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Synthesis of 4-fluoroalkyl-substituted pyridazines from fluorinated diazodiketones

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Abstract

Two approaches are reported for the preparation of 3,4,6-trisubstituted pyridazines from fluoroalkyl-containing diazodiketones: the sequence of Wittig/Staudinger/*diaza*-Wittig and Staudinger/Wittig/*diaza*-Wittig reactions. The implementation of the Wittig reaction at the first stage gives rise to considerably higher yields of the targeted pyridazines than through initial phosphazines. In both approaches the final stages of the synthesis (the formation of vinylphosphazines and the subsequent *diaza*-Wittig reaction) occur as a tandem process. R^F-activated carbonyls are much more reactive in Wittig olefination of diazodicarbonyl and 1,3-dioxophosphazine molecules, than non-fluorinated acyl and aroyl carbonyl groups ($R^FCO \gg$ COAlk, COAr), and as a result non-fluorinated diazodiketones and their phosphazines do not produce pyridazines under the same conditions.

Keywords: 2-Diazo-1,3-diketones; Fluoroalkyl-containing vinyldiazoketones; Phosphazines; *Diaza*-Wittig reaction; Pyridazines

1. Introduction

Pyridazine structures are a rarity in nature, but most synthetic objects of this series exhibit biological activity [1]. Furthermore, incorporation of fluorine atoms into pyridazine molecule could considerably modify their biological properties and enhance physiological activity [2]. For example, fluoroalkyl-containing triazolopyridazines are reported to be central nervous system stimulants [2d], while trifluoromethyl-substituted pyridazinylquinolines may be used to modulate specific *in vivo* or *in vitro* receptor activity in humans and domesticated animals [2e]. This article describes two synthetic ways to fluoroalkyl-substituted pyridazines.

Recently the successful synthesis of substituted pyridazines starting from aliphatic diazocarbonyl compounds has been reported, during which the diazofunctionality of the initial substrates was converted into nitrogen atoms of the pyridazine heterocycle [3]. These data as well as publications from the other groups [4,5] prompted us to study the synthesis of substituted pyridazines from fluoroalkyl-containing diazodiketones and other diazodicarbonyl compounds [6,7].

Based on the known reactions of diazo compounds [3–5,8] one may envision several ways to pyridazine structure **A** from diazocarbonyl substrate **B**, two of which (a,b,c) and (b,a,c) are represented in Scheme 1.

Approach (a,b,c) implies the initial ''olefination'' of the carbonyl group of diazo compound **B** using Wittig reaction (a) followed by cyclization of vinyldiazocarbonyl compound **C** into pyridazine structure **A** with the help of consecutive Staudinger (b) and intramolecular *diaza*-Wittig (c) reactions.

The alternative route (b,a,c) implicates at first preparation of phosphazine **D** by the Staudinger reaction (b) and then transformation of this phosphazine to the targeted structure **A** *via* two stage process (a),(c).

In both cases the key stage in the creation of pyridazine structure **A** is the intramolecular *diaza*-Wittig reaction (c) of the vinylphosphazine **E**, which occurs rather rarely in preparative organic synthesis [3–5,9] and is not well understood, unlike the related Wittig [10,11] and *aza*-Wittig [12] reactions.

As is evident from the above scheme, the successful realization of the ways outlined could offer a powerful

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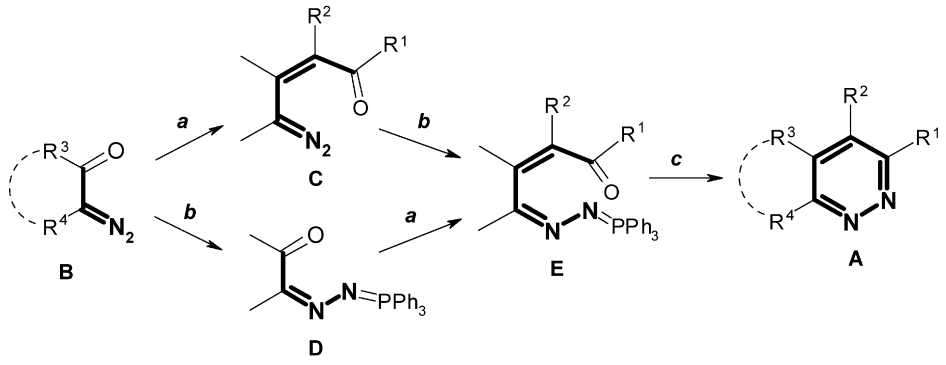


a) Wittig reaction; ***b***) Staudinger reaction; ***c***) *diaza*-Wittig reaction

Scheme 1.

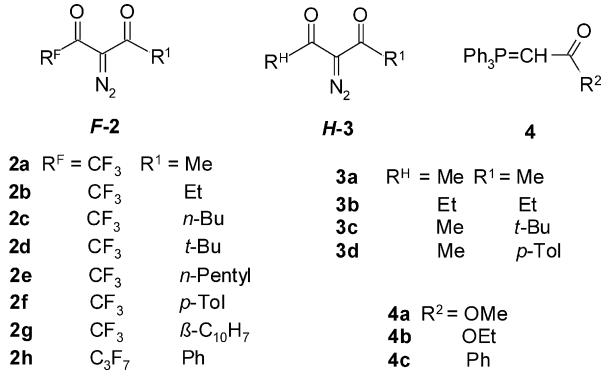
approach for the creation of pyridazine structures with different substituents on heterocycle due to independent variation of them in both reagents—initial diazo compound and Wittig reagent. Our investigations in this area [7] are directed towards elucidation of the structural elements in diazocarbonyl compounds, which enable synthesis of three- and four-substituted pyridazines.

In this article the results of a comparison study of the synthesis of pyridazines **1** from fluorine-containing and non-fluorinated diazodiketones according to Scheme 1 are considered.

2. Results and discussion

2.1. Objects of investigation

A series of fluorine-containing 2-diazo-1,3-diketones ***F*-2a–h** was used in this research, which differ significantly in the nature (Alk, Ar) and bulk of the substituents R^1. To determine the scope and limitations of the processes involved, appropriate non-fluorinated diazodiketones ***H*-3a–d** were also tested in these reactions (Scheme 2). Investigation was carried out with the relatively persistent and easily available Wittig reagents—stabilized (alkoxycarbonyl)methylenetriphenylphosphoranes **4a**,**b** and in part with (benzoyl)methylenetriphenylphosphorane **4c**.



Scheme 2.

Diazodiketones ***F*-2a–h** and ***H*-3a–d** were synthesized from corresponding 1,3-diketones by means of diazotransfer reaction [6,13].

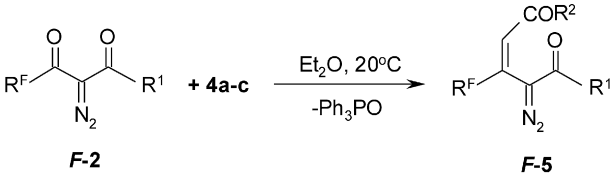
2.2. Synthesis of pyridazines *1* using the approach (a,b,c)

The fluorine-containing vinyldiazoketones ***F*-5** for the first stage of the approach (a,b,c) were obtained from corresponding fluorinated diazodiketones **2a–h** *via* Wittig reaction (a) with alkylidenephosphoranes **4a–c**, according to the recently developed protocol [14] (Scheme 3). The reaction proceeds with a high regio- and stereoselectivity.

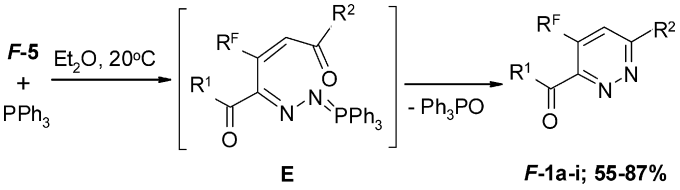
Olefination of unsymmetrically substituted 2-diazo-1,3-diketones ***F*-2**, bearing two different C=O groups in the molecule, occurs solely at the perfluoroacyl carbonyl group. This regioselectivity is in good agreement with previous observation on the R^F-bearing carbonyl olefination of the ethyl diazotrifluoroacetoacetate [3a]. Thus, one can conclude that fluoroalkyl-activated carbonyls are much more reactive in Wittig reaction of diazodicarbonyl molecules than non-fluorinated acyl (aroyl) and alkoxycarbonyl groups ($R^FCO \gg$ COAlk, COAr, CO_2Alk).

As for stereochemistry of the obtained vinyldiazoketones ***F*-5**, the reaction gives rise to only one, *E*-stereoisomer ***F*-5**, which is a characteristic property of the stabilized triphenylphosphonium ylides ($Ph_3PCHCOR'$) olefinations [15].

The Staudinger reaction (b) of fluorinated vinyldiazoketones **5a–i** with PPh_3 was carried out in anhydrous diethyl ether at room temperature (Scheme 4). On completion, the reaction mixture was simply separated on a column packed with silica gel. However, instead of the anticipated vinylphosphazines E after chromatography directly 4-fluoroalkyl-substituted pyridazines **1a–i** were isolated in good yields (55–87%). By this



Scheme 3.



Scheme 4.

Table 1
Vinyldiazoketones **F-5a–i** and pyridazines **F-1a–i**

Compounds ***F*-1**, **5**	R^F	R^1	R^2	Yield (%) of ***F*-1**
a	CF_3	Me	OMe	71
b	CF_3	Et	OEt	82
c	CF_3	*n*-Bu	OMe	55
d	CF_3	*t*-Bu	OMe	74
e	CF_3	*n*-Pentyl	OMe	58
f	CF_3	*p*-Tol	OMe	67
g	CF_3	2-Naphthyl	OEt	67
h	C_3F_7	Ph	OMe	87
i	CF_3	Me	Ph	80

means two-stage process (b,c) occurred here as a one-pot reaction (Table 1).

The structure of the previously unknown 3,4,6-trisubstituted pyridazines ***F*-1** was established by means of ^1H, ^{13}C, ^{19}F NMR spectroscopy; their composition was confirmed by elemental analysis. The molecular structure of 3-(*tert*-butyl)carbonyl-4-trifluoromethyl-6-methoxypyridazine ***F*-1d**, has also been confirmed by X-ray crystallography (Fig. 1).

The compound ***F*-1d** crystallizes in hexagonal space group $P6_5$ with six molecules in the cell. The pyridazine ring is nearly planar, the mean deviation from the least squares plane with the atoms N1, N2, C1, C2, C3 and C4 is 0.018(2)°. The plane with the carbonyl atoms C5, O1 and the atom C6 gives a dihedral angle of 57.7(1)° with the pyridazine ring. The bond distance N1–N2 in the pyridazine ring is 1.362(2) and as well as N–C distances are in a good agreement with other structural data for pyridazines [16].

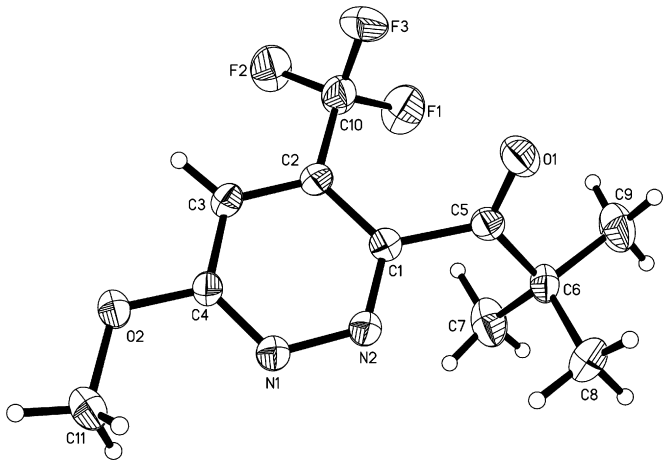


Fig. 1. Molecular structure of pyridazine **1d**. The ellipsoids denote 50% probability.

NMR spectra of compounds ***F*-1** show the required sets of proton, carbon and fluorine signals, which also fit well with the proposed structure. ^1H and ^{19}F chemical shifts of pyridazines ***F*-1** are closely related to the appropriate parameters of the initial vinyldiazoketones ***F*-5** with a general weaker shielding of the corresponding groups in the spectra of pyridazines. A new strong signal of aromatic carbon C6 appears in their ^{13}C NMR spectra at 149–152 ppm instead of a weak signal of the diazocarbon atom at 61–66 ppm. In the IR spectra strong absorption bands of the carbonyl groups were registered at 1665–1722 cm^{-1}, while the absorption of the CN_2 group from the starting compounds at 2080–2095 cm^{-1} disappeared.

Unlike fluorinated diazodiketones ***F*-2** their analogs ***H*-3** did not react with Wittig reagents under the same conditions.[1] Thus, ***H*-vinyldiazoketones 5** were not available by olefination of ***H*-diazodiketones 3** *via* reaction (a) and for this reason a similar approach (a,b,c) for the preparation of pyridazines ***H*-1** from non-fluorinated diazodiketones **3** was not tested.

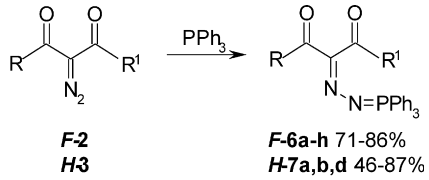
2.3. Synthesis of pyridazines *1* according to the approach (b,a,c)

At the first stage of the approach (b,a,c) phosphazines **6**,**7** were obtained by Staudinger reaction (b) from diazodiketones ***F*-2**, ***H*-3** and triphenylphosphine. This reaction is rather common to a variety of diazo compounds [3–6,8], and usually preparation of crystalline phosphazine derivatives is useful for the identification of liquid, and frequently unstable, aliphatic diazo compounds.

In the course of our experiments with diazodiketones ***F*-2** and ***H*-3** it turned out that reactivity of fluorine-containing diazodiketones **2a–h** and their non-fluorinated counterparts **3a–d** in Staudinger reaction (b) was noticeably different. Thus, interaction of diazodiketones ***F*-2** with PPh_3 is exothermic and gives rise to the formation of corresponding phosphazines ***F*-6a–h** in 10–15 min and in good yields (71–86%). Interaction of ***H*-diazodiketones 3a–d** with triphenylphosphine proceeds much slower (from 1 to 15 days), and in some cases (for example with diazodiketone **3c**) no crystalline adducts with PPh_3 were formed (Scheme 5; Table 2).

The structure of phosphazines ***F*-6a–h** and ***H*-7a,b,d** was confirmed by the data of NMR spectroscopy. Analysis of their parameters shows that in the ^1H and ^{13}C NMR spectra of some phosphazines **6** and **7**, which were recorded just after dissolution of the analytically pure samples in $CDCl_3$, not only the signals of phosphazines ***F*-6**, ***H*-7** were observed, but the patterns related to the initial diazodiketones ***F*-6**, ***H*-7** and PPh_3 were present as well. It is evident that in these cases the dissociation of adducts ***F*-6**, ***H*-7** on the initial components partially takes place in solution. The presence of bulky alkyl and aryl substituents in the structure of phosphazines (as in the case of the compounds **6d**,**f–h**) considerably diminishes the

[1] The Wittig reaction at elevated temperatures, which are usually applied for relatively inert carbonyl compounds [15a], has not been tested in our study, since diazodiketones ***H*-3** decompose at temperatures above 50–60 °C.



Scheme 5.

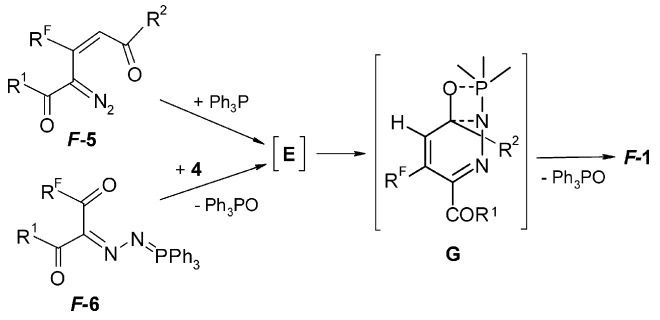
Table 2
Phosphazines **F-6a–h**, **H-7a,b,d**

Compounds ***F*-6**, ***H*-7**	R	R^1	Yield (%)
***F*-6a**	CF_3	Me	84
b	CF_3	Et	85
c	CF_3	*n*-Bu	87
d	CF_3	*t*-Bu	83
e	CF_3	Pentyl	79
f	CF_3	*p*-Tol	86
g	CF_3	2-Naphthyl	83
h	C_3F_7	Ph	76
***H*-7a**	Me	Me	86
b	Et	Et	46
d	Me	*p*-Tol	87

tendency of the adducts for dissociation, while the presence of the linear alkyl groups (such as Me, Et, *n*-Bu, *n*-pentyl in phospazines **6a–c,e**, **7a,b**) conversely favours this process.

The considerable difference in reactivity of diazodiketones ***F*-2a–h** and ***H*-3a–d** with triphenylphosphine in Staudinger reaction (b) is presumably caused by the increasing electrophilic character of the diazofunction (=N_2) on changing the α-acyl to perfluoroacyl group. According to spectroscopic data [6] this replacement cases a noticeable shift of the signals for the key atoms C3 (~17 ppm) and C2 (3–4 ppm) in the ^{13}C NMR spectra. The latter upfield shift may be considered as an indirect evidence of the stronger shielding (and the larger electronic density on) the carbon atoms C2 of diazogroup in diazodiketones ***F*-2**, and accordingly as an argument in favour of the enhancement of the positive charge on the diazofunction in the molecule of these diazodiketones.

The reaction (a) of phosphazines ***F*-6**, ***H*-7** with Wittig reagent **4a** was studied for the compounds ***F*-6a,c,f** and ***H*-7a,b,d** in diethyl ether solution at 18–20 °C using 20% excess of phosphorane **4a** (Scheme 6). And as already observed in the approach (a,b,c), after flash-chromatography of the reaction mixture on silica gel directly 4-fluoroalkyl-containing pyridazines **1a,c,f** were isolated from ***F*-phospazines 6a,c,f** with yields 17–60%. The compounds **1a,c,f** obtained were in every respect identical to the corresponding pyridazines prepared with the approach (a,b,c).



Scheme 7.

All attempts to carry out Wittig reaction (a) with non-fluorinated phosphazines **7a,b,d**, and thus to obtain pyridazines ***H*-1** using (b,a,c) approach, did not give positive results. Only initial compounds **7** or their dissociation products – diazodiketones ***H*-3** and triphenylphosphine – were recovered after ordinary work-up procedure of the reaction mixtures. It seems that non-fluorinated phosphazines ***H*-7**, as well as ***H*-diazodiketones 3** [14], do not react with Wittig reagents **4** at usual conditions.

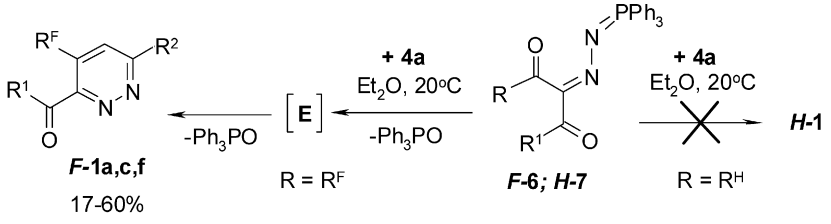
2.4. Concluding remarks

It is evident from the results obtained, that the formation of fluoroalkyl-containing pyridazines **1** takes place *via* a two-stage tandem process in both approaches considered; initially vinylphosphazine E is formed and then in the course of the spontaneous *diaza*-Wittig reaction intramolecular cyclization of this intermediate occurs with the elimination of triphenylphosphine oxide and production of pyridazine **1** (Scheme 7).

The extremely easy occurrence of the *diaza*-Wittig reaction-cyclization at stage (c) is clearly assisted by the *E*-configuration of the initial vinyldiazoketones ***F*-5** [14], because their stereochemistry strongly favours the formation of the typical for Wittig reaction transition state **G** [10–12,15].

Lower yields of pyridazines ***F*-1** in approach (b,a,c) perhaps may be explained by partial dissociation of starting phosphazines ***F*-6** into diazodiketones ***F*-2** and PPh_3 in solution of the reaction mixture and/or owing to the lower reactivity of them in Wittig reaction as compared with diazodiketones ***F*-2**.

In summary, application of two different approaches – the sequence of Wittig/Staudinger/*diaza*-Wittig and Staudinger/Wittig/*diaza*-Wittig reactions – for the synthesis of 4-fluoroalkyl-substituted pyridazines *via* essentially two-stage processes from fluorine-containing diazodiketones has been demonstrated with higher yields in the first one. In both cases the two final reactions occur as a tandem process and at usual



Scheme 6.

reaction conditions vinylphosphazines cannot be isolated from the reaction mixture. Non-fluorinated diazodiketones and the relevant triphenylphosphazines do not interact with (alkoxycarbonyl)methylenetriphenylphosphoranes and thus do not produce corresponding pyridazines.

3. Experimental

3.1. General

^{1}H, ^{13}C and ^{19}F NMR spectra were recorded at 200, 300, 600 MHz (^{1}H), 50, 75, 150 MHz (^{13}C), 188, 282 MHz (^{19}F) and at 81 MHz (^{31}P) with Varian Gemini-2000, Varian Mercury-300 or Bruker DRX-600 NMR spectrometers in $CDCl_3$ solution using TMS, $CFCl_3$ and H_3PO_4 as internal standards. IR spectra were recorded on a spectrophotometer Genesis FTIR Unicam Analytical System (ATI Mattson) with KBr pellets. Microanalysis was performed on a Heraeus CHNO Rapid Analyser. UV–vis spectra were recorded on a Beckman DU 650; λ_{max} in nm ($\log \varepsilon$). Melting points were measured on Boetius micro-melting-point apparatus and are corrected. All reactions were carried out in carefully purified and dried solvents and were monitored by thin-layer chromatography (TLC) on plates of Silufol UV/VIS 254 nm (KAVALIER) using UV light and iodine as visualizing agents. Preparative column chromatography was carried out on neutral silica gel (CHEMAPOL L 40/100 or MERCK 70–230 mesh) with petroleum (40–70 °C) and diethyl ether as eluents in gradient regime.

3.2. General procedure for the synthesis of phosphazines *F*-*6a–h*, *H*-*7a,b,d*

The stirred and cooled to 0–5 °C solution of 0.83 g (3.15 mmol) PPh_3 in Et_2O (5 mL) was treated dropwise with 2-diazo-1,3-diketones **2**,**3** (3 mmol). After stirring for 1–2 h the mixture was cooled in refrigerator to −10 to 15 °C, precipitated bright-yellow crystals of phosphazines **6**,**7** were isolated by filtration, washed with cold Et_2O (2× 5 mL) and dried on air.

3.2.1. 1,1,1-Trifluoro-3-(triphenylphosphoranylidene)azino-2,4-pentanedione (*6a*)

Bright-yellow crystals; yield: 1.12 g (84%); mp 102–103 °C [6a]. ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.58 (3H, s), 7.51–7.58 (6H, m), 7.63–7.71 (9H, m). ^{19}F NMR (282 MHz, $CDCl_3$): δ −70.7 (s, 3F). ^{13}C NMR (150 MHz, $CDCl_3$): δ 31.4, 117.5 (q, $^{1}J_{C-F}$ = 293 Hz), 125.0 (d, $^{1}J_{C-P}$ = 95 Hz), 129.0 (d, $^{3}J_{C-P}$ = 12 Hz), 133.5 (d, $^{4}J_{C-P}$ = 2 Hz), 133.6 (d, $^{2}J_{C-P}$ = 9 Hz), 149.2 (d, $^{3}J_{C-P}$ = 44 Hz), 175.7 (q, $^{2}J_{C-F}$ = 33 Hz), 199.8. Anal. calcd for $C_{23}H_{18}O_2N_2F_3P$: C, 62.5; H, 4.1; N, 6.3. Found: C, 62.3; H, 4.2; N, 6.1.

3.2.2. 1,1,1-Trifluoro-3-(triphenylphosphoranylidene)azino-2,4-hexanedione (*6b*)

Bright-yellow crystals; yield: 1.16 g (85%); mp 83–85 °C [6a]. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.20 (3H, t), 2.90 (2H, q), 7.50–7.59 (6H, m), 7.65–7.75 (9H, m). ^{19}F NMR (282 MHz, $CDCl_3$): δ −70.7 (s, 3F). Anal. calcd for $C_{24}H_{20}O_2N_2F_3P$: C, 63.2; H, 4.4; N, 6.1. Found: C, 63.2; H, 4.5; N, 6.2.

3.2.3. 1,1,1-Trifluoro-3-(triphenylphosphoranylidene)azino-2,4-octanedione (*6c*)

Bright-yellow crystals; yield: 1.26 g (87%); mp 77–79 °C [6a]. ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.89 (3H, t, J = 7 Hz), 1.38 (2H, m, J = 7 Hz), 1.67 (2H, m, J = 7 Hz), 2.80 (2H, t, J = 7 Hz), 7.53–7.57 (6H, m), 6.64–7.70 (9H, m). ^{19}F NMR (282 MHz, $CDCl_3$): δ −70.7 (s, 3F). ^{13}C NMR (150 MHz, $CDCl_3$): δ 14.0, 22.5, 27.4, 43.4, 117.5 (q, $^{1}J_{C-F}$ = 292 Hz), 125.2 (d, $^{1}J_{C-P}$ = 95 Hz), 129.1 (d, $^{3}J_{C-P}$ = 12 Hz), 133.4 (d, $^{4}J_{C-P}$ = 2 Hz), 133.6 (d, $^{2}J_{C-P}$ = 9 Hz), 149.8 (d, $^{3}J_{C-P}$ = 46 Hz), 175.7 (q, $^{2}J_{C-F}$ = 33 Hz), 204.0. Anal. calcd for $C_{26}H_{24}O_2N_2F_3P$: C, 64.5; H, 5.0; N, 5.8. Found: C, 64.3; H, 5.0; N, 5.7.

3.2.4. 5,5-Dimethyl-1,1,1-trifluoro-3-(triphenylphosphoranylidene)azino-2,4-hexanedione (*6d*)

Bright-yellow crystals; yield: 1.20 g (83%); mp 131–133 °C [6a]. ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.23 (9H, s), 7.50–7.53 (6H, m), 7.63–7.66 (9H, m). ^{19}F NMR (282 MHz, $CDCl_3$): δ −70.8 (s, 3F). ^{13}C NMR (150 MHz, $CDCl_3$): δ 26.4, 44.0, 117.3 (q, $^{1}J_{C-F}$ = 292 Hz), 125.5 (d, $^{1}J_{C-P}$ = 95 Hz), 129.1 (d, $^{3}J_{C-P}$ = 12 Hz), 133.3 (d, $^{4}J_{C-P}$ = 2 Hz), 133.5 (d, $^{2}J_{C-P}$ = 9 Hz), 151.1 (d, $^{3}J_{C-P}$ = 47 Hz), 175.9 (q, $^{2}J_{C-F}$ = 33 Hz), 214.6. Anal. calcd for $C_{26}H_{24}O_2N_2F_3P$: C, 64.5; H, 5.0; N, 5.8. Found: C, 64.5; H, 4.9; N, 5.7.

3.2.5. 1,1,1-Trifluoro-3-(triphenylphosphoranylidene)azino-2,4-nonanedione (*6e*)

Bright-yellow crystal; yield: 1.20 g (79%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.90–1.70 (9H, m), 2.83 (2H, t), 7.51–7.58 (6H, m), 6.66–7.71 (9H, m). ^{19}F NMR (282 MHz, $CDCl_3$): δ −70.7 (s, 3F). Anal. calcd for $C_{27}H_{26}O_2N_2F_3P$: C, 65.1; H, 5.3; N, 5.6. Found: C, 65.2; H, 5.4; N, 5.6.

3.2.6. 4-(4-Methylphenyl)-1,1,1-trifluoro-3-(triphenylphosphoranylidene)azino-2,4-butanedione (*6f*)

Bright-yellow crystals; yield: 1.34 g (86%); mp 143–145 °C [6b]. ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.40 (3H, s), 7.22 (2H, d, J = 8 Hz), 7.75 (2H, d, J = 8 Hz), 7.48–7.49 (6H, m), 7.53–7.57 (6H, m), 7.63 (3H, t, J = 7 Hz). ^{19}F NMR (282 MHz, $CDCl_3$): δ −70.6 (s, 3F). ^{13}C NMR (150 MHz, $CDCl_3$): δ 21.8, 117.5 (q, $^{1}J_{C-F}$ = 292 Hz), 125.2 (d, $^{1}J_{C-P}$ = 85 Hz), 128.0 (d, $^{3}J_{C-P}$ = 12 Hz), 128.7, 129.2, 133.3 (d, $^{4}J_{C-P}$ = 2 Hz), 133.6 (d, $^{2}J_{C-P}$ = 9 Hz), 134.0, 144.1, 148.8 (d, $^{3}J_{C-P}$ = 47 Hz), 175.9 (q, $^{2}J_{C-F}$ = 33 Hz), 195.9. Anal. calcd for $C_{29}H_{22}O_2N_2F_3P$: C, 67.2; H, 4.3; N, 5.4. Found: C, 67.1; H, 4.3; N, 5.4.

3.2.7. 4-(2-Naphthyl))-1,1,1-trifluoro-3-(triphenylphosphoranylidene)azino-2,4-butanedione (*6g*)

Bright-yellow crystals; yield: 1.38 g (83%); mp 153–155 °C [6b]. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.33–8.29 (22 H, m). ^{19}F NMR (282 MHz, $CDCl_3$): δ −70.5 (s, 3F). ^{13}C NMR (75 MHz, $CDCl_3$): δ 117.6 (q, $^{1}J_{C-F}$ = 293 Hz), 124.0, 124.4, 125.3 (d, $^{1}J_{C-P}$ = 95 Hz), 127.9, 128.5, 128.5, 129.1 (d, $^{3}J_{C-P}$ = 12 Hz),

129.7, 131.5, 132.9, 133.4 (d, $^4J_{C-P}$ = 2 Hz), 133.6 (d, $^2J_{C-P}$ = 9 Hz), 148.5 (d, $^3J_{C-P}$ = 46 Hz), 176.0 (q, $^2J_{C-F}$ = 33 Hz), 196.3. Anal. calcd for $C_{32}H_{22}O_2N_2F_3P$: C, 69.3; H, 4.0; N, 5.1. Found: C, 69.4; H, 4.1; N, 5.0.

3.2.8. 1,1,1,2,2,3,3-Heptafluoro-4-phenyl-3-(triphenylphosphoranylidene)azino-2,4-butanedione (**6h**)

Bright-yellow crystals; yield: 1.38 g (76%); mp 108–110 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.42 (2H, t, *J* = 8 Hz), 7.43–7.49 (6H, m), 7.50–7.56 (7H, m), 7.62 (3H, t, *J* = 7 Hz), 7.85 (2H, d, *J* = 8 Hz). ^{19}F NMR (282 MHz, $CDCl_3$): δ −80.0 (t, 3F, *J* = 9 Hz), −113.6 (t, 2F, *J* = 9 Hz), −124.8 (s, 2F). ^{13}C NMR (150 MHz, $CDCl_3$): δ 108.9 (tq, $^1J_{C-F}$ = 267 Hz, $^2J_{C-F}$ = 37 Hz), 111.2 (tq, $^1J_{C-F}$ = 268 Hz, $^2J_{C-F}$ = 33 Hz), 117.9 (qt, $^1J_{C-F}$ = 288 Hz, $^2J_{C-F}$ = 34 Hz), 128.6, 128.9 (d, $^1J_{C-P}$ = 95 Hz), 129.0, 129.5 (d, $^3J_{C-P}$ = 12 Hz), 133.2, 133.4 (d, $^4J_{C-P}$ = 2 Hz), 133.5 (d, $^2J_{C-P}$ = 9 Hz), 136.4, 150.7 (d, $^3J_{C-P}$ = 47 Hz), 177.0 (t, $^2J_{C-F}$ = 23 Hz), 196.7. Anal. calcd for $C_{30}H_{20}O_2N_2F_7P$: C, 59.6; H, 3.3; N, 4.6. Found: C, 59.4; H, 3.4; N, 4.6.

3.2.9. 3-(Triphenylphosphoranylidene)azino-2,4-pentanedione (**7a**)

Bright-yellow crystals; yield: 1.00 g (86%); mp 112–113 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.19 (6H, s), 7.51–7.57 (6H, m), 7.62–7.73 (9H, m). ^{31}P NMR (81 MHz, $CDCl_3$): δ 22.4. ^{13}C NMR (50 MHz, $CDCl_3$): δ 28.5, 126.7 (d, $^1J_{C-P}$ = 94 Hz), 128.6 (d, $^3J_{C-P}$ = 13 Hz), 132.9 (d, $^4J_{C-P}$ = 3 Hz), 133.7 (d, $^2J_{C-P}$ = 18 Hz), 154.3 (d, $^3J_{C-P}$ = 43 Hz), 195.8, 205.9. Anal. calcd for $C_{23}H_{21}O_2N_2P$: C, 71.1; H, 5.5; N, 7.2. Found: C, 71.4; H, 5.4; N, 7.3.

3.2.10. 4-(Triphenylphosphoranylidene)azino-3,5-heptanedione (**7b**)

Bright-yellow crystals; yield: 0.58 g (46%); mp 73–75 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.15 (4H, t), 2.74 (6H, q), 7.47–7.52 (6H, m), 7.61–7.68 (9H, m). ^{31}P NMR (81 MHz, $CDCl_3$): δ 23.0. Anal. calcd for $C_{25}H_{25}O_2N_2P$: C, 72.1; H, 6.1; N, 6.7. Found: C, 71.9; H, 6.1; N, 6.0.

3.2.11. 1-(4-Methylphenyl)-2-(triphenylphosphoranylidene)azino-1,3-butanedione (**7d**)

Bright-yellow crystals; yield: 1.21 g (87%); mp 88–90 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.26 (3H, s), 2.35 (3H, s), 7.43–7.75 (15H, m). ^{31}P NMR (81 MHz, $CDCl_3$): δ 22.7. ^{13}C NMR (50 MHz, $CDCl_3$): δ 21.7, 25.0, 126.6 (d, $^1J_{C-P}$ = 92 Hz), 127.5, 128.7 (d, $^3J_{C-P}$ = 12 Hz), 129.2, 131.9, 132.7 (d, $^4J_{C-P}$ = 3 Hz), 133.3 (d, $^2J_{C-P}$ = 9 Hz), 143.5, 154.5 (d, $^3J_{C-P}$ = 43 Hz), 196.2, 199.8. Anal. calcd for $C_{29}H_{25}O_2N_2P$: C, 75.0; H, 5.4; N, 6.0. Found: C, 74.8; H, 5.4; N, 5.9.

3.3. General procedure for the synthesis of pyridazines ***F*-1a–i** from vinyldiazoketones ***F*-5a–i**

To a magnetically stirred solution of 0.45 g (1.7 mmol) triphenylphosphine in Et_2O (5 mL) vinyldiazoketone **5a–i** (1.4 mmol) was added dropwise. The reaction mixture was stirred for approximately 24 h until disappearance of diazo-compound **5**. Solid matter was removed by filtration, resultant filtrate was concentrated *in vacuo* and charged on to a small column with silica gel; the gradient elution was performed with petroleum ether and diethyl ether mixture. On removing the solvents pyridazines ***F*-1** were obtained as white solids in the case of ***F*-1a,b,d,f–i** or as a liquids in the case of ***F*-1c,e**.

3.4. General procedure for the synthesis of pyridazines ***F*-1a,c,f** from phosphazines ***F*-6a,c,f**

To a stirred suspension of 0.77 g (2.3 mmol) (methoxycarbonyl)methylenetriphenylphosphorane **4a** in Et_2O (5 mL) the solution of phosphazine ***F*-6a,c,f** (1.9 mmol) in Et_2O (2 mL) was added dropwise. The reaction mixture was stirred for a 3–4 days at rt. After disappearance of phosphazine ***F*-6** in the reaction mixture solid matter was removed by filtration, the resultant filtrate was concentrated *in vacuo* and the obtained residue was purified by column chromatography to furnish pyridazines ***F*-1a,c,f**.

3.4.1. 6-Methoxy-3-methylcarbonyl-4-trifluoromethylpyridazine (**1a**)

White solid; yield: 0.22 g (71%) (Section 3.3), 0.25 g (60%) (Section 3.4); mp 56–58 °C. IR (KBr): ν 1717 cm^{-1} (C=O). UV ($CHCl_3$): 243 (3.92), 275 (3.42). ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.76 (3H, s), 4.24 (3H, s), 7.29 (1H, s). ^{19}F NMR (282 MHz, $CDCl_3$): δ −63.0 (s, 3H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 28.0, 56.2, 116.3 (q, $^3J_{C-F}$ = 6 Hz), 121.3 (q, $^1J_{C-F}$ = 274 Hz), 131.2 (q, $^2J_{C-F}$ = 37 Hz), 150.1, 166.0, 196.4. Anal. calcd for $C_8H_7O_2N_2F_3$: C, 43.6; H, 3.2; N, 12.7. Found: C, 43.6; H, 3.2; N, 12.4.

3.4.2. 6-Ethoxy-3-ethylcarbonyl-4-trifluoromethylpyridazine (**1b**)

White solid; yield: 0.28 g (82%) (Section 3.3); mp 31–33 °C. IR (KBr): ν 1717 cm^{-1} (C=O). UV ($CHCl_3$): 244 (3.92), 277 (3.37). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.15 (3H, t, *J* = 7 Hz), 1.43 (3H, t, *J* = 7 Hz), 3.20 (2H, q, *J* = 7 Hz), 4.64 (2H, q, *J* = 7 Hz), 7.23 (1H, s). ^{19}F NMR (188 MHz, $CDCl_3$): δ −63.0 (s, 3H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 7.7, 14.3, 33.5, 65.1, 116.3 (q, $^3J_{C-F}$ = 6 Hz), 121.4 (q, $^1J_{C-F}$ = 274 Hz), 131.2 (q, $^2J_{C-F}$ = 36 Hz), 150.0, 165.8, 199.6. Anal. calcd for $C_{10}H_{11}O_2N_2F_3$: C, 48.4; H, 4.4; N, 11.3. Found: C, 48.5; H, 4.4; N, 11.2.

3.4.3. 3-(n-Butyl)carbonyl-6-methoxy-4-trifluoromethylpyridazine (**1c**)

White oil; yield: 0.20 g (55%) (Section 3.3), 0.16 g (32%) (Section 3.4). IR (KBr): ν 1707 cm^{-1} (C=O). UV ($CHCl_3$): 242 (3.48), 281 (3.32). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.89 (3H, t, *J* = 8 Hz), 1.37 (2H, m, *J* = 8 Hz), 1.67 (2H, m, *J* = 8 Hz), 3.21 (2H, t, *J* = 8 Hz), 4.23 (3H, s), 7.28 (1H, s). ^{19}F NMR (282 MHz, $CDCl_3$): δ −62.8 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.9, 22.3, 25.8, 39.9, 56.2, 116.3 (q, $^3J_{C-F}$ = 6 Hz), 121.4 (q, $^1J_{C-F}$ = 274 Hz), 131.3 (q, $^2J_{C-F}$ = 37 Hz), 150.5, 165.9, 199.2. Anal. calcd (%) for $C_{11}H_{13}O_2N_2F_3$: C, 50.4; H, 5.0; N, 10.7. Found: C, 50.4; H, 4.7; N, 10.6.

*3.4.4. 3-(t-Butyl)carbonyl-6-methoxy-4-trifluoromethylpyridazine (**1d**)*

White solid; yield: 0.27 g (74%) (Section 3.3); mp 55–57 °C. IR (KBr): ν 1716 cm^{-1} (C=O). UV ($CHCl_3$): 245 (3.91). ^1H NMR (300 MHz, $CDCl_3$): δ 1.33 (9H, s), 4.20 (3H, s), 7.25 (1H, s). ^{19}F NMR (282 MHz, $CDCl_3$): δ −62.2 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 27.3, 44.8, 56.0, 116.0 (q, $^3J_{C-F}$ = 5 Hz), 121.4 (q, $^1J_{C-F}$ = 274 Hz), 131.0 (q, $^2J_{C-F}$ = 36 Hz), 152.3 (q, $^3J_{C-F}$ = 2 Hz), 165.0, 206.5. Anal. calcd for $C_{11}H_{13}O_2N_2F_3$: C, 50.4; H, 5.0; N, 10.7. Found: C, 50.3; H, 5.0; N, 10.4.

*3.4.5. 6-Methoxy-3-(n-pentyl)carbonyl-4-trifluoromethylpyridazine (**1e**)*

White oil; yield: 0.22 g (58%) (Section 3.3). IR (KBr): ν 1716 cm^{-1} (C=O). UV ($CHCl_3$): 245 (3.96), 281 (3.62). ^1H NMR (300 MHz, $CDCl_3$): δ 0.85 (3H, t, J = 7 Hz), 1.31 (2H, m, J = 7 Hz), 1.69 (2H, m, J = 7 Hz), 3.20 (2H, t, J = 7 Hz), 4.23 (3H, s), 7.28 (1H, s). ^{19}F NMR (282 MHz, $CDCl_3$): δ −62.8 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.9, 22.5, 23.3, 23.4, 40.2, 56.1, 116.3 (q, $^3J_{C-F}$ = 6 Hz), 121.4 (q, $^1J_{C-F}$ = 275 Hz), 131.3 (q, $^2J_{C-F}$ = 36 Hz), 150.5, 165.9, 199.3. Anal. calcd for $C_{12}H_{15}O_2N_2F_3$: C, 52.2; H, 5.4; N, 10.1. Found: C, 51.8; H, 5.3; N, 10.0.

*3.4.6. 6-Methoxy-3-(p-tolyl)carbonyl-4-trifluoromethylpyridazine (**1f**)*

White solid; yield: 0.28 g (67%) (Section 3.3), 0.10 g (17%) (Section 3.4); mp 91–93 °C. IR (KBr): ν 1671 cm^{-1} (C=O). UV ($CHCl_3$): 270 (4.15). ^1H NMR (200 MHz, $CDCl_3$): δ 2.31 (3H, s), 4.15 (3H, s), 7.17 (2H, d, J = 8 Hz), 7.26 (1H, s), 7.71 (2H, d, J = 8 Hz). ^{19}F NMR (188 MHz, $CDCl_3$): δ −62.3 (s, 3H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 21.8, 56.0, 115.8 (q, $^3J_{C-F}$ = 5 Hz), 121.5 (q, $^1J_{C-F}$ = 275 Hz), 129.4, 130.9, 131.8 (q, $^2J_{C-F}$ = 36 Hz), 132.9, 145.6, 151.4, 165.2, 190.1. Anal. calcd for $C_{14}H_{11}O_2N_2F_3$: C, 56.8; H, 3.7; N, 9.5. Found: C, 56.9; H, 3.9; N, 9.7.

*3.4.7. 6-Ethoxy-3-(2-naphthyl)carbonyl-4-trifluoromethylpyridazine (**1g**)*

White solid; yield: 0.32 g (67%) (Section 3.3); mp 104–106 °C. IR (KBr): ν 1665 cm^{-1} (C=O). UV ($CHCl_3$): 258 (4.76), 268 (4.71). ^1H NMR (200 MHz, $CDCl_3$): δ 1.51 (3H, t, J = 7 Hz), 4.74 (2H, q, J = 7 Hz), 7.38 (1H, s), 7.47–8.34 (7H, m). ^{19}F NMR (188 MHz, $CDCl_3$): δ −63.2 (s, 3H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 14.6, 65.2, 116.2 (q, $^3J_{C-F}$ = 5 Hz), 121.7 (q, $^1J_{C-F}$ = 275 Hz), 125.1, 127.1, 128.1, 128.9, 129.5, 130.2, 132.2 (q, $^2J_{C-F}$ = 35 Hz), 132.9, 134.3, 136.3, 151.3, 165.3, 190.6. Anal. calcd for $C_{18}H_{13}O_2N_2F_3$: C, 62.4; H, 3.8; N, 8.1. Found: C, 62.6; H, 3.7; N, 8.0.

*3.4.8. 4-Heptafluoropropyl-6-methoxy-3-phenylcarbonylpyridazine (**1h**)*

White solid; yield: 0.47 g (87%) (Section 3.3); mp 59–61 °C. IR (KBr): ν 1688 cm^{-1} (C=O). UV ($CHCl_3$): 199 (3.96), 256 (4.13). ^1H NMR (200 MHz, $CDCl_3$): δ 4.19 (3H, s), 7.22 (1H, s), 7.38 (2H, dd, J = 8 Hz), 7.54 (1H, dd, J = 8 Hz), 7.74 (2H, d, J = 8 Hz). ^{19}F NMR (188 MHz, $CDCl_3$): δ −124.3 (s, 2F), −108.2 (m, 2F, J = 8 Hz), −80.6 (t, 3F, J = 11 Hz). ^{13}C NMR (50 MHz, $CDCl_3$): δ 56.1, 108.4 (tq, $^1J_{C-F}$ = 267 Hz, $^2J_{C-F}$ = 39 Hz), 114.0 (tt, $^1J_{C-F}$ = 260 Hz, $^2J_{C-F}$ = 39 Hz), 117.7 (qt, $^1J_{C-F}$ = 288 Hz, $^2J_{C-F}$ = 34 Hz), 117.8 (tt, $^3J_{C-F}$ = 8 Hz, $^4J_{C-F}$ = 2 Hz), 128.8, 130.6, 130.6 (t, $^2J_{C-F}$ = 26 Hz), 134.3, 135.6, 152.0, 165.1, 190.2. Anal. calcd for $C_{15}H_9O_2N_2F_7$: C, 47.2; H, 2.3; N, 7.3. Found: C, 47.2; H, 2.2; N, 7.2.

*3.4.9. 3-Methylcarbonyl-6-phenyl-4-trifluoromethylpyridazine (**1i**)*

White solid; yield: 0.30 g (80%) (Section 3.3); mp 68–70 °C. IR (KBr): ν 1722 cm^{-1} (C=O). UV ($CHCl_3$): 276 (4.09). ^1H NMR (300 MHz, $CDCl_3$): δ 2.91 (3H, s), 7.58 (3H, m), 8.17 (3H, m). ^{19}F NMR (282 MHz, $CDCl_3$): δ −62.5 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.5, 121.7 (q, $^3J_{C-F}$ = 5 Hz), 121.9 (q, $^1J_{C-F}$ = 275 Hz), 127.7, 129.0 (q, $^2J_{C-F}$ = 33 Hz), 129.6, 131.9, 134.2, 152.3, 161.2, 197.3. Anal. calcd for $C_{13}H_9ON_2F_3$: C, 58.7; H, 3.4; N, 10.5. Found: C, 58.7; H, 3.4; N, 10.4.

4. X-ray crystal structure analysis

Single crystals of the compound **1d** suitable for X-ray diffraction were obtained from solution of petroleum ether. The intensities were measured on an IPDS1 diffractometer (Fa. STOE). The structures were solved by direct methods, and refinement was performed with SHELX-97 [17]. The details of the structure analyses have been deposited at the Cambridge Crystallographic Data Centre, CCDC-625100. The copies of the data can be obtained, free of charge, from CCDC, Cambridge, UK (fax: +44 1233 336033; e-mail: deposite@ccdc.cam.ac.uk, internet: www.ccdc.cam.ac.uk).

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