A FACILE SYNTHESIS OF NEW PYRAZOLO- AND TRIAZOLO[5,1-C][1,2,4]TRIAZEPINE DERIVATIVES *VIA* INTERMOLECULAR WITTIG RING-CLOSURE REACTION

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Abstract: Starting from the readily available 5-amino-3-phenyl-1*H*-pyrazole and 5-amino-1*H*-1,2,4-triazole new pyrazolo- and triazolo[5,1-c][1,2,4]triazepines were prepared *via* intermolecular Wittig reaction.

Introduction: In view of the potential biological activity of fused azepines[1-4] and in connection with our interest in the synthesis of new heterocycles,[5-8] we report here on the synthesis of the title triazepines, a type of compounds rarely mentioned in literature as possible effective drugs.[9-11]

Results: The reaction pathway is proceed according to Scheme 1. Thus, treatment of 5-amino-3-phenyl-1*H*-pyrazole 1a and 5-amino 1*H*-1,2,4-triazole 1b with nitrous acid afforded the azo- compound 2a,b which was then coupled with α-chloroketones to yield the hydrazonoyl chlorides 3a,b in good yields. The structures of 3 were confirmed based on spectral and elemental analysis. The **IR** spectra of 3 revealed absorption bands at ν 3260, 3230, 2980, 1585 cm^{-1}. The **^{1}H NMR** spectra of 3a showed signals at δ 5.2, 7.1-7.8, 11.2 ppm assigned for NH of pyrazole, aromatic and a one proton of hydrazonoyl group, respectively. The hydrazonoyl compounds 3a,b reacted smoothly with triphenylphosphine in dry acetonitrile at room temperature in the presence of a catalytic amount of triethylamine to give new azomethylene-triphenylphosphoranes 4 and 14 in good yields. The structures of 4 and 14 were confirmed based on spectral and elemental analysis. Thus, the phosphoranes 4a,b reacted easily with ethyl 2-chloro-3-oxobutanoate 6a in toluene at room temperature to yield the triazepines 10a,b as well as reacted also with 3-chloropentan-2,4-dione 6b under the same reaction conditions to give 10c,d. However, phenacyl bromides 7a,b reacted with 4a,b in toluene at reflux temperature to yield the corresponding 1,5-diaryl derivatives 11a-d in good yields, whereas chloroacetyl chloride 8 reacted smoothly at room temperature with 4a,b to afford the 5-chloro derivatives 12a,b. Similarly, chloroacetamide 9 reacted with 4 in toluene at reflux to give the amino derivatives 13a, b (Scheme 2). The structures of 10-13 were confirmed based on spectral and microanalysis data. The **MS** of 10a showed m/z at 369 (M+1, 38), 368 (M, 82), 313 (M-2C_2H_4, 100), 280 (62), 267 (46), 255 (10), 220 (69), 168 (100), 120 (92), 104 (76), 92 (69) and 80 (48 %). Also, the **MS** of 11b showed m/z at 343 (M+1, 9), 277 (11), 262 (100), 183 (55), 152 (12), 107 (26 %). Also, the **MS** of 12a showed m / z at 318 (M+2, 15), 316 (M, 6), 301 (45), 288 (100), 260 (8), 239 (14), 183 (79), 165 (30), 102 (18), 77 (36) and 51 (33). The **^{13}C NMR** spectrum of 10a showed signals at δ 14 ($2CH_3$-CH_2), 21 (CH_3), 62 (2-O-CH_2-), 123-129 (phenyl), 130 (C-4), 140 (C-9), 142 (C-5), 145 (C-6), 150 (C-1), 152 (C-8a), 162 (2 CO).

The reactivity of the new 1,2,4-triazoloazophosphorane 14a,b which prepared in analogy to the reaction sequence of 4a,b was investigated. Thus, compounds 14a,b reacted with α-haloketones 6-9 under the same reaction conditions to yield the corresponding 1,2, 4-triazolo[5,1-c][1,2,4]triazepines 15-18 *via* the same reaction mechanism. The structures

of 15-18 were confirmed based on spectral and elemental analysis. The **MS** of 16a showed m/z at 283 (M, 5), 277 (21), 255 (11), 199 (12), 183 (57), 105 (100), 77 (58 %); and the **MS** of 16b showed m/z at 253 (M, 12), 213 (25), 185 (29), 167 (35), 149 (100), 105 (46), 91 (91), 77 (28), 55 (79 %). The **^{13}C NMR** of 16a showed absorption signals at δ 14 ($2CH_3$-CH_2), 21 (CH_3), 62 (2-O-CH_2-), 135 (C-5), 140 (C-6), 145 (C-7), 150 (C-2), 158 (C-9a) and 165 (2 CO).

Discussion: Alemagna et al have shown that arylazomethylenephosphoranes have ever given an intermolecular Wittig reaction, probably because of the presence of the additional electron withdrawing azo group.[12,13] However, from the above results, it comes out that the formation of the products cannot be explained in terms of intramolecular nucleophilic attack of the azo group on the carbonyl carbon atom, and can only be explained *via* intermolecular Wittig reaction. Thus, intermolecular Wittig reaction of 4 and 14 with α-haloketones 6-9 afforded the highly reactive intermediate 5 which subsequently undergo a nucleophilic attack of the ring nitrogen to the generated carbon center followed by a ring closurure *via* elimination of a halo acid to yield the pyrazolo- and triazolo[5,1-c][1,2,4]triazepines 10-13 and 15-18.

Conclusion: In conclusion the method described here affords a new and simple one - pot route to prepare such a new and biological important pyrazolo- and triazolo[5,1-c][1,2,4]triazeppines.

EXPERIMENTAL

Merck silica gel (pf_{254}) were used for chromatographic separation. All melting points were measured on a Gallen-Kamp melting point apparatus and are uncorrected. Mass spectra were taken on a Varian MAT 311 A spectrometer. **^{1}H NMR** spectra (deuterodimethylsulfoxide, δ = ppm) were recorded on a Varian Spectrometer (90 MHz) and Tetramethylsilane was used as internal standard. **IR** spectra (potassium bromide, $\nu = cm^{-1}$) were run on Nicolet FT IR model 205 Spectrophotometer and all with the Microanalysis were performed at Microanalytical Center, Cairo University, Egypt.

Preparation of hydrazonoyl chloride derivatives 3a-d

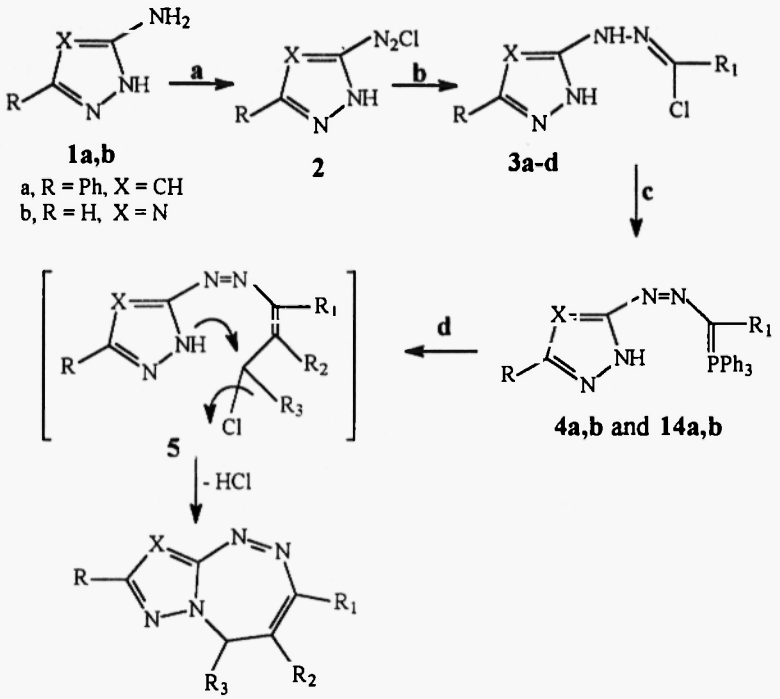
General procedure: To a stirred solution of 100 ml of ethanol containing ethyl 2-chloro-3-oxobutanoate 6a (1.64 g, 10 mmoles) or 3-chloro-pentan-2,4-dione 6b (1.34 g, 10 mmoles) and 3.0 g (36 mmoles) of sodium acetate at 0 ^{0}C, the appropriate diazoinium salts 2a,b (10 mmoles each) was added and stirred for additional 2h at 0-5 ^{0}C. The reaction mixture left for 6h at refrigerator and then diluted with cold water and the product so formed was collected by filtration, washed with water and recrystallized from ethanol to give the corresponding hydrazonoyl chlorides 3a-d. The physical, analytical and spectral data were listed in Table 1.

3-Phenyl-1*H*-pyrazoloazophosphorane 4a,b and 1,2,4-1*H*-triazoloazophos-phorane 14a,b.

General procedure: Equimolar amounts of hydrazonoyl chloride 3a (2.6 g, 0.01 mmoles) and triphenylphosphine (0.3 g, 0.01 mmoles) were stirred in 30 ml of acetonitrile at room temperature in the presence of 0.1 ml of triethylamine for 30 min. The solid product was collected by filtration and recrystallized from ethanol to give 4a. Similarly, the chloride 3b reacted with triphenylphosphine (0.01 mmoles for each) under the same reaction conditions to give 4b. 1,2,4-Triazolohydrazonoyl chlorides 3c,d reacted analogously with triphenylphosphine (0.01mmoles for each) to give the corresponding triazoloazophosphorane 14.

5-Methyl-1-phenylpyrazolo[5,1-c][1,2,4]triazepine derivatives 10a-d

General procedure:



1a,b
a, R = Ph, X = CH
b, R = H, X = N

2

3a-d

4a,b and 14a,b

5

10-13 and 15-18

a) HCl / $NaNO_2$; b) $CH_3COCH(Cl)R_1$ / CH_3COONa / EtOH;
c) PPh_3 / Et_3N / CH_3CN / r.t., d) $R_2COCH(Cl)R_3$ / toluene or CH_2Cl_2

No	X	R	R_1	R_2	R_3
10a	CH	Ph	CO_2Et	CH_3	CO_2Et
10b	CH	Ph	$COCH_3$	CH_3	CO_2Et
10c	CH	Ph	CO_2Et	CH_3	$COCH_3$
10d	CH	Ph	$COCH_3$	CH_3	$COCH_3$
11a	CH	Ph	CO_2Et	Ph	H
11b	CH	Ph	CO_2Et	Ph-p-Me	H
11c	CH	Ph	$COCH_3$	Ph	H
11d	CH	Ph	$COCH_3$	Ph-p-Me	H
12a	CH	Ph	CO_2Et	Cl	H
12b	CH	Ph	$COCH_3$	Cl	H
13a	CH	Ph	CO_2Et	NH_2	H
13b	CH	Ph	$COCH_3$	NH_2	H
15a	N	H	CO_2Et	CH_3	CO_2Et
15b	N	H	$COCH_3$	CH_3	CO_2Et
15c	N	H	CO_2Et	CH_3	$COCH_3$
15d	N	H	$COCH_3$	CH_3	$COCH_3$
16a	N	H	CO_2Et	Ph	H
16b	N	H	CO_2Et	Ph-p-Me	H
16c	N	H	$COCH_3$	Ph	H
16d	N	H	$COCH_3$	Ph-p-Me	H
17a	N	H	CO_2Et	Cl	H
17b	N	H	$COCH_3$	Cl	H
18a	N	H	CO_2Et	NH_2	H
18b	N	H	$COCH_3$	NH_2	H

Scheme 1

To a mixture of pyrazoloazophosphorane 4a (0.5 g, 0.001 mmoles) and ethyl 2-chloro-3-oxobutanoate 6a (0.16 ml, 0.001 mmoles) in 20 ml of dry toluene an 0.1 ml of triethylamine was added. The mixture was stirred at room temperature for 3 h and the precipitate so formed during stirring was filtered and recrystallized from ethanol into 10a as yellow crystals in 75% yield. Similarly, 4a reacted with 6b (0.01 mmoles for each) under the same reaction conditions to yield 10b as yellow crystals. Compound 4b reacted analogously with 6a,b (0.01 m moles for each) under the same reaction conditions to give the triazepines 10c,d.

1,5-Diarylpyrazolo[5,1-c][1,2,4]triazepine derivatives 11a-d

General procedure:

To a suspension of azophosphorane 4a (0.5 g, 0.001 mmoles) in 20 ml of dry toluene an 0.19 g of phenacyl bromide 7a (0.001 mmoles) was added dropwise. The reaction mixture was heated at bath temperature for 2 h in the presence of 0.1 ml of triethylamine. The yellow precipitate formed during reflux was collected by filtration and recrystallized from ethanol as yellow crystals in 69% yield. Similarly, compound 4a reacted with 7b to yield 11b, whereas zophosphorane 4b reacted analogously with 7a,b (0.001 mmoles for each) to give the corresponding pyrazolo[5,1-c][1,2,4]triazepine derivatives 11c,d (Table 1).

5-Chloro-1-phenylpyrazolo[5,1-c][1,2,4]triazepine derivatives 12a,b

General procedure:

To a suspension of pyrazoloazophosphorane 4a (0.5 g, 0.001 mmoles) in 20 ml of dry toluene, an 0.1 ml of chloroacetyl chloride 8 (0.01 mmoles) was added dropwise. The reaction mixture was stirred in the presence of 0.1 ml of triethylamine at room temperature for 5 h. The formed product 12a was collected by filtration and recrystallized as buff crystals in 70 % yield. However, azophosphorane 4b reacted with 8 under the same reaction conditions (0.001 mmoles for each) to yield triazepine derivative 12b (Table 1).

5-Amino-1-phenylpyrazolo[5,1-c][1,2,4]triazepine derivatives 13a,b

General procedure:

A mixture of pyrazoloazophosphorane 4a (0.5 g, 0.001 mmoles), chloroacetamide 9 (0.1 g, 0.001 mmoles) and 0.1 ml of triethylamine was refluxed for 2 h in 20 ml of dry toluene. The solvent was evaporated under vacuum and the resulting solid was collected by filtration and recrystallized from dioxan to yield 13a in 68 % yield. In analogy, azophosphorane 4b reacted with 9 under the same reaction conditions to yield the amino derivative 13b in 65 % yield.

6-Methyl-1,2,4-triazolo[5,1-c][1,2,4]triazepine derivatives 15a-d

General procedure:

A mixture of triazoloazophosphorane 14a (0.4 g, 0.001 mmoles), ethyl 2-chloro-3-oxobutanoate 6a (0.16 ml, 0.001 mmoles) and 0.3 ml of triethylamine in 20 ml dry toluene was stirred at room temperature for 8 h. The formed yellow precipitate 15a was collected by filtration and recrystallized from methanol in 0.16 g yield (61 %). Similarly, 14a reacted with 6b (0.001 mmoles for each) under the same reaction conditions to yield 15b. Compound 14b reacted analogously with 6a,b (0.001 mmoles for each) under the same reaction conditions to give the triazepines 15c,d (Table 2).

6-Aryl-1,2,4-triazolo[5,1-c][1,2,4]triazepine derivatives 16a-d

General procedure:

To a suspension of triazoloazophosphorane 14a (0.5 g, 0.001 mmoles) in 20 ml of dry toluene an 0.19 g of phenacyl bromide 7a (0.001 mmoles) was added dropwise. The reaction mixture was heated in the presence of 0.3 ml of triethylamine at bath temperature for 10 h. The solvent was evaporated under vacuum and the residue was triturated with

Table 1: The physical, analytical and spectral data for the new compounds 3, 4, 10-13

Comp. No	X	R	R_1	R_2	R_3	Mp (°C) Solvent	Yield %	M. Formula (M. Wt.)	Analysis % Calcd./ Found C H N	Spectral Data ^{1}H NMR δ ppm	MS [M$^+$] m/z
3a	CH	Ph	COOEt	---	---	125-26 EtOH	70	$C_{13}H_{13}ClN_2O_2$ (292.72)	53.34 4.48 19.17 53.19 4.38 19.02	1.1(t, 3H, CH_3), 4.2 (q, 2H, CH_2), 5.2 (s, 1H, NH), 7.1-7.8 (m, 6H, Ar-H), 10.0 (s, 1H, NH)	294
3b	CH	Ph	$COCH_3$	---	---	130-32 EtOH	68	$C_{12}H_{11}ClN_2O$ (262.70)	54.87 4.22 21.33 54.71 4.13 21.16	1.3 (s, 3H, CH_3), 5.3 (s, 1H, NH), 7.1-7.8 (m, 6H, Ar-H), 10.3 (s, 1H, NH)	263
3c	N	H	COOEt	---	---	215-17 MeOH	65	$C_5H_6ClN_3O_2$ (217.51)	33.12 3.71 32.18 33.36 3.56 32.05	1.3 (t, 3H, CH_3), 4.2 (q, 2H, CH_2), 5.3 (s, 1H, NH), 8.1 (s, 1H, CH), 9.5 (s, 1H, NH)	219
3d	N	H	$COCH_3$	---	---	205-07 EtOH	70	$C_5H_6ClN_3O$ (187.59)	32.01 3.22 37.33 31.89 3.09 37.17	1.3 (s, 3H, CH_3), 5.3 (s, 1H, NH), 8.1(s, 1H, CH), 9.6 (s, 1H, NH)	188
4a	CH	Ph	COOEt	---	---	155-57 EtOH	72	$C_{31}H_{27}PN_2O_2$ (518.57)	71.66 5.43 10.78 71.52 5.29 10.63	1.3 (t, 3H, CH_3), 4.2 (q, 2H, CH_2), 5.2 (s, 1H, NH), 7.1-7.8 (m, 21H, Ar-H)	520
4b	CH	Ph	$COCH_3$	---	---	120-22 EtOH	70	$C_{30}H_{25}PN_4O$ (488.55)	73.60 5.35 11.44 73.47 5.21 11.30	1.3 (s, 3H, CH_3), 5.2 (s, 1H, NH), 7.1-7.8 (m, 21H, Ar-H)	490
10a	CH	Ph	COOEt	CH_3	COOEt	280-81 EtOH	75	$C_{19}H_{20}N_4O_4$ (368.39)	61.95 5.47 15.21 61.81 5.32 15.04	1.1 (s, 3H, CH_3), 1.2 (t, 6H, $2CH_3$), 4.2 (q, 4H $2CH_2$), 6.4 (s, 1H, CH), 7.1-7.8 (m, 6H, Ar-H).	368
10b	CH	Ph	$COCH_3$	CH_3	COOEt	140-42 EtOH	72	$C_{18}H_{18}N_4O_3$ (338.36)	63.90 5.36 16.56 63.75 5.19 16.41	1.1 (s, 3H, CH_3), 1.2 (s, 3H, CH_3), 1.3 (t, 3H, CH_3), 4.2 (q, 2H, CH_2), 6.3 (s, 1H, CH), 7.1-7.8 (m, 6H, Ar-H).	338
10c	CH	Ph	COOEt	CH_3	$COCH_3$	170-71 MeOH	67	$C_{18}H_{18}N_4O_3$ (338.36)	63.90 5.36 16.56 63.77 5.21 16.45	1.1 (s, 3H, CH_3), 1.2 (s, 3H, CH_3), 1.3 (s, 3H, CH_3), 4.2 (q, 2H, CH_2), 6.5 (s, 1H, CH), 7.1-7.8 (m, 6H, Ar-H).	338
10d	CH	Ph	$COCH_3$	CH_3	$COCH_3$	165-67 EtOH	65	$C_{17}H_{16}N_4O_2$ (308.34)	66.22 5.23 18.17 66.05 5.10 18.03	1.1 (s, 3H, CH_3), 1.2 (s, 6H, $2CH_3$), 6.3 (s, 1H, CH), 7.1-7.8 (m, 6H, Ar-H).	308
11a	CH	Ph	COOEt	Ph	H	220-21 EtOH	69	$C_{21}H_{18}N_4O_2$ (358.40)	70.38 5.06 5.63 70.21 5.22 15.50	1.2 (t, 3H, CH_3), 4.2 (q, 2H, CH_2), 5.2 (s, 2H, CH_2), 7.1-7.8 (m, 11H, Ar-H).	358
11b	CH	Ph	COOEt	Ph-p-Me	H	190-91 benzene	65	$C_{22}H_{20}N_4O_2$ (372.42)	70.95 5.41 15.04 70.81 5.26 15.22	1.1(s,3H, CH), 1.2 (t, 3H, CH_3), 4.1 (q, 2H CH_2), 5.2 (s, 2H, CH_2), 7.1-7.8 (m, 10H, Ar-H).	372
11c	CH	Ph	$COCH_3$	Ph	H	180-82 MeOH	60	$C_{20}H_{16}N_4O$ (328.37)	73.16 4.91 17.05 73.03 4.74 17.21	1.2 (s,3H, CH_3), 5.4 (s, 2H, CH_2), 7.1-7.9 (m, 11H, Ar-H).	328
11d	CH	Ph	$COCH_3$	Ph-p-Me	H	225-27 benzene	65	$C_{21}H_{18}N_4O$ (342.40)	73.67 5.30 16.36 73.51 5.14 16.19	1.4 (s, 6H, $2CH_3$), 5.3 (s, 2H, CH_2), 7.1-7.9 (m, 10H, Ar-H).	342
12a	CH	Ph	COOEt	Cl	H	163-65 DMF	70	$C_{15}H_{13}ClN_4O_2$ (316.75)	56.88 4.14 17.69 56.74 4.02 17.53	1.1(t, 3H, CH_3), 4.1(q, 2H, CH_2), 5.2 (s, 2H, CH_2), 7.2-8.1 (m, 6H, Ar-H).	318
12b	CH	Ph	$COCH_3$	Cl	H	210-12 Dioxan	66	$C_{14}H_{11}ClN_4O$ (286.72)	58.65 3.87 19.54 58.51 3.72 19.38	1.3 (s, 3H, CH_3), 5.2 (s, 2H, CH_2) 7.1-7.9 (m, 6H, Ar-H).	288
13a	CH	Ph	COOEt	NH_2	H	270-71 Dioxan	68	$C_{15}H_{15}N_5O_2$ (297.32)	60.60 5.08 23.55 60.46 5.23 23.43	73.67 (t, 3H, CH_3), 4.2 (q, 2H, CH_2), 5.2 (s, 2H, CH_2), 7.1-7.9 (m, 6H, Ar-H), 9.1 (s, 2H, NH_2)	297
13b	CH	Ph	$COCH_3$	NH_2	H	210-11 benzene	65	$C_{14}H_{13}N_5O$ (267.29)	62.91 4.90 26.20 62.76 4.74 26.03	1.2 (s, 3H, CH_3), 5.4 (s,2H, CH_2), 7.1-7.8 (m, 6H, Ar-H), 9.1 (s, 2H, NH_2)	267

Table 2: The physical, analytical and spectral data for the new compounds 14-18

Comp No.	X	R	R_1	R_2	R_3	Mp (°C) Solvent	Yield %	M. Formula (M. W.)	Analysis % Calcd / Found C H N	Spectral Data ^{1}H NMR δ ppm	MS [M^+] m/z
14a	N	H	COOEt	---	---	165-67 EtOH	65	$C_{14}H_{12}N_5O_2P$ (441.47)	65.00 5.00 15.79 64.13 5.12 15.64	1.3 (t, 3H, CH_3), 4.2 (q, 2H, CH_2), 5.7 (s, 1H, NH), 6.8 (s, 1H, CH)	443
14b	N	H	$COCH_3$	---	---	210-12 EtOH	62	$C_{21}H_{20}N_5OP$ (413.45)	66.82 4.83 16.94 66.69 4.76 16.81	1.4 (s, 3H, CH_3), 5.5 (s, 1H, NH), 6.9 (s, 1H, CH)	413
15a	N	H	COOEt	CH_3	COOEt	200-02 MeOH	61	$C_{12}H_{15}N_5O_4$ (293.28)	49.14 5.15 23.88 49.01 5.02 23.71	1.1 (s, 3H, CH_3), 1.2 (t, 6H, $2CH_3$) 4.2 (q, 4H, $2CH_2$), 6.4 (s, 1H, CH), 6.9 (s, 1H, CH)	293
15b	N	H	$COCH_3$	CH_3	COOEt	210-12 MeOH	54	$C_{11}H_{13}N_5O_3$ (263.25)	50.19 4.98 26.60 50.05 4.83 26.47	1.1 (s, 3H, CH_3), 1.2 (s, 3H, CH_3),1.3 (t, 3H, CH_3), 4.2 (q, 2H, CH_2), 6.3 (s, 1H, CH), 6.9 (s, 1H, CH)	263
15c	N	H	COOEt	CH_3	$COCH_3$	201-03 MeOH	60	$C_{11}H_{13}N_5O_3$ (263.25)	50.19 4.98 26.60 50.07 4.86 26.43	1.1 (s, 3H, CH_3), 1.2 (s, 3H, CH_3),1.3 (t, 3H, CH_3), 4.2 (q, 2H, CH_2), 6.5 (s, 1H, CH), 6.8 (s, 1H, CH)	263
15d	N	H	$COCH_3$	CH_3	$COCH_3$	195-97 EtOH	54	$C_{10}H_{11}N_5O_2$ (233.23)	51.50 4.75 30.02 51.36 4.61 30.16	1.2 (s, 3H, CH_3), 1.3 (s 6H, $2CH_3$), 6.4 (s, 1H CH), 6.8 (s, 1H, CH)	233
16a	N	H	COOEt	Ph	H	165-67 benzene	60	$C_{14}H_{13}N_5O_2$ (283.29)	59.36 4.63 24.72 59.21 4.50 24.58	1.1 (t, 3H, CH_3), 4.2 (q, 2H, CH_2) 5.2 (s 2H CH_2), 6.9 (s 1H, CH), 7.1-7.9 (m, 5H, Ar-H)	283
16b	N	H	COOEt	Ph-p-Me	H	180-82 MeOH	55	$C_{15}H_{15}N_5O_2$ (297.32)	60.60 5.08 23.55 60.48 5.22 23.40	1.1(t, 3H, CH_3) 1.2 (s, 3H, CH_3), 4.2 (q 2H, CH_2), 5.3 (s, 2H CH_2), 6.9 (s 1H, CH), 7.1-7.8 (m, 4H, Ar-H)	297
16c	N	H	$COCH_3$	Ph	H	185-87 benzene	50	$C_{13}H_{11}N_5O$ (253.26)	61.65 4.38 27.65 61.52 4.25 27.52	1.3 (s, 3H, CH_3), 5.2 (s, 2H, CH_2), 6.8 (s, 1H, CH) 7.1-7.9 (m, 5H Ar-H)	253
16d	N	H	$COCH_3$	Ph-p-Me	H	150-52 MeOH	58	$C_{14}H_{13}N_5O$ (267.29)	62.91 4.90 26.20 62.76 4.73 26.04	1.1 (s, 3H, CH_3), 1.3 (s, 3H, CH3), 5.4 (s, 2H, CH), 6.8 (s, 1H, CH), 7.1-7.8 (m, 4H, Ar-H)	267
17a	N	H	COOEt	Cl	H	170-72 MeOH	55	$C_8H_8ClN_5O_2$ (241.64)	39.76 3.34 28.98 39.62 3.19 28.82	1.1 (t, 3H, CH_3), 4.2 (q 2H, CH_2), 5.6 (s, 2H, CH_2), 6.9 (s 1H, CH)	243
17b	N	H	$COCH_3$	Cl	H	270-21 EtOH	60	$C_7H_6ClN_5O$ (211.61)	39.73 2.86 33.10 39.61 2.74 33.01	1.1 (s, 3H, CH_3), 5.6 (s, 2H CH_2), 6.9 (s 1H, CH)	213
18a	N	H	COOEt	NH_2	H	230-32 benzene	60	$C_{10}H_{10}N_6O_2$ (222.21)	43.24 4.54 37.82 43.05 4.41 37.65	1.1 (t, 3H, CH_3), 4.1 (q, 2H, CH_2), 5.7 (s 2H, CH_2), 6.8 (s 1H, CH), 9.2 (s, 2H, NH_2)	222
18b	N	H	$COCH_3$	NH_2	H	130-32 benzene	61	$C_9H_8N_6O$ (192.18)	43.75 4.20 43.73 43.64 4.06 43.61	1.2 (s, 3H CH_3), 5.4 (s, 2H, CH_2), 6.8 (s, 1H CH), 8.9 (s, 2H, NH_2)	192

methanol. The resulting solid product was collected by filtration and recrystallized from methanol as yellow crystals to yield 16a in 0.15 g (60 %). Similarly, 14a reacted with 7b (0.001 mmoles for each) under the same reaction conditions to yield 16b. Compound 14b reacted analogously with 7a,b (0.001 mmoles for each) under the same reaction conditions to give the triazepine derivatives 16c,d (Table 2).

6-Chloro-1,2,4-triazolo[5,1-c][1,2,4]triazepine derivatives 17a,b

General procedure:

To a suspension of triazoloazophosphorane 14a (0.4 g, 0.001 mmoles) in 20 ml of dry toluene, an 0.1 ml of chloroacetyl chloride 8 (0.001 mmoles) and 0.3 ml of triethylamine were added and the reaction mixture was stirred at room temperature for 12 h. The solvent was evaporated under vacuum and the residue triturated with dilute methanol. The formed product was collected by filtration and recrystallized from methanol to yield 17a in 0.11 g (55 %) as buff crystals. Similarly, 14b reacted with 8 (0.001 mmoles for each) under the same reaction conditions to yield 17b.

6-Amino-1,2,4-triazolo[5,1-c][1,2,4]triazepine derivatives 18a,b

General procedure:

A mixture of triazoloazophosphorane 14a (0.4 g, 0.001 mmoles), chloroacetamide 9 (0.09 g, 0.001 mmoles) and 0.3 ml of triethylamine was refluxed in 20 ml of toluene for 8h. The solvent was evaporated under vacuum and the residue was triturated with methanol. The formed solid was collected by filtration and recrystallized from benzene to yield 18a in 0.12 g (60 %) as buff crystals. Similarly, 14b reacted with 9 (0.01 mmoles for each) under the same reaction conditions to yield 18b, the spectral, physical and analytical data were listed in Table 2.

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Received on September 20, 2000