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PREPARATION OF ALKYL- AND PHENYL-SUBSTITUTED PYRIMIDINES

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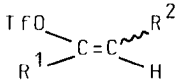
Abstract.- Vinyltrifluoromethanesulfonates (triflates)



1, which are obtained from the corresponding ketones, react in an excess of pure nitriles (acetonitrile, propionitrile, benzonitrile) at 80ºC (20h) to form substituted pyrimidines 5 and 8 in good yields.

Tri and tetrasubstituted pyrimidines are an important class of compounds which have been widely used as drugs1), flavours2), herbizides3) and liquid cristals3). The syntheses of substituted pyrimidines 5 and 8 known so far are often somewhat complicated4) or restricted to such systems which are partly substituted with aromatic groups3).

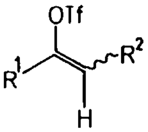
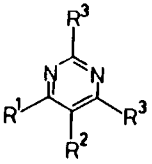
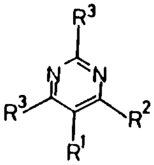
We report now a new and simple procedure for the synthesis of substituted pyrimidines 5 and 8: Z/E-isomeric vinyltriflates 1 (R^1=alkyl, aryl; R^2=H, alkyl) (20 mmol) are treated with an excess of pure alkyl- or arylcyanide R^3-CN (R^3=alkyl, aryl) (0.1 mol) at 80ºC for 20 h to form the substituted pyrimidines 5 or 8 in yields of 54-71%. (Examples: see Table 1).

If Z/E-triflates 1, with R^1=alkyl and R^2=H are used only uniformly substituted pyrimidines 5 are obtained. The pyrimidines 5 are isolated after removal of the excess nitrile by distillation, washing the residue with 10% NaOH solution and extraction with methylene chloride. If triflates 1 are used in which $R^1 \neq R^2 \neq H$, then a mixture of two isomeric pyrimidines 5 and 8 is formed, which however can be separated by column chromatography.

All triflates 1 are obtained in high yield by the reaction of the appropriate ketone with trifluoromethanesulfonic anhydride (Tf_2O) and sodium carbonate in methylene chloride 5,6).

The pyrimidines 5 and 8 listed in Table 1 were characterized by IR, ^{13}C-^{1}H-NMR, MS and elemental analysis.

Table 1

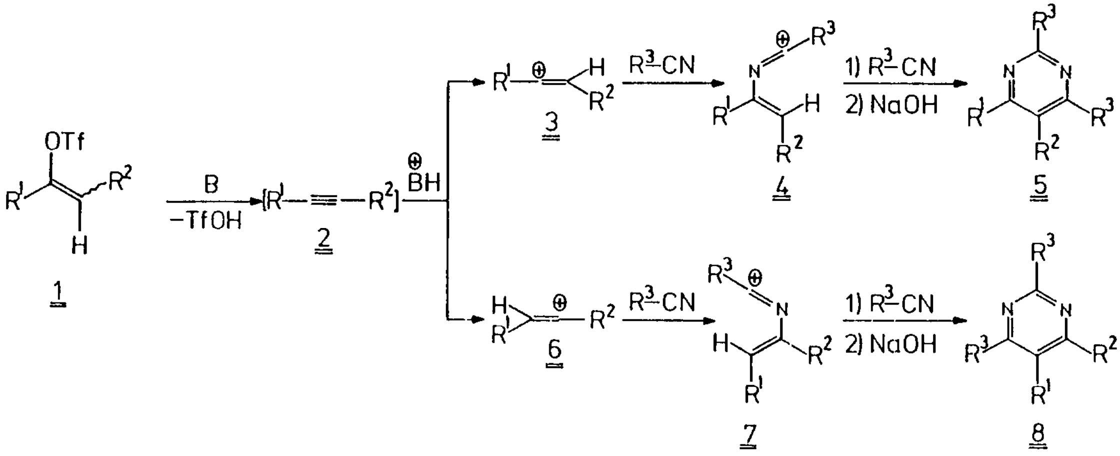
Triflate			Nitrile	Products		Yield[b] (%)	b.p.[°C]/torr or m.p.[°C] [c]
			R^3-CN				
1 (E/Z-ratio)[a]				5[a]	8[a]		
	R^1	R^2	R^3				
1a	t-C_4H_9	H	CH_3	5a	-	56	61-62/4.5
1a	t-C_4H_9	H	C_2H_5	5b	-	54	74-76/4.0
1a	t-C_4H_9	H	C_6H_5	5c	-	65	83-84 3)
1b	C_6H_5	H	CH_3	5d	-	71	95-96/0.7
1b	C_6H_5	H	C_2H_5	5e	-	70	86-88/0.1
1b	C_6H_5	H	C_6H_5	5f	-	75	184-185 3)
1c	i-C_4H_9 (72/28)	i-C_3H_7	CH_3	5g(56%)	8g(44%)	71	71-73/1.0
1c	i-C_4H_9 (72/28)	i-C_3H_7	C_2H_5	5h(56%)	8h(44%)	70	93-94/2.0

[a] Determined by G.L.C. (OV-101, 25m, 80ºC).

[b] Of isolated product.

[c] Recristallized from EtOH.

The formation of two isomeric pyrimidines 5g-h and 8g-h from triflates 1c leads us to propose the following mechanism: (Scheme 1)



Scheme 1

In the first step the triflates 1 form the alkynes 2 by elimination of TfOH, the excess nitrile serving as a weak base. By protonation of the alkynes 2 the vinyl cations 3 and 6 are obtained which react with two mol of nitrile R^3-CN via 4 and 7 respectively to form the pyrimidines 5 and 8.

As has been shown recently, such nitriles, which do not contain hydrogen atoms in the α-position, can be reacted with alkynes in presence of phosphoric acid and BF_3 to yield pyrimidines$^{3)}$. The synthesis of substituted pyrimidines using our method is not restricted to certain substituents and common available ketones, which are easily transformed into the corresponding triflates 1, are used as starting materials.

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References.-

1.- A. Kreutzberger, M. Sellheim, *Chem. Ztg.*, **108**, 326 (1984); C.A., **102**. 24572 p.

2.- R. Przybylski, E. Kaminski, *Nahrung*, **27**, 487 (1983); C.A., **99**, 86878 w.

3.- Ali-Akbar, *Ger. Offen.*, DE 3319843 A1 (1984); C. A., **102**, 95667 j.

4.- F. Krönke, E. Schmidt, W. Zecher, *Chem. Ber.*, **97**, 1163 (1964).

5.- P. J. Stang, M. Hanack, L. R. Subramanian, *Synthesis*, 85 (1982).

6.- C. J. Collins, A. García Martínez, R. Martínez Alvarez, J. Arranz Aguirre, *Chem. Ber.*, **117**, 2815 (1984).

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