A New Route to 5-Substituted 1*H*-1,2,4-Triazole-3-carboxylic Acid Esters

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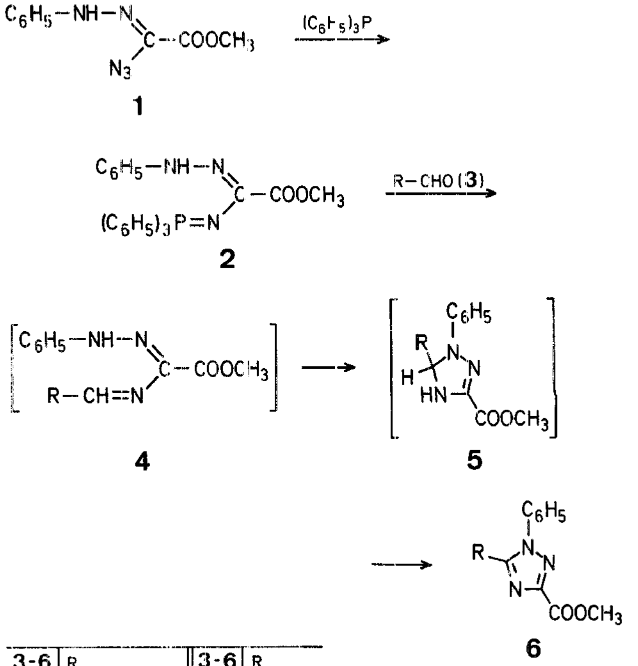
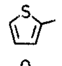
On continuing our studies on the chemistry of *C*-azidohydrazones[1,2], we considered the reaction of methyl azido-(phenylhydrazono)-acetate (**1**) with triphenylphosphine as an entry to a new type of azaphosphoranes of potential utility in heterocyclic syntheses. This report deals with the preparation of the azaphosphorane **2** and its reaction with aldehydes leading to 1*H*-1,2,4-triazoles **6**.

Treatment of the azidohydrazone **1** with an equimolar amount of triphenylphosphine in ether gave the desired azaphosphorane **2** as the only product. The latter compound reacted with a wide variety of aldehydes (**3**) in boiling hydrocarbon solvents to afford the triazole derivatives **6** in yields ranging from 29 to 70%. Triphenylphosphine oxide was usually obtained as a side-product.

The formation of the cyclization products **6** can be assumed to proceed via the following reaction sequence: (1) aza-Wittig condensation[3] between **2** and the aldehyde **3** to afford the imine **4**, (2) ring closure of the latter intermediate through nucleophilic participation of the hydrazone moiety, and (3) oxidation of the so-formed triazolines **5** to the triazoles **6**. That 4,5-dihydro-1*H*-1,2,4-triazoles can be spontaneously oxidized by exposure to air is a documented fact[4].

Although several methods are known for the preparation of 1*H*-1,2,4-triazoles[5], the synthetic approach reported here may be useful in view of the pharmacological interest of this class of compounds[6].



3-6	R	3-6	R
a	H	f	
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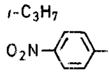
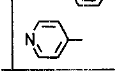
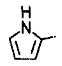
d			
e		h	

Methyl 2-(Phenylhydrazono)-2-(triphenylphosphinimino)-acetate (2): A solution of compound **1**[2] (6.1 g, 27.8 mmol) and triphenylphosphine (7.3 g, 27.8 mmol) in dry diethyl ether (1000 ml) is refluxed for 1 h. The precipitate is collected by filtration and washed with diisopropyl ether to give compound **2**; yield: 10.8 g (85%); m.p. 203–204 °C (from choroform/diisopropyl ether).

$C_{27}H_{24}N_3O_2P$	calc.	C 71.51	H 5.33	N 9.27
(453.5)	found	71.73	5.10	9.45

M.S.: m/e = 453 (M^+).

Table. 5-Substituted Methyl 1-Phenyl-1*H*-1,2,4-triazole-3-carboxylates (**6**)

6	Solvent (at reflux)	Reaction time [h]	Eluant	Yield [%]	m.p. [°C][a,b]	Molecular Formula[c] or Lit. m.p. [°C]	^{1}H-N.M.R. ($CDCl_3$/TMS_{int}) δ [ppm][d]
a	benzene	54	ethyl acetate	53	113°	114–116°[7]	–
b	benzene	30	ethyl acetate	70	102°	101.5–102.5°[8]	–
c	toluene	63	ethyl acetate	51	126°	126°[2]	–
d	toluene	10	diethyl ether/ light petroleum (2/1)	41	162–163°	$C_{16}H_{12}N_4O_4$ (324.3)	4.10 (s, 3H); 7.3–7.7 (m, 5H); 7.78 (d, 2H, *J* = 8 Hz); 8.25 (d, 2H, *J* = 8 Hz)
e	toluene	27	ethyl acetate/ ethanol (1:1)	60	156–157°	$C_{15}H_{12}N_4O_2$ (280.3)	4.10 (s, 3H); 7.3–7.7 (m, 7H); 8.5–8.8 (m, 2H)
f	toluene	90	diethyl ether/ light petroleum (2/1)	43	143–144°	$C_{14}H_{11}N_3O_2S$ (285.3)	4.10 (s, 3H); 6.9–7.0 (m, 1H); 7.2–7.3 (m, 1H); 7.4–7.7 (m, 6H)
g	toluene	60	benzene/ ethyl acetate (2/1)	29[e]	161–162°	$C_{14}H_{11}N_3O_3$ (269.2)	4.10 (s, 3H); 6.4–6.5 (m, 1H); 6.7–6.8 (m, 1H); 7.3–7.7 (m, 6H)
h[f]	toluene	140	benzene/ ethyl acetate (2/1)	33[e]	197–198°	$C_{14}H_{12}N_4O_2$ (268.3)	4.10 (s, 3H); 5.8–5.9 (m, 1H); 6.1–6.2 (m, 1H); 6.9–7.0 (m, 1H); 7.4–7.6 (m, 5H); 9.5 (br. s, 1H)

[a] Uncorrected.

[b] From diisopropyl ether.

[c] Satisfactory microanalyses were obtained for the new compounds: C ±0.30, H ±0.25, N ±0.25.

I.R. (Nujol): ν = 3290, 1690 cm^{-1}.

^{1}H-N.M.R. ($CDCl_3$/TMS_{int}): δ = 3.57 (s, 3H); 7.0–7.8 (m, 20H); 9.0 ppm (br. s, 1H).

^{31}P-N.M.R. ($CDCl_3$/H_3PO_{4ext}): δ = 10.2 ppm.

5-Substituted Methyl 1-Phenyl-1*H*-1,2,4-triazole-3-carboxylates (6); General Procedure:

A solution of compound **2** (2 mmol) and aldehyde **3** (20 mmol) in the appropriate solvent (100 ml) is refluxed as indicated in the Table. The solvent is evaporated and the residue is chromatographed on a silica gel column to give compound **6** (Table).

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