

## Polyhalogenoheterocyclic Compounds. Part 35.<sup>1</sup> Reactions of Fluorinated Alkenes and Cycloalkenes with Enolate Anions

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Reactions of compounds that are oligomers of tetrafluoroethylene, with enolate anions derived from ethyl acetoacetate and acetylacetone, give fluorinated pyran derivatives whereas an uncyclised product is obtained from diethyl malonate. Similar reactions with perfluoro-but-2-ene, -cyclohexene, and -cyclopentene give furan or pyran derivatives. The different behaviour of these systems is rationalised.

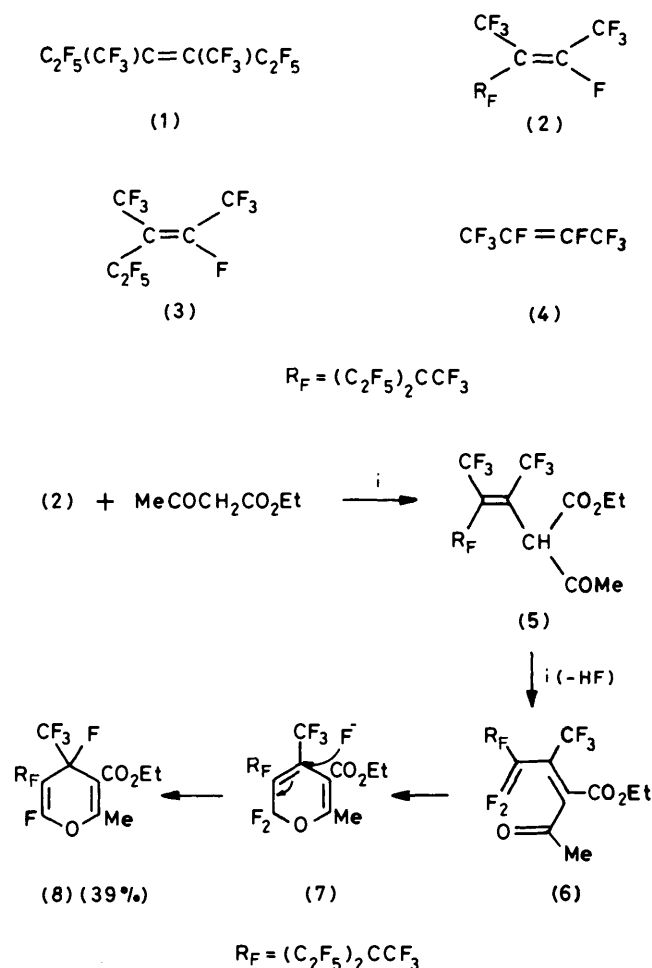
We have recently described the synthesis of fluorinated pyran derivatives<sup>2</sup> from reaction of perfluoro-3,4-dimethylhex-3-ene (1) with various enolate anions. Here, we describe an extension of this investigation to other appropriate fluorinated alkenes and cycloalkenes for the synthesis of heterocyclic compounds.

Compounds (1)–(4) are all oligomers of tetrafluoroethylene and are available either directly or indirectly from this compound.<sup>3,4</sup> Reaction of (2) with ethyl acetoacetate gave a pyran derivative (8) in 39% yield in a cyclisation process that can be rationalised as in Scheme 1. The intermediates (5) and (6) were not isolated in this case but compounds of structure similar to (6) will be described below. Compound (7) is not isolated, apparently because of the very unfavourable steric requirements of the bulky fluorocarbon groups in an enforced *cis* arrangement on a double bond [*cf.* compound (2) which exists exclusively as the geometric isomer shown].

Different results are obtained with compound (3) although, formally, this compound is very similar to (2), having a vinylic fluorine atom. Reaction occurred readily with ethyl acetoacetate and with diethyl malonate, but only in the former case was a cyclic product (11) obtained, together with a diene derivative (10). Diethyl malonate gave diene (9) as the sole product of reaction. Dienes of this type, *e.g.* (6), have been postulated as intermediates in the formation of the fluorinated pyran derivative (8) (Scheme 1) and elsewhere,<sup>5</sup> but this is the first case of their isolation. Surprisingly, the dienes (9) and (10) were not significantly converted into the corresponding pyran derivatives on being heated at *ca.* 110 °C, and this implies that (11) arises from a specific geometric isomer of (10).

Formation of benzofuran derivatives in reactions of enolate anions with fluorinated benzenes is well known<sup>6</sup> but, surprisingly, analogous syntheses involving fluorinated alkenes have not been described. We have now shown that furan derivatives (13) and (14) can be obtained in reactions of perfluorobut-2-ene (4) with acetylacetone and with ethyl acetoacetate (see Scheme 2). Nevertheless, the apparently analogous reaction of (4) with diethyl malonate gave a pyran derivative (16) rather than a furan, presumably by a mechanism analogous to that shown in Scheme 1 which gives (7). The reason for this quite different behaviour probably stems from the relative amounts of charge on carbon *versus* oxygen in anions (12) and (15), which is reflected in the acidities of the enolate ion precursors, and it is informative that diethyl malonate is the least acidic of the reagents shown on Scheme 2. Similar arguments have been used previously to account for other well-known differences in the chemistry of these reagents.<sup>7</sup>

Analogous products are formed from perfluorocyclohexenes (18), (19), and (21), and perfluorocyclopentenes (17) and (20)

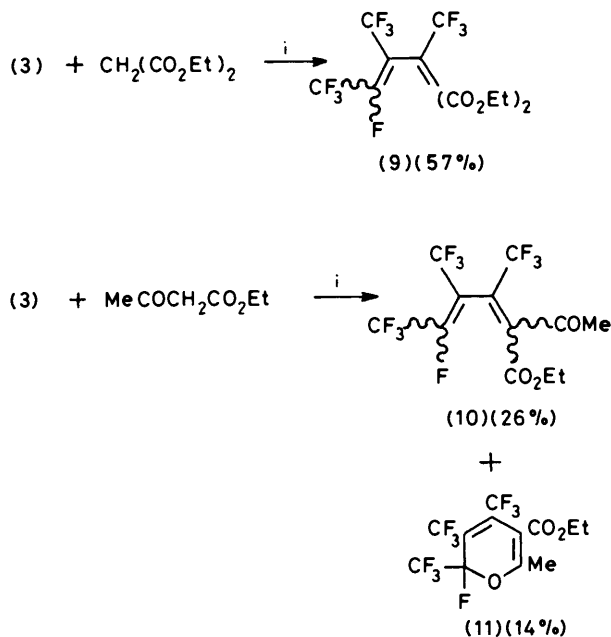


Scheme 1. Reagents: i, NaH, tetraglyme, 20 °C

(Scheme 3), although in the latter case only low yields were obtained. Attempted reactions using perfluorocyclobutene, however, gave only tars from which no identifiable products could be obtained.

Clearly, reactions of enolate anions with various unsaturated fluorocarbons have considerable potential for the synthesis of partially fluorinated heterocycles, and the further chemistry of these systems is being pursued.

Spectroscopic data and assignments for the compounds



Reagents: i, NaH, tetraglyme, 20 °C

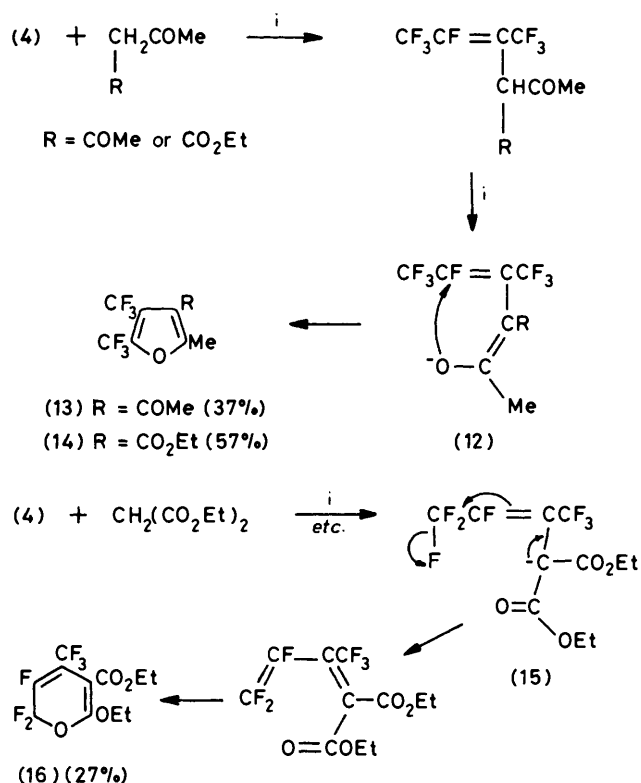
described here are contained in the Experimental section and it will be clear that, in most cases, structures follow from these data in an unambiguous manner. The assignment of structures (20) and (21), rather than structures involving cyclisation through oxygen, was more difficult and depends on comparison of <sup>19</sup>F n.m.r. chemical shifts with various model systems.

### Experimental

<sup>19</sup>F N.m.r. spectra were measured at 40 °C, using a Varian EM360L spectrometer, with trichlorofluoromethane as external reference; upfield shifts are quoted as positive. <sup>1</sup>H N.m.r. spectra were measured under the same conditions using tetramethylsilane as external reference; shifts are quoted relative to the δ scale. Gas chromatography was carried out using columns packed with 20% 'Krytox' fluid on Chromosorb W (Column K) and 30% silicone gum rubber SE-30 on Chromosorb P (Column O). Percentage yields quoted were measured by g.l.c. analysis, using a gas-density balance detector, and are based on the actual fluorocarbon consumed. I.r. spectra were recorded on a Perkin-Elmer 577 instrument and mass spectra on a VG Micromass 12.

**Reaction of Perfluoro-4-ethyl-3,4-dimethylhex-2-ene (2) with Ethyl Acetoacetate.**—The reaction procedure and work-up described immediately below was used in all cases. When the fluorocarbon starting material was gaseous, the reaction was carried out in a flask fitted with a 'rotaflo' tap and the fluorocarbon was transferred under vacuum by cooling the reaction flask in liquid air.

Compound (2) (5.00 g, 10.0 mmol) was added to tetraglyme (5 ml), containing the anion derived from treating ethyl acetoacetate (2.70 g, 21.0 mmol) with an equimolar amount of sodium hydride, and the mixture was stirred at room temperature for 16 h. Water (50 ml) was then added, the lower oily layer thus formed was removed, volatile material from it was dried (P<sub>2</sub>O<sub>5</sub>) and transferred under vacuum to a cold trap. The resultant liquid (5.43 g) was shown by g.l.c. (columns K and O) to contain starting materials together with one major product. A sample of this product was obtained pure by

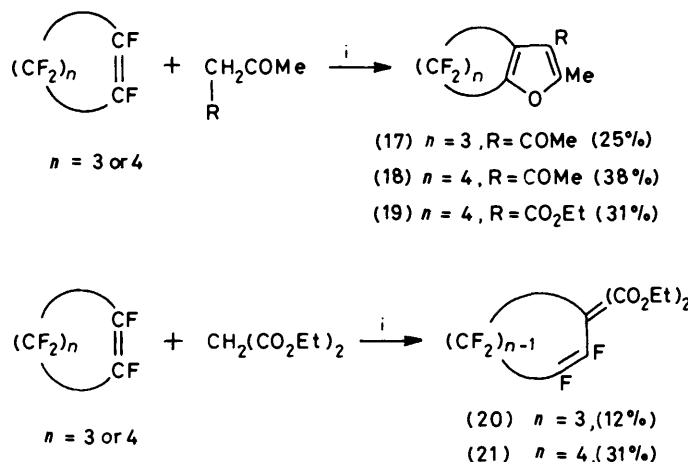


Scheme 2. Reagents: i, NaH, tetraglyme, room temp

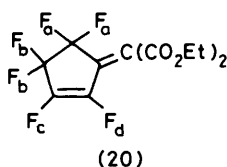
preparative scale g.l.c. (column K) and was identified as 5-ethoxycarbonyl-2,4-difluoro-6-methyl-3-(perfluoro-1-ethyl-1-methylpropyl)-4-trifluoromethylpyran (8) (39%) (Found: C, 30.3; H, 1.5; F, 57.8%; (*P* - 45), 545; (*P* - 69), 521. C<sub>16</sub>H<sub>8</sub>F<sub>18</sub>O<sub>3</sub> requires C, 30.5; H, 1.36; F, 58.0%; *M*, 590);  $\nu_{\max}$  2 990, 2 880, 1 735, 1 700, 1 650, and 1 635 cm<sup>-1</sup>;  $\delta_F$  58.0 (m, 3F), 62.3 (m, 1F), 78.3 (br, s, 3F), 79.8 (br, s, 6F), 103.7 (m, 4F), and 158.7 p.p.m. (q, *J* 53 Hz, 1F);  $\delta_H$  0.96 (t, *J* 7 Hz, 3 H), 2.00 (s, 3 H), and 3.86 (q, *J* 7 Hz, 2 H).

**Reaction of Perfluoro-3-methylpent-2-ene (3) with Diethyl Malonate.**—A mixture containing (3) (3.00 g, 10.0 mmol), diethyl malonate (2.40 g, 15.0 mmol), sodium hydride (15 mmol), and tetraglyme (5 ml) gave, after work-up, a liquid which contained one major product, subsequently identified as a 1 : 4 mixture of *E* and *Z* isomers of 1,1-bis(ethoxycarbonyl)-2,3-bis(trifluoromethyl)tetrafluoropenta-1,3-diene (9) (57%) (Found: C, 37.0; H, 2.45; F, 45.4%; *M*<sup>+</sup>, 420. C<sub>13</sub>H<sub>10</sub>F<sub>10</sub>O<sub>4</sub> requires C, 37.1; H, 2.38; F, 45.2%; *M*, 420);  $\nu_{\max}$  2 990 and 1 740 cm<sup>-1</sup>;  $\delta_H$  0.80 (br, 6 H) and 3.87 (br, 4 H);  $\delta_F$  (*Z* isomer) 62.7 (d, *J* 17 Hz, 3F), 65.3 (br, s, 3F), 72.0 (br, d, *J* 9 Hz, 3F), and 111.7 (q, of q, *J* 9, 17 Hz, 1F);  $\delta_F$  (*E* isomer) 59.2 (m, 3F), 65.3 (br, s, 3F), 71.3 (m, 3F), and 108.3 p.p.m. (br, 1F).

**Reaction of (3) with Ethyl Acetoacetate.**—Compound (3) (3.00 g, 10.0 mmol), ethyl acetoacetate (1.95 g, 15.2 mmol), sodium hydride (15.2 mmol), and tetraglyme (5 ml) gave two products, (10) (26%) and (11) (14%); (*Z/E,Z/E*)-1-acetyl-1-ethoxycarbonyl-2,3-bis(trifluoromethyl)tetrafluoropenta-1,3-diene (10) (Found: C, 37.1; H, 2.15; F, 49.1%; *M*<sup>+</sup>, 390. C<sub>12</sub>H<sub>8</sub>F<sub>10</sub>O<sub>3</sub> requires C, 36.9; H, 2.05; F, 48.7%; *M*, 390);  $\nu_{\max}$  2 990, 1 720, and 1 650 cm<sup>-1</sup>;  $\delta_H$  1.15 (br, 3 H), 2.90 (s, 3 H), and 5.70 (br, 2 H);  $\delta_F$  (CF<sub>3</sub> groups *trans*) 62.3 (d, *J* 17 Hz, 3F), 63.3 (s, 3F), 71.7 (br, d, *J* 7.5 Hz, 3F), and 111.3 (q of q, *J* 7.5, 17 Hz, 1F);  $\delta_F$  (CF<sub>3</sub> groups *cis*) 58.7 (br, 3F),



Scheme 3. Reagents: i, NaH, tetraglyme, room temp.



Numbering scheme for n.m.r. assignments

63.3 (s, 3F), 71.7 (br, 3F), and 108.3 (m, 1F). 5-Ethoxycarbonyl-2-fluoro-6-methyl-2,3,4-tris(trifluoromethyl)-2H-pyran (11) (Found: C, 36.8; H, 2.1; F, 48.9%;  $M^+$ , 390.  $C_{12}H_8F_{10}O_3$  requires C, 36.9; H, 2.05; F, 48.7%;  $M$ , 390);  $v_{max}$  2990, 1740, 1655, and 1580  $cm^{-1}$ ;  $\delta_H$  1.20 (t,  $J$  7 Hz, 3 H), 2.33 (s, 3 H), and 4.20 (q,  $J$  7 Hz, 2 H);  $\delta_F$  58.0 (m, 3F), 59.0 (m, 3F), 82.3 (q,  $J$  11 Hz, 3F), and 102.0 p.p.m. (m, 1F).

**Reaction of Perfluorobut-2-ene (4) with Diethyl Malonate.**—Reaction of (4) (3.64 g, 182 mmol), diethyl malonate (3.14 g, 19.6 mmol), sodium hydride (19.6 mmol), and tetraglyme (5 ml) gave 5-ethoxycarbonyl-6-ethoxy-2,2,3-trifluoro-4-trifluoromethyl-2H-pyran (16) (27%) (Found: C, 41.1; H, 3.1; F, 35.8%;  $M^+$  320.  $C_{11}H_{10}F_6O_4$  requires C, 41.3; H, 3.1; F, 35.6%;  $M$ , 320);  $v_{max}$  2910, 1740, 1690, and 1625  $cm^{-1}$ ;  $\delta_F$  60.7 (d,  $J$  26 Hz, 3F), 62.3 (d,  $J$  21 Hz, 2F), and 183.0 p.p.m. (m, 1F);  $\delta_H$  1.2 (br, 6 H) and 4.2 (br, 4 H).

**Reaction of (4) with Acetylacetone.**—Reaction of (4) (4.93 g, 24.7 mmol), acetylacetone (3.06 g, 30.6 mmol), sodium hydride (31.0 mmol), and tetraglyme (10 ml) gave 4-acetyl-5-methyl-2,3-bis(trifluoromethyl)furan (13) (37%) (Found: C, 41.3; H, 2.2; F, 44.3%;  $M^+$ , 260.  $C_9H_6F_6O_2$  requires C, 41.5; H, 2.3; F, 43.9%;  $M$ , 260).  $v_{max}$  2930, 1695, 1640, and 1565  $cm^{-1}$ ;  $\delta_F$  57.3 (q,  $J$  9 Hz, 3F) and 63.7 p.p.m. (q,  $J$  9 Hz, 3F);  $\delta_H$  2.00 (s, 3 H) and 2.17 (s, 3 H).

**Reaction of (4) with Ethyl Acetoacetate.**—Reaction of (4) (4.06 g, 20.3 mmol), ethyl acetoacetate (3.00 g, 23.0 mmol), sodium hydride (23.0 mmol), and tetraglyme (5 ml) gave 4-ethoxycarbonyl-5-methyl-2,3-bis(trifluoromethyl)furan (14) (57%) (Found: C, 41.7; H, 2.9; F, 39.8%;  $M^+$ , 290.  $C_{10}H_8F_6O_3$  requires C, 41.4; H, 2.8; F, 39.3%;  $M$ , 290).  $v_{max}$  2990, 1730, 1630, and 1585  $cm^{-1}$ ;  $\delta_F$  60.0 (q,  $J$  9.4 Hz, 3F) and 63.7 p.p.m. (q,  $J$  9.4 Hz, 3F);  $\delta_H$  0.80 (t,  $J$  7 Hz, 3 H), 2.14 (s, 3 H), and 3.73 (q,  $J$  7 Hz, 2 H).

**Reaction of Decafluorocyclohexene with Acetylacetone.**—Reaction of decafluorocyclohexene (4.16 g, 15.9 mmol), acetylacetone (2.50 g, 25.0 mmol), sodium hydride (25.0 mmol), and tetraglyme (10 ml) gave 3-acetyl-2-methyl-4,4,5,5,6,6,7,7-octafluoro-4,5,6,7-tetrahydrobenzofuran (18) (38%) (Found: C, 41.1; H, 2.0; F, 46.9%;  $M^+$ , 322.  $C_{11}H_6F_8O_2$  requires C, 41.0; H, 1.9; F, 47.2%;  $M$ , 322);  $v_{max}$  2930, 1690, 1620, and 1560  $cm^{-1}$ ;  $\delta_F$  106.8 (br, m, 2F), 113.2 (br, m, 2F), 134.0 (br, m, 2F), and 134.8 p.p.m. (br, m, 2F);  $\delta_H$  2.33 (s, 3 H) and 2.60 (s, 3 H).

**Reaction of Decafluorocyclohexene with Ethyl Acetoacetate.**—Reaction of decafluorocyclohexene (4.08 g, 15.6 mmol), ethyl acetoacetate (2.04 g, 15.8 mmol), sodium hydride (15.8 mmol), and tetraglyme (5 ml) gave 3-ethoxycarbonyl-2-methyl-4,4,5,5,6,6,7,7-octafluoro-4,5,6,7-tetrahydrobenzofuran (19) (31%) (Found: C, 41.2; H, 2.3; F, 43.2%;  $M^+$ , 352.  $C_{12}H_8F_8O_3$  requires C, 40.9; H, 2.3; F, 43.2%;  $M$ , 352);  $v_{max}$  2990, 1725, 1630, and 1580  $cm^{-1}$ ;  $\delta_F$  108.7 (br, m, 2F), 113.3 (br, m, 2F), 134.0 (br, m, 2F), and 135.0 p.p.m. (br, m, 2F);  $\delta_H$  1.27 (t,  $J$  7 Hz, 3 H), 2.60 (s, 3 H), and 4.30 (q,  $J$  7 Hz, 2 H).

**Reaction of Decafluorocyclohexene with Diethyl Malonate.**—Decafluorocyclohexene (6.30 g, 24.0 mmol), diethyl malonate (5.82 g, 36.4 mmol), sodium hydride (36.4 mmol), and tetraglyme (10 ml) gave 3-bis(ethoxycarbonyl)methyleneoctafluorocyclohexene (21) (31%) (Found: C, 40.8; H, 2.7; F, 40.2%;  $M^+$ , 382.  $C_{13}H_{10}F_8O_4$  requires C, 40.8; H, 2.6; F, 39.8%;  $M$ , 382);  $v_{max}$  2995, 1750, and 1700  $cm^{-1}$ ;  $\delta_F$  116.3 (br, m, 2F), 120.2 (br, m, 2F), 130.0 (br, m, 1F), 134.3 (br, m, 2F), and 152.0 p.p.m. (t,  $J$  21 Hz, 1F);  $\delta_H$  1.20 (t,  $J$  7 Hz, 3 H) and 4.27 (q,  $J$  7 Hz, 2 H).

**Reaction of Octafluorocyclopentene with Acetylacetone.**—Octafluorocyclopentene (3.65 g, 17.2 mmol), acetylacetone (3.0 g, 30.0 mmol), sodium hydride (30.0 mmol), and tetraglyme (10 ml) gave 3-acetyl-2-methyl-4,4,5,5,6,6-hexafluorocyclopenta[b]furan (17) (25%) (Found: C, 44.4; H, 2.4; F, 41.6%;  $M^+$ , 272.  $C_{10}F_6H_6O_2$  requires C, 44.1; H, 2.2; F, 41.9%;  $M$ , 272);  $v_{max}$  2930, 1690, 1620, 1565, and 1550  $cm^{-1}$ ;  $\delta_F$  104.8 (s, 2F), 111.3 (s, 2F), and 121.3 p.p.m. (s, 2F);  $\delta_H$  2.27 (s, 3 H) and 2.53 (s, 3 H).

**Reaction of Octafluorocyclopentene with Diethyl Malonate.**—Octafluorocyclopentene (4.58 g, 21.6 mmol), diethyl malonate

(3.20 g, 20.0 mmol), sodium hydride (20.0 mmol), and tetraglyme (5 ml) gave 3-bis(ethoxycarbonyl)methylenehexafluorocyclopentene (20) (12%) (Found: C, 43.6; H, 3.2; F, 34.7%;  $M^+$ , 332.  $C_{12}H_{10}F_6O_4$  requires C, 43.4; H, 3.0; F, 34.3%;  $M$ , 332);  $\nu_{\max}$  2 990, 1 745, and 1 720;  $\delta_F$  116.2 (d,  $J_{ad}$  4.7 Hz,  $F_a$ ), 120.2 (d, of d,  $J_{b,d}$  11 Hz,  $J_{b,c}$  14 Hz,  $F_b$ ), 133.7 (t,  $J_{b,d}$  11, of t,  $J_{a,d}$  4.7 Hz,  $F_d$ ), and 151.0 p.p.m. (t,  $J_{b,c}$  14 Hz,  $F_c$ );  $\delta_H$  1.20 (t,  $J$  7 Hz, 3 H), and 4.20 (q,  $J$  7 Hz, 2 H).

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