Chemistry of Diazocarbonyl Compounds: XXX.* Development of a Synthetic Approach to Pyridazine Structure via Wittig Reaction of Fluoroalkyl-Containing Diazo Keto Esters

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Abstract—3,4,6-Trisubstituted pyridazines were synthesized from fluoroalkyl-containing diazo keto esters in three steps along two different reaction sequences: (1) Wittig, Staudinger, and diaza-Wittig and (2) Staudinger, Wittig, and diaza-Wittig. According to the first of these with the initial Wittig reaction, the yield of the target 4-fluoroalkyl-substituted pyridazines is almost twice as large as in the reaction sequence involving the corresponding *N*-phosphanylidene derivatives as intermediates. In both sequences, the final steps (synthesis of vinylphosphazenes and the subsequent diaza-Wittig reaction) occurred as a tandem process, and intermediate vinylphosphazenes could not be isolated. Non-fluorinated diazo keto esters and the respective phosphazenes failed to react with alkoxycarbonylmethylidene(triphenyl)phosphoranes under the same conditions.

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Pyridazine structures are uncommon for naturally occurring compounds, but most synthetic pyridazine derivatives exhibit biological activity [2, 3]. Guillaume et al. [4] recently reported on a successful synthesis of substituted pyridazines from diazocarbonyl compounds, which involved transformation of the diazo group in the initial compound into the endocyclic pyridazine nitrogen atoms. These results, as well as the data reported by other authors [5, 6], prompted us to use in the synthesis of substituted pyridazines fluoroalkyl-containing diazodicarbonyl compounds which were prepared by us for the first time [7].

Taking into account published data [4–6, 8, 9], several ways of building up pyridazine structure **A** from diazocarbonyl substrate **B** may be proposed; Scheme 1

illustrates two synthetic approaches including reaction sequences (*a*, *b*, *c*) and (*b*, *a*, *c*). The (*a*, *b*, *c*) path implies initial "olefinization" of the carbonyl group in diazocarbonyl compound **B** via the Wittig reaction (*a*) and subsequent cyclization of vinyldiazocarbonyl derivative **C** to pyridazine **A** as a result of successive Staudinger (*b*) and diaza-Wittig reactions (*c*). An alternative approach (*b*, *a*, *c*) is based on initial Staudinger reaction (*b*) to obtain intermediate phosphazene **D** and transformation of the latter into the target structure **A** via reactions (*a*) and (*c*). In both cases, the key step in the formation of pyridazine structure **A** is the diaza-Wittig reaction (*c*) which is still rarely used in synthetic practice [4–6, 10, 11]; unlike related Wittig [12, 13] and aza-Wittig reactions [14], the diaza-Wittig reaction has been studied very poorly.
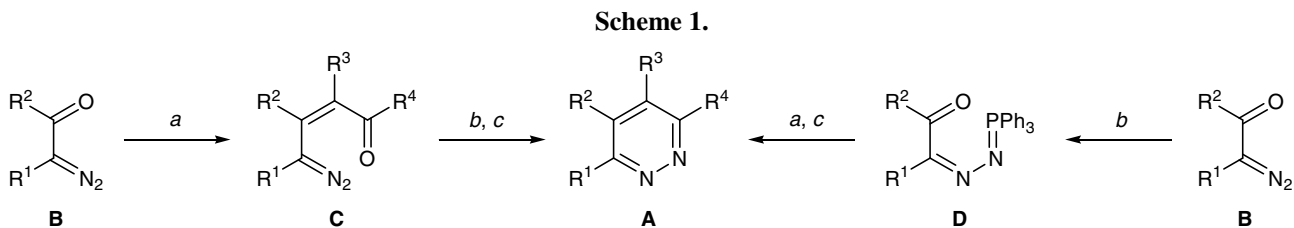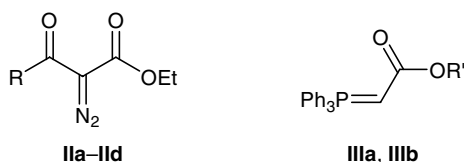
Scheme 1.

a: Wittig reaction; *b*: Staudinger reaction; *c*: diaza-Wittig reaction.

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* For communication XXIX, see [1].

As follows from Scheme 1, successful implementation of the above approaches could give rise to an efficient method for building up pyridazine structures having various substituents in the heteroring via appropriate choice of substituents in the initial diazo compound (R^1, R^2) and Wittig reagent (R^3, R^4). Our studies in this line [15] are aimed at elucidating structural factors in diazocarbonyl compounds with a view to obtain pyridazine derivatives with three and four substituents in the heteroring. In the present work we examined reactions of fluoroalkyl-containing and fluorine-free diazo keto esters, leading to pyridazines **I** according to schemes (*a, b, c*) and (*b, a, c*); no analogous studies have been reported so far.

As diazocarbonyl compounds we used ethyl 2-diazo-4,4,4-trifluoro-3-oxobutanoate (**IIa**), ethyl 2-diazo-4,4,5,5,6,6,6-heptafluoro-3-oxohexanoate (**IIb**), and their non-fluorinated analogs, ethyl 2-diazo-3-oxobutanoate (**IIc**) and ethyl 2-diazo-3-oxohexanoate (**IId**). The Wittig reagents were relatively stable and readily accessible methyl and ethyl (triphenyl-λ^5-phosphanylidene)acetates **IIIa** and **IIIb**.

**II**, R = CF$_3$ (**a**), C$_3$F$_7$ (**b**), Me (**c**), Pr (**d**); **III**, R' = Me (**a**), Et (**b**).

Initial diazo keto esters **IIa–IId** were synthesized from the corresponding 3-oxo esters by the diazo transfer reaction (Scheme 2). In the synthesis of readily hydrolyzable perfluoroalkyl-containing diazodicarbonyl compounds **IIa** and **IIb** [16], the most satisfactory yields (58–64%) were obtained using *m*-nitrobenzenesulfonyl azide and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in methylene chloride [7, 17]; the reactions were accompanied by side formation of the corresponding fluorinated carboxylic acid and ethyl diazoacetate. When the reaction was carried out in diethyl ether–pentane or in the presence of trimethylamine as a base instead of DBU, as well as under other conditions, the yields of diazo keto esters **IIa** and **IIb** were lower (30–50%). The diazo transfer reaction with
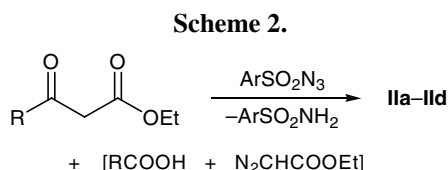
p-toluenesulfonyl azide in benzene in the presence of triethylamine [18] gave only 7–8% of compound **IIa**, while the major product was ethyl diazoacetate. Fluorine-free diazo keto esters **IIc** and **IId** were prepared under standard conditions for diazo group transfer [19, 20], i.e., with the use of *p*-toluenesulfonyl or *m*-nitrobenzenesulfonyl azide and trimethyl- or triethylamine. Unlike compounds **IIa** and **IIb**, nonfluorinated analogs **IIc** and **IId** were stable, and they did not undergo hydrolysis during their synthesis.

The structure of diazo keto esters **IIa–IId** was confirmed by the ^{1}H and ^{13}C NMR spectra. Replacement of the alkyl group by perfluoroalkyl in going from diazo keto esters **IIc** and **IId** to **IIa** and **IIb** leads to upfield shift of the C^1–C^3 signals. The largest shift is observed for the ketone carbonyl carbon atom (C^3, $\Delta\delta_C \approx 17$–17.5 ppm), while the chemical shifts of C^2 and C^1 change by 0.3–0.9 and 2.6–3.0 ppm, respectively.

Synthesis of pyridazines I according to scheme (*a, b, c*). The reactions of diazo keto esters **IIa–IId** with (alkoxycarbonyl)methylidenephosphoranes **IIIa** and **IIIb** were carried out under standard Wittig conditions [12, 13], at 18–20°C in diethyl ether using 20% excess of phosphorane **III**. In the reactions with fluorinated compounds **IIa** and **IIb** the corresponding unsaturated diazo esters **IVa–IVd** were obtained; they were isolated in high yields (75–99%) by flash chromatography on silica gel (Scheme 3). The structure of compounds **IVa–IVd** was confirmed by the ^{1}H and ^{13}C NMR spectra, as well as by comparing their spectral parameters with those reported previously for related structures [4, 21, 22]. Diazo esters **IVa–IVd** were formed as a single stereoisomer and were assigned *E* configuration at the double C=C bond on the basis of published data for vinyl diazo ketones [22] and other compounds [23].

Scheme 3.

R_F = CF$_3$, R = Me (**a**), Et (**b**); R_F = C$_3$F$_7$, R = Me (**c**), Et (**d**).
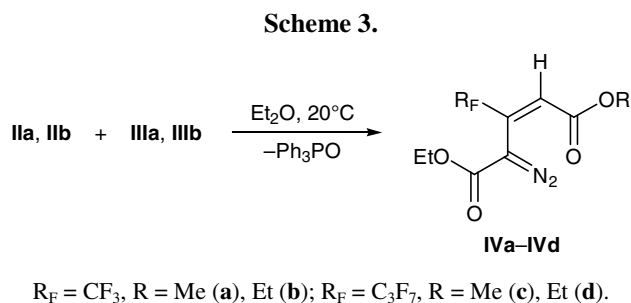
Fluorine-free diazo keto esters **IIc** and **IId** failed to react with phosphoranes **IIIa** and **IIIb** under analogous

Scheme 2.

conditions or on prolonged heating of the reactants in boiling diethyl ether (7–10 days). After prolonged heating, the only change observed in the reaction mixture was the appearance of an appreciable amount of PPh$_3$ (detected by TLC), while no triphenylphosphine oxide (the expected Wittig reaction product) was present. We did not try more severe conditions (which may be useful in some cases for relatively weakly reactive carbonyl compounds [24]), for diazo esters **IIc** and **IId** are known to be unstable above 60°C.

The formation of triphenylphosphine in the reaction mixtures on heating may result from partial dissociation of phosphonium ylide **IIIa** or **IIIb**, the other dissociation product being alkoxycarbonylcarbene. Examples of generation of carbene by decomposition of ylides [25], including phosphoranes [26], have been reported. However, we obtained no experimental proofs for the formation of ethoxycarbonylcarbene in the examined reactions.
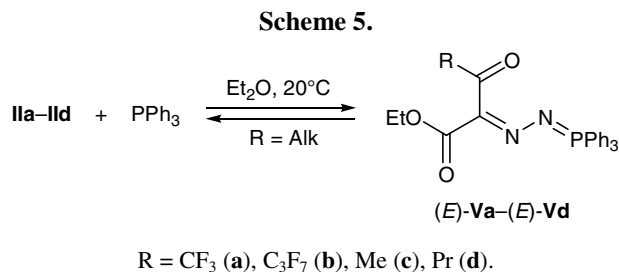
The different behaviors of fluorine-containing diazo keto esters **IIa** and **IIb** and their fluorine-free analogs **IIc** and **IId** may be interpreted in terms of enhanced electrophilicity of the carbonyl carbon atom in the perfluoroacyl fragment of the former. Similar differences were also observed for simple fluorinated and non-fluorinated ketones [27], but we were the first to reveal such differences while studying chemical properties of diazo keto esters.

The Staudinger (*b*) reactions of fluorine-containing diazo diesters **IVa–IVd** with triphenylphosphine were carried out in diethyl ether at room temperature; however, chromatographic separation of the reaction mixtures gave 57–65% of pyridazines **Ia–Id** rather than the expected phosphoranes **E** (Scheme 4). The product
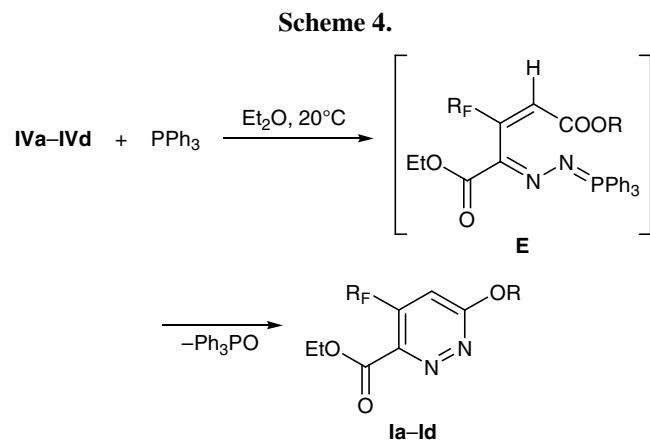
structure was determined on the basis of their ^{1}H and ^{13}C NMR and mass spectra. The NMR spectra of **Ia**–**Id** contained sets of proton and carbon signals consistent with their structure as fluoroalkyl-substituted pyridazines, and the signal positions insignificantly differed from those observed in the spectra of initial diazo esters **IVa–IVd**. All carbon signals in the spectra of **Ia–Id** were located slightly downfield relative to the corresponding signals of initial compounds **IVa–IVd**, and a new signal appeared in the aromatic region (δ_C 145–148 ppm) from the C^6 atom instead of the C=N signal (δ_C 57–63 ppm).

Synthesis of pyridazines I according to scheme (*b*, *a*, *c*). Following the (*b*, *a*, *c*) sequence, we preliminarily synthesized phosphazenes **Va–Vd** (Scheme 5). Experiments showed that, as in the above reactions, fluorine-containing diazo keto esters **IIa** and **IIb** and their non-fluorinated analogs **IIc** and **IId** behaved differently in the reaction with triphenylphosphine. The reactions of diazo compounds **IIa** and **IIb** with PPh$_3$ were accompanied by heat evolution and were complete in 2–3 min to give the corresponding phosphazenes **Va** and **Vb** in high yield (85–93%). By contrast, no heat evolution was observed upon addition of fluorine-free compounds **IIc** and **IId** to a solution of triphenylphosphine, products **Vc** and **Vd** began to separate from the reaction mixture in 7–10 days, and their yields did not exceed 60% after 2–3 weeks.

Scheme 5.

IIa–IId + PPh$_3$ $\xrightarrow[\text{R = Alk}]{\text{Et}_2\text{O, 20°C}}$

(*E*)-**Va**–(*E*)-**Vd**

R = CF$_3$ (**a**), C$_3$F$_7$ (**b**), Me (**c**), Pr (**d**).

In the ^{13}C and ^{1}H NMR spectra of **Vc** and **Vd** in CDCl$_3$ some signals were doubled. The ^{13}C NMR spectra of **Vc** and **Vd** contained only one signal at δ_C 149.8 ppm, which was assigned to the C=N carbon atom. After dissolution of analytically pure samples of **Vc** and **Vd** in CDCl$_3$, a weak signal appeared at δ_C 76.3 ppm, which is typical of initial diazo ester. Therefore, we concluded that adducts **Vc** and **Vd** in chloroform undergo partial dissociation into the initial components, diazo keto ester **IIc** or **IId** and triphenylphosphine.

Fluorine-containing derivatives **Va** and **Vb** showed in the NMR spectra (CDCl$_3$) only one set of signals,

Scheme 4.

IVa–IVd + PPh$_3$ $\xrightarrow{\text{Et}_2\text{O, 20°C}}$

E

$\xrightarrow{-\text{Ph}_3\text{PO}}$

Ia–Id

R$_F$ = CF$_3$, R = Me (**a**), Et (**b**); R$_F$ = C$_3$F$_7$, R = Me (**c**), Et (**d**).

indicating that these compounds are relatively stable in solution and that they exist as a single stereoisomer. The NOESY spectrum of compound **Va** revealed a correlation between the fluorine atoms in the CF$_3$ group and *ortho* protons in the aromatic ring on the phosphorus. These findings suggest *E* configuration of the substituents at the C=N bond in **V**.

Va
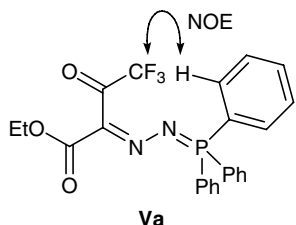
An appreciable difference in the reactivity of diazo keto esters **IIa** and **IIb**, on the one hand, and **IIc** and **IId**, on the other, toward triphenylphosphine is likely to result from increased electrophilicity of the diazo fragment in molecules **II** having perfluoroacyl groups. This assumption is confirmed by the upfield shift of the C^2 signal in the ^{13}C NMR spectra of **IIa** and **IIb** (see above, $\Delta\delta \approx 0.3$–0.9 ppm) relative to the corresponding signal of **IIc** and **IId**. In other words, fluorinated diazo compounds **IIa** and **IIb** are characterized by increased contribution of canonical structure **G** (Scheme 6) where the diazo group is clearly more electrophilic.

Scheme 6.
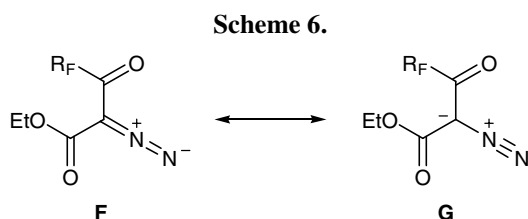
Phosphazenes **Va**–**Vd** were brought into the Wittig reaction with 1.2 equiv of compounds **IIIa** and **IIIb** in diethyl ether at room temperature (18–20°C). After appropriate treatment of the reaction mixtures obtained from compounds **Va** and **Vb**, we isolated by flash chromatography on silica gel fluoroalkyl-substituted pyridazines **Ia**–**Id** in relatively poor yields (25–29%; Scheme 7), i.e., the products were the same as in the reaction sequence (*a, b, c*). Under analogous conditions, only the initial compounds were isolated in the

Scheme 7.
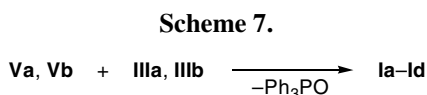
reactions with non-fluorinated derivatives **Vc** and **Vd** (yield 40–45%).

Presumably, both the examined reaction sequences lead to fluoroalkyl-substituted pyridazines **Ia**–**Id** via a two-step (tandem) process including initial formation of phosphazene **E** and its subsequent intramolecular cyclization via spontaneous diaza-Wittig reaction (Scheme 8). The easy diaza-Wittig reaction is likely to be favored by the *E* configuration of initial fluorine-containing diazo esters **IV** and phosphazenes **V**; such configuration facilitates formation of a four-membered transition state assumed for the Wittig reaction [12, 13, 24]. Non-fluorinated diazo keto esters **IIc** and **IId**, as well as the corresponding phosphazenes **Vc** and **Vd**, do not react with phosphoranes **III** under analogous conditions; therefore, no subsequent diaza-Wittig reaction occurs, and pyridazines **I** are not formed.

Scheme 8.
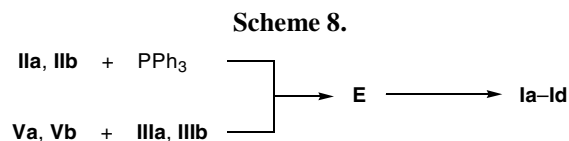
Thus we demonstrated the possibility for synthesizing 3,4,6-trisubstituted pyridazines from fluoroalkyl-containing diazo keto esters following two different reaction sequences: Wittig, Staudinger, and diaza-Wittig reactions or Staudinger, Wittig, and diaza-Wittig reactions. The first of these ensures greater yields of the target products by a factor of ~2. The two final steps in both sequences, i.e., the formation of phosphazene and diaza-Wittig reaction, occur as a tandem process, so that intermediate phosphazene cannot be isolated.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker 300 instrument at 300 and 75.5 MHz, respectively, using CDCl$_3$ as solvent and tetramethylsilane as internal reference. The mass spectra (electron impact, 70 eV) of compounds **IIa** and **IIb** were obtained with direct sample admission into the ion source. The elemental compositions were determined on a Heraeus CHNO Rapid Analyzer. The reaction mixtures were separated by column or flash chromatography on neutral silica gel (Silicagel L, 40–100 μm; gradient elution with petroleum ether–diethyl ether mixtures). The progress of reactions was monitored by TLC on Silufol UV-254 plates; R_f values were measured using petroleum ether–diethyl ether (1:1) as eluent.

Wittig reagents **IIIa** and **IIIb** were prepared from commercial ethyl or methyl chloroacetate and triphenylphosphine according to the procedure described in [28] and were additionally purified by recrystallization from ethyl acetate. All reactions were performed in anhydrous solvents.

Diazo keto esters IIa–IId (*general procedure*). 3-Nitrobenzenesulfonyl azide, 3.22–7.27 g (13–30 mmol), and the corresponding keto ester, 13–30 mmol, were dissolved in 10–15 ml of methylene chloride, the solution was cooled to 0–5°C, and 0.2–0.4 ml (1–4 mmol) of DBU was added under stirring and cooling. After 10 min, the cooling bath was removed, and the mixture was stirred for 1–2 h at room temperature until the reaction was complete. The precipitate of arenesulfonamide was separated by filtration through a layer of calcined silica gel (3.5 g) on a Schott filter and washed with CH_2Cl_2–hexane (1:1, 2×6 ml). The solvent was distilled off under reduced pressure (10–15 mm), and the residue was distilled at 0.5–2.0 mm on a microdistillation setup.

The most efficient procedure for the separation of ethyl diazoacetate formed by hydrolysis of diazo keto esters **IIa** and **IIb** was vacuum distillation of the reaction mixture at a residual pressure of 0.5–0.6 mm. Under these conditions, volatile ethyl diazoacetate is collected in a trap, and it does not contaminate fluorine-containing diazo esters **IIa** and **IIb** that are distilled at 35–48°C (0.5–0.6 mm).

Ethyl 2-diazo-4,4,4-trifluoro-3-oxobutanoate (IIa) was obtained from 3.9 g (21 mmol) of ethyl 4,4,4-trifluoro-3-oxobutanoate and 4.9 g (21 mmol) of *m*-nitrobenzenesulfonyl azide. Yield 4.2 g (66%), bp 35–37°C (0.6 mm), $n_D^{20} = 1.4276$, R_f 0.71 [29]. ^{1}H NMR spectrum, δ, ppm: 1.35 t (3H, CH_3, $J = 7.1$ Hz), 4.36 q (2H, CH_2, $J = 7.1$ Hz). ^{13}C NMR spectrum, $δ_C$, ppm: 14.2 (CH_3), 62.8 (CH_2), 76.0 (CN_2), 115.8 q (CF_3, [1]$J_{CF} = 288.5$ Hz), 158.5 (**C**OOEt), 172.6 q (C=O, [2]$J_{CF} = 40.2$ Hz).

Ethyl 2-diazo-4,4,5,5,6,6,6-heptafluoro-3-oxo-hexanoate (IIb) was obtained from 3.76 g (13 mmol) of ethyl 4,4,5,5,6,6,6-heptafluoro-3-oxohexanoate and 3.03 g (13 mmol) of *m*-nitrobenzenesulfonyl azide. Yield 2.47 g (61.4%), bp 44–48°C (0.6 mm), $n_D^{20} = 1.3964$, R_f 0.70 [30]. ^{1}H NMR spectrum, δ, ppm: 1.36 t (3H, CH_3, $J = 7.1$ Hz), 4.37 q (2H, CH_2, $J = 7.1$ Hz). ^{13}C NMR spectrum, $δ_C$, ppm: 14.2 (CH_3), 63.0 (CH_2), 75.4 (CN_2), 108.7 t.q (CF_3**C**F_2, [1]$J_{CF} = 266.7$, [2]$J_{CF} = 39.0$ Hz), 109.8 t.t (CF_3**C**$F_2$$CF_2$, [1]$J_{CF} = 268.7$, [2]$J_{CF} = 33.7$ Hz), 117.6 q.t (CF_3, [1]$J_{CF} = 288.4$, [2]$J_{CF} = 33.3$ Hz), 158.9 (**C**OOEt), 172.7 t (C=O, [2]$J_{CF} = 27.6$ Hz).

Ethyl 2-diazo-3-oxobutanoate (IIc) was obtained from 3.4 g (26 mmol) of ethyl 3-oxobutanoate and 5.95 g (26 mmol) of *m*-nitrobenzenesulfonyl azide. Yield 3.22 g (79.5%), bp 40–42°C (0.6 mm), $n_D^{20} = 1.4725$, R_f 0.77 [31]. ^{1}H NMR spectrum, δ, ppm: 1.34 t (3H, CH_3, $J = 7.1$ Hz), 2.47 s (CH_3), 4.31 q (2H, CH_2, $J = 7.1$ Hz). ^{13}C NMR spectrum, $δ_C$, ppm: 14.4 (**C**H_2CH_3), 28.3 (CH_3), 61.5 (CH_2CH_3), 76.3 (CN_2), 161.5 (**C**OOEt), 190.1 (C=O).

Ethyl 2-diazo-3-oxohexanoate (IId) was obtained from 4.79 g (30 mmol) of ethyl 3-oxohexanoate and 7.27 g (30 mmol) of *m*-nitrobenzenesulfonyl azide. Yield 4.76 g (86%), bp 46–47°C (0.1 mm), $n_D^{20} = 1.4722$, $R_f = 0.76$ [29]. ^{1}H NMR spectrum, δ, ppm: 0.90 t (3H, $CH_2CH_2CH_3$, $J = 7.5$ Hz), 1.27 t (3H, OCH_2CH_3, $J = 7.5$ Hz), 1.6 m ($CH_2CH_2CH_3$), 2.76 t (2H, **C**$H_2CH_2CH_3$, $J = 7.1$ Hz), 4.23 q (2H, OCH_2, $J = 7.1$ Hz). ^{13}C NMR spectrum, $δ_C$, ppm: 14.0 ($CH_2CH_2CH_3$), 14.6 (OCH_2CH_3), 18.1 ($CH_2CH_2CH_3$), 42.4 (**C**$H_2CH_2CH_3$), 61.6 (OCH_2), 76.1 (CN_2), 161.7 (**C**OOEt), 193.1 (C=O).

Diazo esters IVa–IVd (*general procedure*). Diazo keto ester **IIa** or **IIb**, 0.40–1.47 g (1.3–7 mmol), was added dropwise under stirring to a suspension of 0.68–3.51 g (1.95–10.5 mmol) of triphenylphosphorane **IIIa** or **IIIb** in 7–30 ml of diethyl ether. The mixture was stirred for 1–2 h until the reaction was complete, 10 ml of petroleum ether was added, the precipitate was filtered off and washed with petroleum ether (4×5 ml), the solvent was distilled off under reduced pressure (10–15 mm), and the residue was subjected to chromatography in a column charged with 10 g of silica gel (gradient elution with petroleum ether–diethyl ether). Fractions containing compounds **IVa–IVd** were dried over anhydrous $MgSO_4$ and evaporated under reduced pressure (10–15 mm), and the residue was distilled at 0.1–0.05 mm using a microdistillation setup.

5-Ethyl 1-methyl 4-diazo-3-trifluoromethylpent-2-enedioate (IVa) was obtained from 1.47 g (7 mmol) of diazo ester **IIa** and 3.51 g (10.5 mmol) of phosphorane **IIIa**. Yield 1.4 g (75%), bright yellow oily substance, bp 38–40°C (0.5 mm), R_f 0.67 [32]. ^{1}H NMR spectrum, δ, ppm: 1.30 t (3H, CH_2CH_3, $J = 7.2$ Hz), 3.80 s (3H, OCH_3), 4.27 q (2H, OCH_2, $J = 7.2$ Hz), 6.45 s (1H, CH). ^{13}C NMR spectrum, $δ_C$, ppm: 14.3 (CH_2CH_3), 52.4 (OCH_3), 58.4 (CN_2), 62.0 (**C**H_2CH_3), 122.3 q (CF_3, [1]$J_{CF} = 276.1$ Hz), 123.6 (C=**C**H), 128.6 q (**C**=CH, [2]$J_{CF} = 33.2$ Hz), 163.2 (**C**OOEt), 165.9 (**C**OOMe).

Diethyl 4-diazo-3-trifluoromethylpent-2-enedioate (IVb) was obtained from 0.44 g (2.1 mmol) of

diazo ester **IIa** and 1.10 g (3.2 mmol) of phosphorane **IIIb**. Yield 0.50 g (85%), bright yellow oily substance, bp 38–40°C (0.5 mm), n_D^{20} = 1.4722, R_f 0.67 [4]. ^{1}H NMR spectrum, δ, ppm: 1.29 t (3H, CH$_3$, J = 7.0 Hz), 1.31 t (3H, CH$_3$, J = 7.7 Hz), 4.24 q (2H, CH$_2$, J = 7.6 Hz), 4.27 q (2H, CH$_2$, J = 7.1 Hz), 6.45 s (1H, CH). ^{13}C NMR spectrum, δ$_C$, ppm: 14.3 (CH$_3$), 14.5 (CH$_3$), 58.4 (CN$_2$), 61.8 (CH$_2$), 62.1 (CH$_2$), 122.4 q (CF$_3$, $^1J_{CF}$ = 277.0 Hz), 124.6 q (C=**CH**, $^3J_{CF}$ = 4.6 Hz), 128.5 q (**C**=CH, $^2J_{CF}$ = 32.2 Hz), 163.4 (**C**OOEt), 165.5 (**C**OOEt).

5-Ethyl 1-methyl 4-diazo-3-heptafluoropropyl-pent-2-enedioate (IVc) was obtained from 1.24 g (4 mmol) of diazo ester **IIb** and 2.01 g (6 mmol) of phosphorane **IIIa**. Yield 1.30 g (83%), bright yellow oily substance, bp 45–48°C (2 mm), R_f 0.66. ^{1}H NMR spectrum, δ, ppm: 1.27 t (3H, CH$_2$**CH$_3$**, J = 7.7 Hz), 3.80 s (3H, OCH$_3$), 4.25 q (2H, OCH$_2$, J = 6.9 Hz), 6.43 s (1H, CH). ^{13}C NMR spectrum, δ$_C$, ppm: 14.3 (CH$_2$**CH$_3$**), 52.5 (OCH$_3$), 62.1 (OCH$_2$), 58.1 (CN$_2$), 104.5–119.7 m (C$_3$F$_7$), 126.8 t (**C**=CH, $^2J_{CF}$ = 24.1 Hz), 128.5 t (C=**CH**, $^3J_{CF}$ = 7.1 Hz), 163.3 (**C**OOMe), 163.7 (**C**OOEt).

Diethyl 4-diazo-3-heptafluoropropylpent-2-ene-dioate (IVd) was obtained from 0.40 g (1.3 mmol) of diazo ester **IIb** and 0.68 g (1.95 mmol) of phosphorane **IIIb**. Yield 0.5 g (99.8%), bright yellow heavy oily substance, bp 38–40°C (0.5 mm), R_f 0.66. ^{1}H NMR spectrum, δ, ppm: 1.27 t (3H, CH$_3$, J = 6.8 Hz), 1.32 t (3H, CH$_3$, J = 7.1 Hz), 4.26 q (2H, CH$_2$, J = 7.1 Hz), 4.26 q (2H, CH$_2$, J = 7.1 Hz), 6.43 s (1H, CH). ^{13}C NMR spectrum, δ$_C$, ppm: 14.1 (CH$_3$), 14.3 (CH$_3$), 57.9 (CN$_2$), 61.8 (CH$_2$), 62.1 (CH$_2$), 108.3 t.q (CF$_3$**CF$_2$**, $^1J_{CF}$ = 265.8, $^2J_{CF}$ = 38.4 Hz), 114.6 t.t (CF$_3$**CF$_2$**CF$_2$, $^1J_{CF}$ = 289.7, $^2J_{CF}$ = 32.5 Hz), 117.8 q.t (**CF$_3$**, $^1J_{CF}$ = 288.1, $^2J_{CF}$ = 33.8 Hz), 126.6 t (**C**=CH, $^2J_{CF}$ = 24.3 Hz), 129.3 (C=**CH**), 163.3 (**C**OOEt), 163.5 (**C**OOEt).

Phosphazenes Va–Vd (*general procedure*). Diazo ester **IIa–IId**, 0.8–1.22 g (3–4.7 mmol), was added to a solution of 0.79–1.22 g (3–4.7 mmol) of triphenylphosphine in 5–12 ml of diethyl ether (in the synthesis of fluorine-containing phosphazenes **Va** and **Vb**, the reaction was exothermic; therefore, the mixture was cooled in an ice bath, and diazo ester **IIa** or **IIb** was added in small portions). The mixture was kept at room temperature for 2–3 min (in the synthesis of **Va** and **Vb**) or 3–4 weeks (in the synthesis of **Vc** and **Vd**). The precipitate was filtered off on a Schott filter, washed with 2 ml of diethyl ether and 5 ml of petroleum ether, and dried in air.

Ethyl 4,4,4-trifluoro-3-oxo-2-(triphenyl-λ^5-phosphanylidenehydrazono)butanoate (Va) was obtained from 0.98 g (4.7 mmol) of diazo ester **IIa** and 1.22 g (4.7 mmol) of triphenylphosphine. Yield 1.9 g (85%), bright yellow crystalline substance, mp 119–120°C [29]. ^{1}H NMR spectrum, δ, ppm: 1.36 t (3H, CH$_3$, J = 7.3 Hz), 4.38 q (2H, CH$_2$, J = 7.3 Hz), 7.25–7.65 m (15H, H$_{arom}$). ^{13}C NMR spectrum, δ$_C$, ppm: 14.4 (CH$_2$**CH$_3$**), 60.9 (OCH$_2$), 121.2 q (CF$_3$, $^1J_{CF}$ = 291.0 Hz), 124.9 d (C^i, $^1J_{CP}$ = 94.2 Hz), 129.0 d (C^m, $^3J_{CP}$ = 12.6 Hz), 133.5 (C^p), 133.7 d (C^o, $^2J_{CP}$ = 9.3 Hz), 143.3 d (C=N, $^3J_{CP}$ = 48.2 Hz), 164.0 (**C**OOEt), 174.9 q (**C**=O, $^2J_{CF}$ = 33.3 Hz). Found, %: C 61.26, 61.00; H 4.34, 4.40; N 6.17, 6.02. C$_{24}$H$_{20}$F$_3$N$_2$O$_3$P. Calculated, %: C 61.10; H 4.28; N 5.93.

Ethyl 4,4,5,5,6,6,6-heptafluoro-3-oxo-2-(triphenyl-λ^5-phosphanylidenehydrazono)hexanoate (Vb) was obtained from 0.93 g (3.0 mmol) of compound **IIb** and 0.79 g (3.0 mmol) of triphenylphosphine. Yield 1.6 g (93%), bright yellow crystalline substance, mp 107–108°C. ^{1}H NMR spectrum, δ, ppm: 1.35 t (CH$_3$, 3H, J = 7.3 Hz), 4.38 q (2H, OCH$_2$, J = 7.3 Hz), 7.27–7.65 m (15H, H$_{arom}$). ^{13}C NMR spectrum, δ$_C$, ppm: 14.4 (CH$_2$**CH$_3$**), 61.0 (OCH$_2$), 104.8–120.1 m (C$_3$F$_7$), 124.9 d (C^i, $^1J_{CP}$ = 95.9 Hz), 129.1 d (C^m, $^3J_{CP}$ = 11.3 Hz), 133.5 d (C^o, $^2J_{CP}$ = 9.2 Hz), 133.3 (C^p), 146.1 d (C=N, $^3J_{CP}$ = 49.4 Hz), 164.6 (**C**OOEt), 175.9 t (**C**=O, $^2J_{CF}$ = 24.1 Hz). Found, %: C 54.52, 54.85; H 3.57, 3.67; N 5.04, 5.22. C$_{26}$H$_{20}$F$_7$N$_2$O$_3$P. Calculated, %: C 54.54; H 3.53; N 4.89.

Ethyl 3-oxo-2-(triphenyl-λ^5-phosphanylidenehydrazono)butanoate (Vc) was obtained from 0.52 g (3.0 mmol) of compound **IIc** and 0.84 g (3.0 mmol) of triphenylphosphine. Yield 0.37 g (27%), pale yellow crystalline substance, mp 103–104°C [29]. ^{1}H NMR spectrum, δ, ppm: 1.36 t (3H, CH$_2$**CH$_3$**, J = 7.0 Hz), 2.5 s (3H, CH$_3$), 4.29 q (2H, OCH$_2$CH$_3$, J = 7.2 Hz), 7.25–7.62 m (15H, H$_{arom}$). ^{13}C NMR spectrum, δ$_C$, ppm: 14.3 (CH$_2$**CH$_3$**), 28.2 (CH$_3$), 60.5 (**CH$_2$**CH$_3$), 126.6 d (C^i, $^1J_{CP}$ = 94.3 Hz), 128.8 d (C^m, $^3J_{CP}$ = 11.5 Hz), 132.8 (C^p), 133.3 d (C^o, $^2J_{CP}$ = 8.1 Hz), 149.7 d (C=N, $^3J_{CP}$ = 43.6 Hz), 166.8 (**C**OOEt), 194.9 (**C**=O). Found, %: C 68.76, 68.92; H 5.67, 5.59; N 7.09, 6.79. C$_{24}$H$_{23}$N$_2$O$_3$P. Calculated, %: C 68.88; H 5.55; N 6.69.

Ethyl 3-oxo-2-(triphenyl-λ^5-phosphanylidenehydrazono)hexanoate (Vd) was obtained from 0.80 g (4.4 mmol) of diazo ester **IId** and 1.15 g (4.4 mmol) of triphenylphosphine. Yield 1.16 g (59%), pale yellow crystalline substance, mp 85–87°C [29]. ^{1}H NMR spectrum, δ, ppm: 0.79 t (3H, CH$_2$**CH$_3$**, J = 7.3 Hz),

1.36 t (3H, OCH$_2$CH$_3$, J = 7.3 Hz), 1.50 m (2H, CH$_2$CH$_3$), 2.54 t (2H, CH$_2$CH$_2$CH$_3$, J = 7.3 Hz), 4.39 q (2H, OCH$_2$, J = 7.0 Hz), 7.49–7.69 m (15H, H$_{arom}$). ^{13}C NMR spectrum, δ_C, ppm: 14.1 (CH$_2$CH$_3$), 14.5 (OCH$_2$CH$_3$), 18.7 (CH$_2$CH$_3$), 38.9 (CH$_2$CH$_2$CH$_3$) 60.5 (OCH$_2$), 126.7 d (C^i, $^1J_{CP}$ = 94.3 Hz), 128.5 d (C^m, $^3J_{CP}$ = 11.5 Hz), 132.1 (C^p), 133.4 d (C^o, $^2J_{CP}$ = 8.1 Hz), 149.2 d (C=N, $^3J_{CP}$ = 44.6 Hz), 166.9 (COOEt), 197.3 (C=O). Found, %: C 71.83, 71.61; H 6.35, 6.24; N 6.58, 6.37. C$_{26}$H$_{27}$N$_2$O$_3$P. Calculated, %: C 69.94; H 6.11; N 6.28.

Pyridazines Ia–Id (*general procedure*). *a. Path b, c.* Diazo ester **IVa–IVd**, 1.07–1.43 g (2.5–4.0 mmol), was added under stirring to a solution of 0.79–1.31 g (3–5.0 mmol) of triphenylphosphine in 10–15 ml of diethyl ether, and the mixture was kept for 24 h at room temperature. When the reaction was complete, the precipitate was filtered off on a Schott filter and washed with petroleum ehter (4×10 ml), the solvent was distilled off from the filtrate under reduced pressure (10–15 mm), and the residue was subjected to column chromatography on 10 g of silica gel (gradient elution with petroleum ether–diethyl ether). Fractions containing pyridazines **Ia–Id** were dried over anhydrous magnesium sulfate and evaporated under reduced pressure (10–15 mm), and the residue was distilled in a vacuum using a microdistillation setup.

b. Path a, c. Compound **Va** or **Vb**, 1.14–1.49 g (2–4 mmol), was added under stirring to a suspension of 0.82–1.61 g (2.4–4.8 mmol) of phosphorane **IIIa** or **IIIb** in 8–12 ml of diethyl ether, and the mixture was left to stand for 24 h at room temperature. When the reaction was complete, the mixture was treated as described above in *a*.

Ethyl 6-methoxy-4-trifluoromethylpyridazine-3-carboxylate (Ia) was obtained from 1.07 g (4 mmol) of diazo ester **IVa** and 1.3 g (5 mmol) of triphenylphosphine or from 1.49 g (4 mmol) of compound **Va** and 1.61 g (4.8 mmol) of phosphorane **IIIa**; yield 0.58 g (58%) (*a*), 0.31 g (29%) (*b*); colorless heavy oily substance, bp 48–50°C (3 mm), R_f 0.49. ^{1}H NMR spectrum, δ, ppm: 1.44 t (3H, CH$_2$CH$_3$, J = 7.3 Hz), 4.27 s (3H, OCH$_3$), 4.51 q (2H, OCH$_2$, J = 7.3 Hz), 7.30 (1H, CH). ^{13}C NMR spectrum, δ_C, ppm: 14.0 (CH$_2$CH$_3$), 56.2 (OCH$_3$), 63.0 (OCH$_2$), 115.3 q (C^5, $^3J_{CF}$ = 5.0 Hz), 121.3 q (CF$_3$, $^1J_{CF}$ = 274.2 Hz), 131.3 q (C^4, $^2J_{CF}$ = 35.9 Hz), 146.0 (C^3), 163.2 (CO$_2$Et), 165.6 (C^6).

Ethyl 6-ethoxy-4-trifluoromethylpyridazine-3-carboxylate (Ib) was obtained from 1.12 g (4.0 mmol)

of diazo ester **IVa** and 1.31 g (5.0 mmol) of triphenylphosphine or from 1.42 g (3.0 mmol) of compound **Va** and 1.25 g (3.0 mmol) of phosphorane **IIIb**; yield 0.22 g (27%) (*a*), 0.61 g (58%) (*b*); colorless heavy oily substance, bp 48–49°C (1–2 mm), R_f 0.50 [4]. ^{1}H NMR spectrum, δ, ppm: 1.45 t (3H, CH$_3$, J = 7.3 Hz), 1.50 t (3H, CH$_3$, J = 7.1 Hz), 4.51 q (2H, OCH$_2$, J = 7.0 Hz), 4.72 q (2H, OCH$_2$, J = 7.0 Hz), 7.30 (1H, CH). ^{13}C NMR spectrum, δ_C, ppm: 14.0 (CO$_2$CH$_2$CH$_3$), 14.3 (6-OCH$_2$CH$_3$), 63.0 (CO$_2$CH$_2$-CH$_3$), 65.2 (6-OCH$_2$), 115.4 (C^5), 121.4 q (CF$_3$, $^1J_{CF}$ = 274.5 Hz), 131.4 q (C^4, $^2J_{CF}$ = 35.7 Hz), 145.8 (C^3), 163.3 (CO$_2$Et), 165.5 (C^6). Mass spectrum, m/z (I_{rel}, %): 264 (47) [M]$^+$, 249 (32), 236 (40), 236 (40), 219 (62), 208 (62), 192 (94), 164 (100), 152 (15), 148 (94), 136 (23), 121 (30), 107 (24), 93 (32), 86 (40), 69 (18), 57 (21), 45 (58).

Ethyl 4-heptafluoropropyl-6-methoxypyridazine-3-carboxylate (Ic) was obtained from 1.42 g (2.5 mmol) of diazo ester **IVb** and 0.79 g (3.0 mmol) of triphenylphosphine or from 1.14 g (2.0 mmol) of compound **Vb** and 0.82 g (2.4 mmol) of phosphorane **IIIa**; yield 0.20 g (29%) (*a*), 0.51 g (58%) (*b*); colorless heavy oily substance, bp 42–46°C (2 mm), R_f 0.54. ^{1}H NMR spectrum, δ, ppm: 1.41 t (3H, CH$_2$CH$_3$, J = 7.3 Hz), 4.27 s (3H, OCH$_3$), 4.49 q (2H, OCH$_2$, J = 7.0 Hz), 7.20 (CH). ^{13}C NMR spectrum, δ_C, ppm: 13.9 (CH$_2$CH$_3$), 56.2 (OCH$_3$), 63.1 (OCH$_2$), 117.1 t (C^5, $^3J_{CF}$ = 7.0 Hz), 108.5 t.q (CF$_3$CF$_2$, $^1J_{CF}$ = 266.6, $^2J_{CF}$ = 39.0 Hz), 113.8 t.t (4-CF$_2$, $^1J_{CF}$ = 258.5, $^2J_{CF}$ = 32.6 Hz), 117.7 q.t (CF$_3$, $^1J_{CF}$ = 288.2, $^2J_{CF}$ = 34.0 Hz), 129.4 t (C^4, $^2J_{CF}$ = 26.0 Hz), 147.5 (C^3), 163.8 (CO$_2$Et), 165.2 (C^6).

Ethyl 6-ethoxy-4-heptafluoropropylpyridazine-3-carboxylate (Id) was obtained from 1.42 g (2.5 mmol) of diazo ester **IVb** and 0.79 g (3.0 mmol) of triphenylphosphine or from 1.14 g (2.0 mmol) of compound **Vb** and 0.84 g (2.4 mmol) of phosphorane **IIIb**; yield 0.16 g (25%) (*a*), 0.59 g (65%) (*b*); colorless heavy oily substance, bp 44–47°C (3 mm), R_f 0.55. ^{1}H NMR spectrum, δ, ppm: 1.40 t (3H, CH$_3$, J = 7.3 Hz), 1.50 t (3H, CH$_3$, J = 7.2 Hz), 4.48 q (2H, CH$_2$, J = 7.3 Hz), 4.71 q (2H, CH$_2$, J = 7.0 Hz), 7.20 (1H, CH). ^{13}C NMR spectrum, δ, ppm: 13.9 (CH$_3$), 14.3 (CH$_3$), 63.0 (CH$_2$), 65.2 (CH$_2$), 117.2 t (C^5, $^3J_{CF}$ = 6.9 Hz), 108.6 t.q (CF$_3$CF$_2$, $^1J_{CF}$ = 265.4, $^2J_{CF}$ = 38.9 Hz), 113.9 t.t (4-CF$_2$, $^1J_{CF}$ = 258.6, $^2J_{CF}$ = 33.3 Hz), 117.7 q.t (CF$_3$, $^1J_{CF}$ = 288.3 Hz, $^2J_{CF}$ = 35.7 Hz), 129.4 t (C^4, $^2J_{CF}$ = 26.4 Hz), 147.2 (C^3), 163.9 (CO$_2$Et), 165.0 (C^6). Mass spectrum, m/z (I_{rel}, %): 364 (68) [M]$^+$, 349

(37), 336 (38), 319 (86), 308 (63), 292 (80), 264 (83), 262 (50), 248 (100), 247 (96), 179 (27), 145 (44), 117 (21), 69 (59), 59 (18), 52 (36), 45 (82).

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