spectrum (EI) of the major product from entry 1: *m/z* 284(M$^+$, 3.4), 252(11.4), 238(13.4), 207(9.8), 150(22.5), 85(58.6), 56(100). Mass spectrum (EI) of the major product from entry 2: *m/z* 298(M$^+$, 3.4), 252(18.7), 226(6.3), 180(22.9), 167(29.1), 165(38.8), 93(69.7), 56(100).

‡ Four peaks (1:5:10:6) were recorded in GC-MS (EI) of AB-type products from entry 3: (isomer 1) *m/z* 242(76.2), 215(9.5), 155(100); (isomer 2) *m/z* 288(M$^+$, 3.1), 256(26.1), 242(26.4), 210(30.5), 155(64.6), 104(100), 91(89.1); (isomer 3) *m/z* 242(54.7), 215(4.7), 155(100); (isomer 4) *m/z* 256(4.8), 228(4.3), 214(5.8), 202(5.8), 188(10.4), 155(22.9), 104(100), 91(43.9).

Two peaks (*ca.* 1:5) were recorded in GC-MS (EI) of AB-type products from entry 4: (isomer 1) *m/z* 256(46.9), 243(3.1), 229(4.3), 169(100), 91(25.4);. (isomer 2) *m/z* 256(31.9), 242(6.6), 228(6.4), 202(36.8), 169(100), 91(65.4). GC-MS (CI) (isomer 1) *m/z* 331(4.6), 303(M$^+$ + 1, 6.1), 257(15.1), 243(11.4), 229(100), 179(21.5); (isomer 2) *m/z* 331(4.9), 303(5.4), 257(100), 243(16.1).

Three peaks (*ca.* 1:5:10) were recorded in GC-MS (EI) of AB-type products from entry 5: (isomer 1) *m/z* 255(M$^+$, 19.2), 226(17.8), 209(8.3), 182(26.1), 180(18.9), 155(11.3), 128(15.6), 115(25.0), 104(100), 91(78.7); (isomer 2) *m/z* 255(25.3), 226(14.0), 210(15.4), 209(12.1), 182(100), 155(36.6), 128(38.4), 115(21.9), 104(24.0), 91(28.4); (isomer 3) *m/z* 255(20.3), 226(11.5), 210(14.2), 182(100), 155(49.6), 128(35.3), 115(20.1), 104(42.5), 91(34.9).

§ Two peaks (*ca.* 2:3) were recorded in GC-MS (EI) of AB-type products from entry 6: (isomer 1) *m/z* 366(M$^+$, 47.8), 337(7.5), 321(5.1), 293(52.6), 261(7.2) 202(22.5), 189(33.5), 151(38.6), 115(38.9), 91(100); (isomer 2) *m/z* 366(10.1), 189(2.5), 164(100), 151(8.7), 128(8.0), 91(11.2).

A single peak was recorded in GC-MS (EI) of AB-type products from entry 7 (there were two vinylic signals of equal strength at δ 6.88 and 7.08 in ^{1}H NMR): *m/z* 396(M$^+$, 8.0), 367(2.0), 351(6.0), 322(26.4), 292(3.2), 245(4.0), 219(8.0), 202(18.9), 104(100), 91(69.8).

Two peaks (*ca.* 5:1) were recorded in GC-MS (EI) of AB-type products from entry 8: (isomer 1) *m/z* 456(M$^+$, 64.5), 427(11.9), 425(6.5), 411(11.7), 383(100), 351(9.6), 245(17.5), 202(28.0), 189(46.3), 151(54.2), 115(41.8), 77(55.1); (isomer 2) *m/z* 456(5.6), 219(2.2), 189(2.1), 181(3.0), 164(100), 151(8.2), 149(9.0), 121(3.2), 115(3.4), 103(6.4), 91(8.6).

¶ A single peak was recorded in GC-MS (EI) of AB-type products from entry 9 (there were two vinylic signals of *ca.* 2:3 ratio at δ 7.12 and 6.92 in ^{1}H NMR): *m/z* 378(M$^+$, 6.9), 347(4.9), 332(52.6), 318(7.3), 304(6.7), 300(8.5), 289(4.4), 273(14.7), 245(100), 244(19.8), 224(6.0), 194(7.2), 181(34.1), 77(66.4), 59(91.5).

benzene afforded biphenyl- and terphenyl-carboxylates in moderate yields (Scheme 2).

In conclusion, the radical-mediated triple component annulation reaction described here provides a viable alternative in synthesizing biphenyl- and terphenyl-carboxylate derivatives.[4]

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