CYCLOADDITION REACTIONS OF THE METHYL ESTER OF TRIFLUOROPYRUVIC ACID

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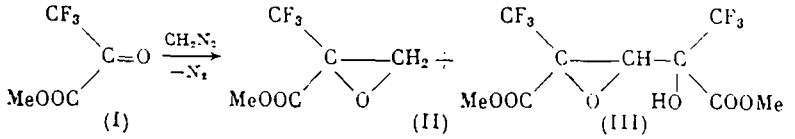
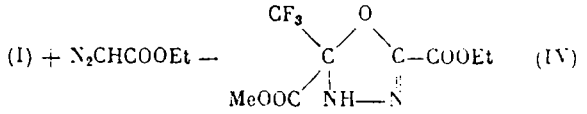
The reactions of polyfluorocarbonyl compounds with carbenes, their precursors, carbenoids, and many unsaturated compounds were systematically studied using hexafluoroacetone as an example [1]. According to [2], the paths of similar reactions are determined by both the characteristics of the frontier orbitals and by the influence of substituents at the reaction centers. In this work cycloaddition reactions of methyl trifluoropyruvate (I) were investigated. Similar reactions of (I) are known with ketene, cyclohexylisonitrile, and trialkylphosphites [3].

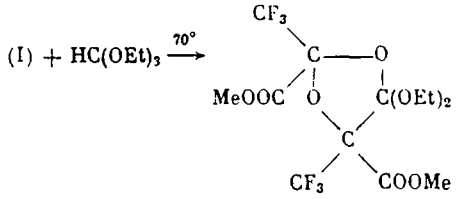
Compound (I) reacts energetically with diazomethane at −50°C with elimination of N_2, forming a mixture of oxiranes (II) and (III)



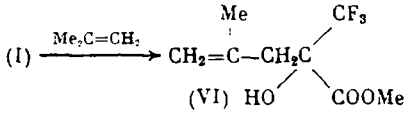
Unlike hexafluoroacetone, compound (I) gives a stable (3 + 2) cycloadduct (IV) with diazoacetic ester, and not the corresponding oxirane



Under unusually mild conditions compound (I) reacts with the diethoxycarbene precursor ethyl orthoformate. As in the case of hexafluoroacetone, the reaction product is a cycloadduct of 2:1 composition — dioxolane (V)



Compound (I) reacts easily only with sufficiently strong π-donating alkenes, as was noted also for hexafluoroacetone [4]. Thus, (I) with vinyl ethyl ester at −50°C forms a mixture of oligomers and not the (2 + 2) cycloadduct. Under slightly more rigid conditions at −20°C (I) reacts with isobutylene by a type of "ene" reaction



Alkenes inactive in reactions with hexafluoroacetone, for example cyclopentene and cyclohexene, react with (I) at 180-200°C, forming esters (VII) and (VIII) with preparative yields

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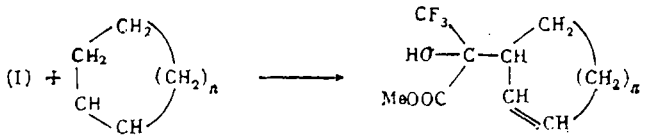
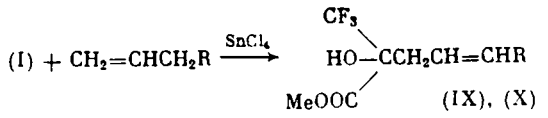


(VII), (VIII)

$n = 1$(VII), $n = 2$(VIII).

Reactions of alkenes with (I), as with hexafluoroacetone [5, 6], are activated by Lewis acids. In the presence of $SnCl_4$ even at −50°C compound (I) with propene and butene-1 forms allyl C-alkylation products (IX) and (X)

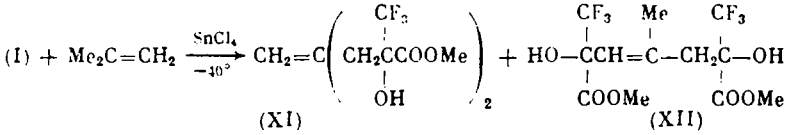


(IX), (X)

R = H(IX), R = Me(X).

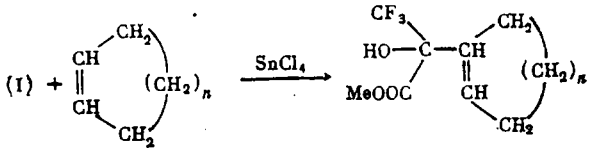
In the same reaction with hexafluoroacetone the vinyl C-alkylation is formed in addition to these [6].

With $SnCl_4$ catalysis isobutylene reacts with 2 equ. of (I) to form a mixture of double allyl and allyl vinyl C-alkylation products (XI) and (XII)



(XI) (XII)

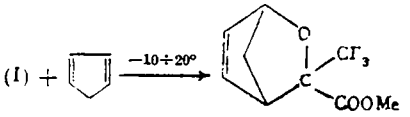
Reactions of (I) with cyclopentene and cyclohexene at 20°C in the presence of $SnCl_4$ proceed with slightly more difficulty to form the products of vinyl C-alkylation (XIII) and (XIV) exclusively



(XIII), (XIV)

$n = 1$ (XIII); $n = 2$ (XIV).

It should be noted that in many cases reactions of (I) with alkenes are accompanied by extensive oligomerization of the latter. This prevented us from obtaining monomeric products from the reactions with vinyl ethyl ester, vinyl acetate, and styrene with or without catalyst. Compound (I) undergoes a Diels—Alder reaction as easily as hexafluoroacetone [7]. 2-Oxabicycloheptene (XV), formed with cyclopentadiene, unlike the analogous hexafluoroacetone derivative is sufficiently stable to be isolated and identified as a (2.5:1) mixture of endo- and exo-isomers

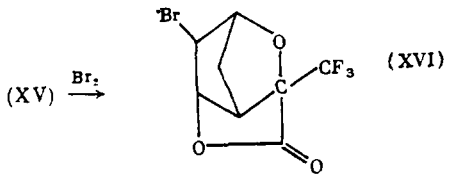


(XV)

On the basis of the results of [3] one can conclude that (I) reacts with unsaturated compounds of the donor type more energetically than hexafluoroacetone. Moreover, compared with

hexafluoroacetone, (I) displays increased inclination to [3 + 2]- and [4 + 2]-cyclization and is not inclined to [2 + 2]-cycloaddition even under strong conditions, including the presence of a catalyst.

The structures of the obtained compounds were confirmed by elemental analysis and spectral data. The structure of (XV) was proved by its bromolactonization into dioxatricyclononanone (XVI)



EXPERIMENTAL

NMR spectra were taken on a Bruker WR-200-SV instrument (^{1}H 200, ^{19}F 188, ^{13}C 50 MHz) with TMS (internal standard) or with CF_3COOH (external standard). IR spectra were recorded on a UR-20 instrument.

Methyl Ester of 2-Trifluoromethyl-2,3-epoxypropionic Acid (II) and Dimethyl Ester of 2-Hydroxy-2,4-bis(trifluoromethyl)-3,4-epoxyglutaric Acid (III). To a solution of 7.4 g methyl trifluoropyruvate in 20 ml dry ether a solution of 2.0 g CH_2N_2 in 80 ml ether was added dropwise with stirring and cooling (−50°C). The mixture was slowly warmed to 20°C and by fractionation compounds (II) and (III) were isolated.

(II): Yield 2.9 g (35.9%), b.p. 42°C (8 mm), n_D^{20} 1.3640. PMR spectrum (δ, ppm, J, Hz): 3.77 s (3H, MeO), 3.20 s (2H, CH_2). ^{13}C NMR spectrum (acetone, δ, ppm, J, Hz): 162.81 (C=O), 120.00 (CF_3, J_{C-F} = 276.2), 51.78 (MeO, J_{C-H} = 148.9) 47.99 (CH_2, J_{C-H} = 185.6). IR spectrum (ν, cm^{-1}): 3040 (CH_2), 1760 (C=O). Found: C 34.98; H 2.69; F 33.99%. $C_5H_5F_3O_3$. Calculated: C 35.29; H 2.94; F 33.53%.

(III): Yield 4.7 g (60.7%), mp 68°C. PMR spectrum (d_6-acetone, δ, ppm, J, Hz): 4.08 s (1H, CH), 3.92 s (3H, MeO), 3.74 s (3H, MeO). ^{13}C NMR spectrum (acetone, δ, ppm, J, Hz): 164.7 (C=O), 159.7 (C=O), 121.5 (CF_3, J_{C-F} = 287.8), 120.5 (CF_3, J_{C-F} = 281.7), 57.6 (CH, J_{C-H} = 185.6), 53.2 (MeO, J_{C-H} = 148.4), 51.4 (MeO, J_{C-H} = 150.4). ^{19}F NMR spectrum (acetone, δ, ppm, J, Hz): −4.0 s (CF_3), −1.1 s (CF_3). IR spectrum (ν, cm^{-1}): 3455 (OH), 3045 (CH), 1785 (C=O), 1770 (C=O). Mass spectrum (m/z): 310 (M^+ − 0), 295 (M^+ − MeO), 267 (M^+ − MeOOC). Found: C 32.83; H 2.59%. $C_9H_8F_6O_6$. Calculated: C 33.13; H 2.45%.

2-Carboethoxy-5-carbomethoxy-5-trifluoromethyl-4,5-dihydro-1,3,4-oxadiazole (IV). To a solution of 5.9 g methyl trifluoropyruvate in 20 ml hexane with stirring and cooling with ice water a solution of 4.3 g diazoacetic ester in 20 ml hexane was added dropwise. The mixture was kept for 12 h at 20°C and fractionated. There was obtained 8.6 g (84.3%) of (IV) with b.p. 58°C (1 mm), n_D^{24} 1.4225. PMR spectrum (d_6-acetone, δ, ppm, J, Hz): 6.03 broad s (1H, NH), 4.19 q (2H, OCH_2, J_{H-H} = 7.5), 3.80 s (3H, MeO), 1.18 t (3H, Me, J_{H-H} = 7.5). ^{13}C NMR spectrum (CCl_4), 164.59 (C=O), 162.29 (C=O), 120.72 (CF_3, J_{C-F} = 286.8), 73.52 (C^5, J_{C-F} = 31.7), 59.65 (OCH_2), 52.05 (MeO), 12.22 (Me). ^{19}F NMR spectrum (CCl_4, δ, ppm): −1.1 s (CF_3). IR spectrum: 3450 (NH), 2120 (NH—N=), 1770 (C=O), 1715 (C=O). Found: C 30.95; H 3.15; n N 9.75%. $C_8H_9F_3N_2O_5$. Calculated: C 30.71; H 3.21; N 10.01%.

2,4-Bis(carbomethoxy)-2,4-bis(trifluoromethyl)-5,5-diethoxy-1,3-dioxolane (V). A mixture of 6.32 g methyl trifluoropyruvate and 3.0 g ethyl orthoformate was heated for 5 h at 70°C and fractionated. There was obtained 2.7 g (100%) of the methyl ester of 2-hydroxy-2-ethoxytrifluoropropionic acid with bp 58°C (20 mm), n_D^{20} 1.3625 [3] and 4.5 g (81.2%) of (V) as a mixture (1:1) of Z- and E-isomers with bp 90°C (1 mm), n_D^{20} 1.3860. PMR spectrum (d_6-acetone, δ, ppm): 3.8 m (10 H, 2 MeO, 2 CH_2O), 1.16 m (6H, 2 Me). ^{19}F NMR (acetone, δ, ppm): −6.7 m (CF_3), 1.8 m (CF_3). Found: C 37.75; H 3.81; F 27.26%. $C_{12}H_{16}F_6O_8$. Calculated: C 37.68; H 3.86; F 27.54%.

Methyl Ester of 2-Hydroxy-2-trifluoromethyl-4-methyl-4-pentenoic Acid (VI). Methyl trifluoropyruvate (5.6 g) and isobutene (5.0 g) were mixed at −70°C, slowly warmed to −20°C, and kept 12 days at this temperature. Unreacted isobutene was recondensed and the residue was

fractionated. There was obtained 5.6 g (73.6%) of (VI) with bp 64°C (11 mm), n_D^{20} 1.3910. PMR spectrum (CCl_4, δ, ppm) 4.85 m and 4.75 m (2H, CH_2), 3.94 s (1H, OH), 3.86 s (3H, MeO), 2.61 m (2H, CH_2), 1.75 s (3H, Me). ^{19}F NMR spectrum (CCl_4, δ, ppm): 0.8 s (CF_3). Found: C 44.92; H 4.93; F 27.12%. $C_8H_{11}F_3O_3$. Calculated: C 45.28; H 5.19; F 26.89%.

Methyl Ester of 2-Hydroxy-2-(2-cyclopenten-1-yl)trifluoropropionic Acid (VII). A mixture of 3.0 g methyl trifluoropyruvate and 1.31 g cyclopentene was heated in a sealed ampul at 160°C for 16 h and fractionated. There was obtained 1.9 g (44.1%) of (VII) with bp 37°C (1 mm), n_D^{20} 1.4190. PMR spectrum (CCl_4, δ, ppm) 5.84 m and 5.58 m (2H, CH=CH), 3.86 s (3H, MeO), 3.35 m (1H, CH), 2.27 m and 1.68 m (4H, CH_2CH_2). ^{13}C NMR spectrum (acetone, δ, ppm, J, Hz) 168.7 (C=O), 133.3 and 126.5 (CH=CH), 123.07 (CF_3, J_{C-F} = 288.3), 80.16 (–C–), 52.24 (MeO), 47.65 (CH), 36.82 and 22.90 (CH_2CH_2). Found: C 47.96; H 4.62; F 25.63%. $C_9H_{11}F_3O_3$. Calculated: C 48.19; H 4.91; F 25.43%.

Methyl Ester of 2-Hydroxy-2-(2-cyclohexen-1-yl)trifluoropropionic Acid (VIII). A mixture of 5.0 g methyl trifluoropyruvate and 2.63 g cyclohexene was heated in a sealed ampul at 200°C for 9 h and fractionated. There was obtained 2.8 g (38.4%) of (VIII) with bp 72°C (1 mm), n_D^{20} 1.4310. PMR spectrum (δ, ppm): 5.70 m (2H, CH=CH), 4.13 s (1H, OH), 3.79 s (3H, MeO), 2.84 m (1H, CH), 1.80 m and 1.47 m [6H, $(CH_2)_3$]. ^{13}C NMR spectrum (acetone, δ, ppm, J, Hz): 168.15 (C=O), 129.63 and 122.66 (CH=CH), 123.20 (CF_3, J_{C-F} = 287.3), 78.98 (–C–, J_{C-F} = 26.7), 51.88 (MeO), 38.26 (CH), 23.33, 22.20, and 20.27 [$(CH_2)_3$]. ^{19}F NMR spectrum (acetone, δ, ppm): –4.6 s (CF_3). Found: C 50.32; H 5.12; F 24.07%. $C_{10}H_{13}F_3O_3$. Calculated: C 50.42; H 5.46; F 23.95%.

Methyl Ester of 2-Hydroxy-2-trifluoromethyl-4-pentenoic Acid (IX). 10.0 g Methyl trifluoropyruvate, 2.7 g propene, 1.65 g $SnCl_4$, and 30 ml hexane were mixed at –70°C, slowly warmed to –50°C, maintained at this temperature until cessation of exothermic reaction, warmed to –10°C, and stirred for 2 h at this temperature. The mixture then was washed with 15 ml of 15% HCl and with water (3 × 15 ml), dried over Na_2SO_4, and fractionated. There was obtained 10.0 g (80%) of (IX) with bp 81°C (60 mm), n_D^{21} 1.3823. PMR spectrum (CCl_4, δ, ppm): 5.66 m (1H, CH=), 5.10 m (2H, CH_2=), 4.07 broad s (1H, OH), 3.79 s (3H, MeO), 2.59 m (2H, CH_2). ^{13}C NMR spectrum (CCl_4, δ, ppm, J, Hz): 167.9 (C=O), 127.93 and 118.40 (CH_2=CH), 121.62 (CF_3, J_{C-F} = 288.8), 75.97 (–C–, J_{C-F} = 30.7), 51.84 (MeO), 34.49 (CH_2). ^{19}F NMR spectrum (CCl_4, δ, ppm): 1.0 s (CF). Found: C 42.22; H 4.28; F 28.74%. $C_7H_9F_3O_3$. Calculated: C 42.42; H 4.54; F 28.79%.

Methyl Ester of 2-Hydroxy-2-trifluoromethyl-4-hexenoic Acid (X). We obtained from 10.0 g methyl trifluoropyruvate, 3.6 g butene-1, and 1.66 g $SnCl_4$ under same conditions as for (IX). The yield was 8.2 g (60%), bp 81°C (20 mm), n_D^{22} 1.3928. PMR spectrum (CCl_4, δ, ppm, J, Hz): 5.58 m and 5.33 m (2H, CH=CH), 4.02 s (1H, OH), 3.82 s (3H, MeO), 2.55 m (2H, CH_2), 1.65 d (3H, Me, J_{H-H} = 6.5). ^{19}F NMR spectrum (CCl_4, δ, ppm): 0.5 s (CF_3). Found: C 44.97; H 5.07; F 27.10%. $C_8H_{11}F_3O_3$. Calculated: C 45.28; H 5.19; F 26.89%.

Dimethyl Ester of 2,6-Dihydroxy-2,6-bis(trifluoromethyl)-4-methylenepimelic Acid (XI) and Dimethyl Ester of 2,6-Dihydroxy-2,6-bis(trifluoromethyl)-4-methyl-3-heptenedioic Acid (XII). Into a solution of 5.7 g methyl trifluoropyruvate and 1.0 g $SnCl_4$ in 20 ml hexane cooled to –40°C, 1.0 g isobutene was added and the mixture was stirred for 2 h at this temperature, then warmed to 20°C, treated with 10 ml 15% HCl, and washed with water. The organic layer was dried over Na_2SO_4 and fractionated. There was obtained 0.8 g of (IX) and 4.2 g (63%) of a mixture (2:1) of (XI) and (XII) with bp 85-92°C (1 mm). Found: C 38.85; H 3.65; F 31.23%. $C_{12}H_{14}F_6O_6$. Calculated: C 39.13; H 3.80; F 30.98%.

(XI): PMR spectrum (CCl_4, δ, ppm): 5.04 s and 4.91 s (2H, CH_2=C), 3.95 s (2H, 2OH), 3.82 s and 3.80 s (6H, 2MeO), 2.73 m (4H, $2CH_2$).

(XII): PMR spectrum (CCl_4, δ, ppm): 5.49 s (1H, CH=C), 3.93 s (2H, 2OH), 3.94 s and 3.92 s (6H, 2MeO), 2.52 m (2H, CH_2), 1.76 m (3H, Me).

Methyl Ester of 2-Hydroxy-2-(1-cyclopenten-1-yl)trifluoropropionic Acid (XIII). A solution of 3.0 g methyl trifluoropyruvate, 0.5 g $SnCl_4$, and 1.31 g cyclopentene in 20 ml CCl_4 was kept at 20°C for 48 h, then treated with 10 ml 15% HCl and washed with water. The organic

layer was separated, dried over Na_2SO_4, and fractionated. There was obtained 3.6 g (83.5%) of (XIII) with bp 39°C (1 mm), n_D^{20} 1.4240. PMR spectrum (d_6-acetone, δ, ppm): 5.97 m (1H, CH=C), 5.30 broad s (1H, OH), 3.78 s (3H, MeO), 2.48-1.76 m [6H, $(CH_2)_3$]. ^{13}C NMR spectrum (acetone, δ, ppm, J, Hz): 167.37 (C=O), 136.30 (–C=), 131.16 (C=CH), 122.46 (CF_3, J_{C-F} = 286.3), 76.53 (–C–), 51.86 (MeO), 31.07, 30.75, and 21.86 [$(CH_2)_3$]. ^{19}F NMR spectrum (acetone, δ, ppm): –2.45 s (CF_3). Found: C 47.83; H 4.63; F 25.57%. $C_9H_{11}F_3O_3$. Calculated: C 48.19; H 4.91; F 25.43%.

Methyl Ester of 2-Hydroxy-2-(1-cyclohexen-1-yl)-trifluoropropionic Acid (XIV). To a solution of 5.0 g methyl trifluoropyruvate and 0.83 g $SnCl_4$ in 20 ml CCl_4 with stirring and cooling with water 2.63 g cyclohexene was added dropwise. The mixture was stirred for 10 h at 20°C, then for 2 h at 50°C. Isolation of the product was carried out as for (XIII). There was obtained 4.0 g (52.4%) of (XIV) with bp 73°C (1 mm), n_D^{20} 1.4370. PMR spectrum (d_6- acetone, δ, ppm): 6.08 m (1H, C=CH), 5.40 broad s (1H, OH), 3.74 s (3H, MeO), 2.2-1.4 m [8H, $(CH_2)_4$]. ^{13}C NMR spectrum (acetone, δ, ppm): 167.50 (C=O), 135.35 (–C=), 126.96 (–C=CH), 122.87 (CF_3, J_{C-F} = 285.8), 78.5 (–C–), 51.43 (MeO), 23.79, 22.95, 21.24, 20.35 [$(CH_2)_4$]. ^{19}F NMR spectrum (CCl_4, δ, ppm): –3.1 s (CF_3). IR spectrum: 3490 (OH), 1750 (C=O), Found: C 50.03; H 5.34; F 23.83%. $C_{10}H_{13}F_3O_3$. Calculated: C 50.42; H 5.46; F 23.95%.

2-Oxa-3-carbomethoxy-3-trifluoromethylbicyclo[2.2.1]hept-5-ene (XV). To 9.0 g methyl trifluoropyruvate in 20 ml dry ether with stirring and cooling (–10°C) 3.8 g cyclopentadiene in 10 ml ether was added dropwise. The mixture was heated and kept for 12 h at 20°C. Ether and easily volatile impurities were removed under vacuum. The residue contained 8.5 g (66.4%) of (XV) as a mixture (2.5:1) of endo and exo isomers.

PMR spectrum of exo isomer (XV) (d_6-acetone, δ, ppm): 6.57 m (1H, HC^5), 6.42 m (1H, HC^6), 5.08 m (1H, HC^1), 3.80 m (1H, HC^4), 3.78 s (3H, MeO), 1.71 m and 1.54 m (2H, H_2C^7). ^{13}C NMR spectrum (acetone, δ, ppm, J, Hz): 167.64 (C=O), 137.69 and 135.06 (CH=CH), 122.65 (CF_3, J_{C-F} = 284.8), 84.02 (OCH), 51.49 (CH), 50.85 (MeO), 46.47 (CH_2). ^{19}F NMR spectrum (acetone, δ, ppm): –10.1 s (CF_3).

PMR spectrum of endo isomer (XV) (d_6-acetone, δ, ppm): 6.48 m (1H, HC^5), 6.39 m (1H, HC^6), 5.08 m (1H, HC^1), 3.74 m (1H, HC^4), 3.63 (3H, MeO), 2.01 m and 1.54 m (2H, CH_2). ^{13}C NMR spectrum (acetone, δ, ppm, J, Hz): 166.43 (C=O), 137.14 and 137.03 (CH=CH), 122.9 (CF_3, J_{C-F} = 264.6), 82.93 (OCH), 51.78 (CH), 49.09 (MeO), 47.88 (CH_2). ^{19}F NMR spectrum (acetone, δ, ppm): –6.6 s (CF_3). Found: C 47.95; H 3.85; F 25.80%. $C_9H_9F_3O_3$. Calculated: C 48.21; H 4.02; F 25.47%.

1-Trifluoromethyl-2,6-dioxa-4-bromo-7-oxotricyclo[3.2.1.$1^{3,8}$]nonane (XVI). To 13.5 g (XV) in 50 ml CCl_4 with stirring and cooling (–20°C) 9.7 g Br_2 in 50 ml CCl_4 was added dropwise. The mixture was kept at 0°C for 6 days and fractionated. There was obtained 10.5 g (45.0%) of (XVI) with bp 93°C (1 mm), which slowly crystallized during standing to colorless crystals with mp 99°C. PMR spectrum (d_6-acetone, δ, ppm): 5.3 m (1H, HC^5), 4.9 m (1H, HC^3), 4.22 m (1H, HC^8), 4.06 m (1H, HC^4), 2.69 m and 2.35 m (2H, CH_2). ^{19}F NMR spectrum (acetone, δ, ppm): –0.8 s (CF_3). Found: C 33.73; H 2.03; F 19.36%. $C_8H_6BrF_3O_3$. Calculated: C 33.45; H 2.09; F 19.86%.

CONCLUSIONS

The methyl ester of trifluoropyruvic acid acts as a stronger π-acceptor than hexafluoroacetone in [3 + 2]- and [4 + 2]-cycloaddition reactions with donor type alkenes and is not inclined to [2 + 2]-cyclization.

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