HEXAFLUOROACETONE IN THE WITTIG REACTION

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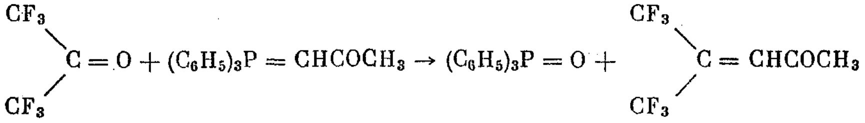
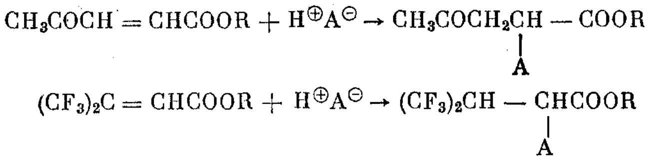
Acetonylidenetriphenylphosphorane (I) undergoes the Wittig reaction with difficulty [1]. Hexafluoroacetone, being, unlike other ketones, a strongly electrophilic compound [2-5], reacts smoothly with (I) in ethereal solution at room temperature with formation of 4,4-bistrifluoromethyl-3-buten-2-one (II), a fluorinated analog of mesityl oxide:



(I) (II)

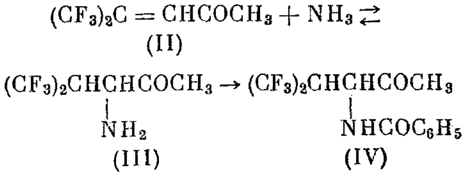
Unlike hexafluoroacetone, acetone does not react at all with (I) under analogous conditions. We studied the direction of the addition of ammonia to the unsaturated ketone (II); this depends on the comparative electron-acceptor strength of the two trifluoromethyl groups, on the one hand, and of the acetyl group, on the other. It is known that the acetyl group attracts the π-electrons of the double bond more strongly than the carboxy or alkoxycarbonyl group does [6, 7]. On the other hand two trifluoromethyl groups also have a greater electron-attracting effect than carbonyl or alkoxycarbonyl [8]



$$CH_3COCH = CHCOOR + H^{\oplus}A^{\ominus} \rightarrow CH_3COCH_2\underset{\displaystyle A}{\underset{|}{C}}H - COOR$$

$$(CF_3)_2C = CHCOOR + H^{\oplus}A^{\ominus} \rightarrow (CF_3)_2CH - \underset{\displaystyle A}{\underset{|}{C}}HCOOR$$

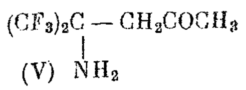
In the case of a double carbon-carbon bond which has two trifluoromethyl groups as neighbors on one side and one acetyl group as a neighbor on the other the π-electrons are displaced toward the trifluoromethyl groups. Actually on reaction of the ketone (II) with ammonia we obtained 3-amino-4,4-bistrifluoromethyl-2-butanone (III). It is interesting that this reaction is reversible; when an attempt is made to purify the amino ketone by distillation, even at reduced pressure (135 mm), it is decomposed into (II) and ammonia. For this reason the amino ketone, without isolation, was benzoylated, when we obtained 3-benzamido-4,4-bistrifluoromethyl-2-butanone (IV)



$$\underset{\text{(II)}}{(CF_3)_2C = CHCOCH_3} + NH_3 \rightleftarrows$$

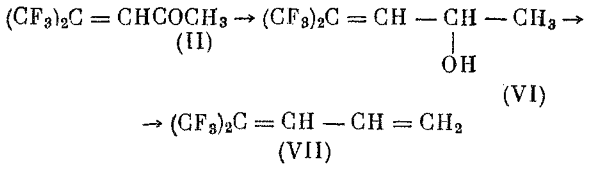
$$\underset{\text{(III)}}{(CF_3)_2CH\underset{\displaystyle NH_2}{\underset{|}{C}}HCOCH_3} \rightarrow \underset{\text{(IV)}}{(CF_3)_2CH\underset{\displaystyle NHCOC_6H_5}{\underset{|}{C}}HCOCH_3}$$

The structure of the benzamido ketone (IV), and therefore also of the amino ketone (II), was proved by the fact that on treatment of (IV) with alcoholic potassium hydroxide in the cold, almost all the fluorine in the molecule was mineralized. Such ready hydrolysis of the trifluoromethyl groups is not compatible with the structure (V), in which there is no hydrogen atom on the carbon adjacent to a trifluoromethyl group (cf. [8]).



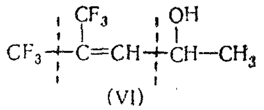
$$(CF_3)_2\underset{\substack{|\\ NH_2}}{C}-CH_2COCH_3 \quad (V)$$

4,4-Bistrifluoromethyl-3-buten-2-one (II) was applied also in the synthesis of 1,1-bistrifluoromethyl-1,3-butadiene in accordance with the scheme:



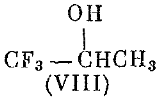
$$\underset{(II)}{(CF_3)_2C=CHCOCH_3} \rightarrow \underset{(VI)}{(CF_3)_2C=CH-\underset{\substack{|\\ OH}}{CH}-CH_3} \rightarrow \underset{(VII)}{(CF_3)_2C=CH-CH=CH_2}$$

The reduction of the unsaturated ketone to 4,4-bistrifluoromethyl-3-buten-2-ol (VI) was effected both by the Meerwein-Ponndorf method and also with the aid of lithium aluminum hydride.* The alcohol (VI) was obtained as an azeotropic mixture with ethanol and was not isolated in the pure state. It is known that the trifluoromethyl group strengthens the bond between a neighboring carbon and hydroxyl [9]. Since the ethylenic alcohol (VI) may be regarded as a vinylog of 1,1,1-trifluoro-2-propanol (VIII),



$$CF_3-\overset{\substack{CF_3\\ |}}{C}=CH-\overset{\substack{OH\\ |}}{CH}-CH_3$$

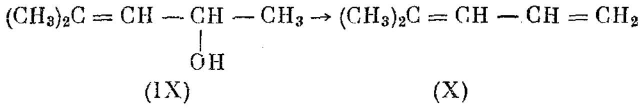
(VI)



$$CF_3-\overset{\substack{OH\\ |}}{C}HCH_3$$

(VIII)

it follows that in this case also the strengthening of the C–O bond is to be expected. Accordingly, the ethylenic alcohol (VI) remains unchanged under the conditions [10] under which its nonfluorinated analog (IX) is readily dehydrated into the corresponding diene (X) (distillation over aniline hydrobromide)



$$\underset{(IX)}{(CH_3)_2C=CH-\underset{\substack{|\\ OH}}{CH}-CH_3} \rightarrow \underset{(X)}{(CH_3)_2C=CH-CH=CH_2}$$

We succeeded in obtaining 1,1-bistrifluoromethyl-1,3-butadiene (VII) only with the aid of such strong dehydrating agents as sulfuric acid and phosphorus pentoxide. Attempts at effecting the thermal, radiation-induced, and chemically initiated polymerization of (VII) were not successful.

EXPERIMENTAL

4,4-Bistrifluoromethyl-3-buten-2-one (II). With continuous agitation 44 g of hexafluoroacetone was passed into a suspension of 80 g of acetonylidenetriphenylphosphorane in 200 ml in dry ether; 65.1 g (93%) of triphenylphosphine oxide, m.p. 151-152°, was filtered off. A mixture with a known sample melted without depression. By fractionation of the filtrate we isolated 31.4 g (61%) of (II); b.p. 68° (135 mm); n_D^{20} 1.3330; d_4^{20} 1.4102. Found: C 34.91; H 1.95; F 54.33%. $C_6H_4F_6O$. Calculated: C 34.95; H 1.94; F 55.34%.

3-Benzamido-4,4-bistrifluoromethyl-2-butanone (IV). Excess of ammonia was passed for ten minutes into a solution of 2 g of (II) in 30 ml of dry ether under cooling with solid carbon dioxide; the coolant was then removed, and ammonia and part of the ether was vacuum-distilled off. The resulting ethereal solution of 3-amino-4,4-bistrifluoromethyl-2-butanone (III)** was cooled with solid carbon dioxide, and gradual addition was made of an ethereal solution of 1.64 g of benzoyl chloride and 1.17 g of triethylamine. Solvent was evaporated from the resulting suspension, and the residue was washed with saturated sodium bicarbonate solution, with water, with dilute hydrochloric acid, and again with water. The precipitate obtained was recrystallized from dichloroethane. We obtained 2.18 g (66%) of (IV), m.p. 119-120°. Found: C 47.91; H 3.48; F 34.84; N 4.17%. $C_{13}H_6F_6O$. Calculated: C 47.70; H 3.36; F 34.86; N 4.28%.

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*Lithium aluminum hydride (0.5 mole) was added at not above 0° to the ketone (1 mole). A higher temperature or the reverse order of addition leads to reduction of the double bond.

**When an attempt was made to isolate (III) by vacuum-fractionation the original reactant (II) was obtained; b.p. 68° (135 mm); n_D^{20} 1.3330.

When (IV) was treated with 0.5% alcoholic potassium hydroxide for one day at room temperature 81% of all the fluorine contained in the (IV) molecule was mineralized.

4,4-Bistrifluoromethyl-3-buten-2-ol (VI). a) A mixture of 5 g of (II) and a solution of aluminum isopropoxide (from 1.32 g of aluminum foil and 40 ml of isopropyl alcohol) was boiled with simultaneous removal of the acetone formed by distillation through a rectification column. When acetone ceased to be liberated, the mixture was cooled to −10°, and acidified with dilute hydrochloric acid until weakly acid to Congo Red. The product was extracted with ether, and by fractionation of the ethereal solution we obtained 3.2 g of an azeotropic mixture of (VI) and ether containing 80.2% of (VI); b.p. 125-126°; n_D^{20} 1.3715; d_4^{20} 1.2702. Found: C 41.69; H 4.92; F 43.93%. 80.2%. $C_6H_6F_6O$ + 19.8% $C_4H_{10}O$. Calculated: C 40.60; H 5.02; F 43.93%. The yield calculated on pure (VI) was 2.6 g (52%).

b) To a solution of 9.13 g of (II) in 50 ml of dry ether at 0-4° we gradually added 0.84 g of lithium aluminum hydride. The mixture was cooled to −18° and carefully acidified with 0.1 N HCl until weakly acid to Congo Red. By distillation of the ether layer we isolated 7 g of an azeotropic mixture of (VI) and ether, identical to the azeotrope obtained in Expt. (a). The yield calculated on pure (VI) was 5.6 g (61%).

1,1-Bistrifluoromethyl-1,3-butadiene (VII). a) 7.06 g of the azeotropic mixture of (VI) and ether was mixed with 15 ml of concentrated sulfuric acid. On the next day crude (VII) was distilled off, washed with water, dried, and again distilled. We obtained 3.6 g (69.5%) of (VII); b.p. 65°; n_D^{20} 1.3447; d_4^{20} 1.3012. Found: C 38.34; H 2.35; F 60.12; MR 31.01. $C_6H_4F_6$. Calculated: C 37.89; H 2.11; F 60.00%; MR 29.83.

b) 3.75 g of the azeotropic mixture of (VI) and ether was mixed with 2 g of phosphorus pentoxide. After 30 minutes (VII) was distilled off. Yield 2.23 g (81.5%); b.p. 65°.

SUMMARY

1. 4,4-Bistrifluoromethyl-3-buten-2-one was prepared by the reaction of hexafluoroacetone with acetonylidenetriphenylphosphorane.

2. 1,1-Bistrifluoromethyl-1,3-butadiene was synthesized by the reduction of 4,4-bistrifluoromethyl-3-buten-2-one with subsequent dehydration of the resulting alcohol.

3. Ammonia adds to 4,4-bistrifluoromethyl-3-buten-2-one with formation of the α-amino ketone.

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