Tetrahedron Letters,Vol.28,No.51,pp 6513-6516,1987
Printed in Great Britain

0040-4039/87 $3.00 + .00
Pergamon Journals Ltd.

IMINOPHOSPHORANE-MEDIATED TRANSFORMATION OF TERTIARY ALCOHOLS INTO t-ALKYLAMINES AND THEIR N-PHOSPHORYLATED DERIVATIVES

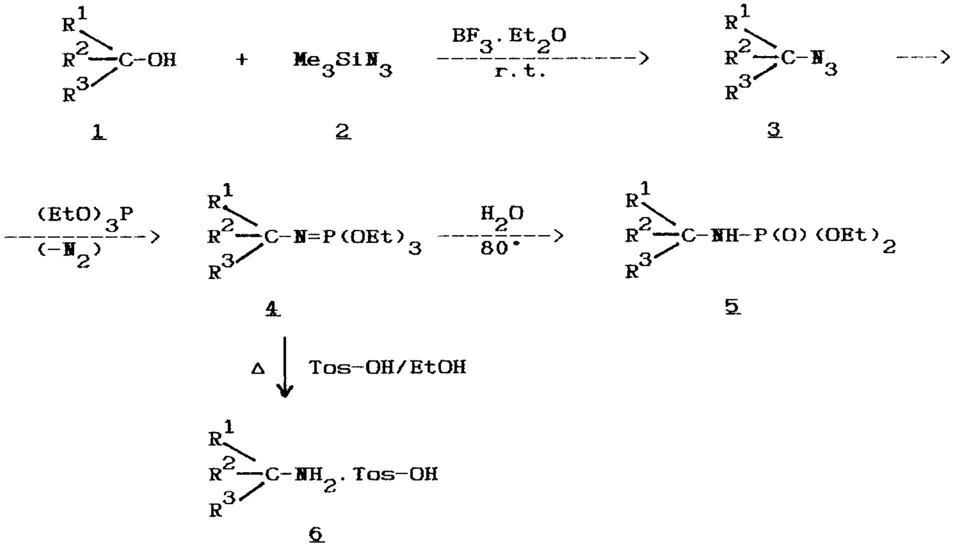
Anna Koziara and Andrzej Zwierzak*
Institute of Organic Chemistry, Technical University, Zwirki 36,
PL-90-924 Lodz, Poland.

Summary: Novel azidation of tertiary alcohols by means of trimetylsilyl azide in the presence of boron trifluoride etherate has been worked out. The Staudinger reaction of crude azides with triethyl phosphite affords the corresponding iminophosphoranes which can be directly transformed into diethyl N-(t-alkyl) phosphoroamidates or t-alkylamine tosylates.

No general and simple approach to t-alkylamines, which are of considerable interest as starting materials for pharmaceuticals and other biologically active compounds, has been so far reported. The Ritter reaction[1] and the Haaf reaction[2], used occasionally for this purpose, suffer from relatively low yields and several preparative inconveniences. Our recently published procedure[3] based on Lewis acid catalyzed azidation of t-alkyl chlorides followed by Staudinger reaction requires long reaction times and does not secure good yields. Although t-alkyl azides, which can be considered as convenient precursors of t-alkylamines, became recently available[4] the necessity of using poisonous and explosive hydrazoic acid limits seriously the preparative applicability of this approach. In order to circumvent this difficulty we reacted tertiary alcohols 1 with the readily accessible trimethylsilyl azide[5] 2 in the presence of boron trifluoride etherate. This reaction is reminiscent of the Ritter amide synthesis. It avoids, however, the strong acids required in that synthesis and occurs regioselectively with tertiary alcohols. Solutions of the corresponding azides 3 thus formed can be treated with triethyl phosphite without cumbersome purification to give the iminophosphoranes 4.

On refluxing with the stoichiometric amount of water the solutions of 4 afford diethyl N-(t-alkyl)phosphoroamidates 5 in good yields (see Table 1). Several iminophosphoranes 4 can be also directly converted into the t-alkylamine tosylates 6 by refluxing with p-toluenesulfonic acid in ethanol. When extensive decomposition was observed on attempted acidolytic cleavage of 4 (compounds 6e and 6d, see Table 2) the solutions of crude azides 3 were reduced with lithium aluminum hydride in refluxing ether directly to the corresponding t-alkylamines.

Scheme



Experimental Procedure

- 3: Boron trifluoride etherate (8.52g, 0.06 mol) is added dropwise at 20-30°C to a stirred solution of 1 (0.05 mol) and 2 (6.91g, 0.06 mol) in benzene (50 mL). After 24h at room temperature the mixture is poured into water (100 mL). The organic phase is separated off and washed with a 10% solution of $NaHCO_3$. The solution is dried over Na_2SO_4.

- 4: Triethyl phosphite (8.3g, 0.05 mol) is added at 25-30°C to a stirred solution of 3; stirring is continued for 6h and the solution is left for 72h at this temperature. The solution of iminophosphorane 4 thus obtained can be directly used for the preparation of 5 or 6.

- 5: Water (0.9g, 0.05 mol) is added to the solution of 4 and the mixture is refluxed with stirring for 1h. The resultant solution of 5 is dried over $MgSO_4$ if necessary, filtered, and evaporated. Crude 5 is distilled under reduced pressure or recrystallized.

- 6: After evaporation of the solvent crude iminophosphorane 4 is dissolved in ethanol (15 mL) and treated with p-toluenesulfonic acid monohydrate (9.51g, 0.05 mol) and water (0.9g, 0.05 mol). The mixture is refluxed for 8h, evaporated, and diluted with ether (100 mL). 6 precipitates out and is recovered by filtration.

Table 1. Yields and properties of diethyl N-(t-alkyl) phosphoroamidates 5.

5	R^1	R^2	R^3	Yield [%][a]	B.p.[°C/torr] (M.p.)	n_D^{20}
a	CH_3	CH_3	CH_3	73	65-66/0.1	1.4276
b	C_2H_5	CH_3	CH_3	62	78/0.15	1.4340
c	C_2H_5	C_2H_5	CH_3	72	86/0.15	1.4392
d	C_6H_5	C_6H_5	CH_3	72	(130-132)[b]	-
e	$C_6H_5CH_2$	CH_3	CH_3	53	128-130/0.05 (43-44)	-
f	$-(CH_2)_5-$		CH_3	67	92-94/0.1	1.4600
g	$-(CH_2)_5-$		$n\text{-}C_3H_7$	49	104/0.05	1.4536

[a] *Yields of distilled, analytically pure products. The structures of all compounds were confirmed analytically and spectroscopically.*

[b] *Crystallized from* CCl_4 *- hexane.*

Table 2. Yields and properties of t-alkylamine tosylates **6**[a]

Compound No.	Yield [%]	M.p. [°C]
6a	59	202-203[b]
6b	54	175-177[c]
6c	29[d]	143-144[c]
6d	0[e]	-
6e	37	169-172[c]
6f	45	184-185[c]

[a] *All compounds gave satisfactory elemental analyses and spectroscopic data.* [b] *Recrystallized by dissolving 0.5g sample in cold ethanol (5 mL) and precipitation with ether (50 mL).* [c] *Recrystallized by dissolving 0.5g sample in cold* $CHCl_3$ *(5 mL), filtration, and precipitation with hexane (50 mL).* [d] *Azidation was performed in pentane. Free amine was obtained in 74% yield, b.p. 106-107°C,* n_D^{20} *- 1.4132 by reduction of crude azide with lithium aluminum hydride in refluxing ether-pentane.* [e] *Free amine contaminated with ca. 5% of 1,1-diphenylethylene (GC) was obtained in 74% yield, b.p. 96-97°C/0.3 torr,* n_D^{20} *- 1.5927 by reduction of crude azide with lithium aluminum hydride in refluxing ether-benzene.*

Acknowledgements

This work was supported by a grant CPBP-01.13.3.3 from Polish Academy of Sciences.

References

1) L.I.Crimen, D.J.Cota, Org. React. **17**, 213, (1969).
2) W.Haaf, Chem. Ber. **96**, 3359, (1963).
3) A.Koziara, K.Osowska-Pacewicka, S.Zawadzki, A.Zwierzak, Synthesis 1987, 487.
4) A.Hassner, R.Fibiger, D.Andisik, J. Org. Chem. **49**, 4237, (1984).
5) H.R.Kricheldorf, Synthesis 1972, 551.

(Received in UK 13 October 1987)