Tetrahedron Letters,Vol.26,No.3,pp 307-310,1985
Printed in Great Britain

0040-4039/85 $3.00 + .00

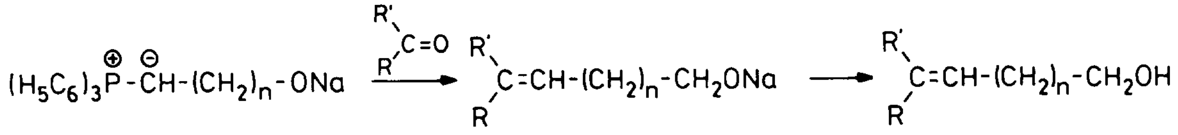
ω-HYDROXYALKYL-PHOSPHONIUM SALTS AS "INSTANT-YLID" COMPONENTS : EXTREMELY CONVENIENT AND HIGHLY CIS-SELECTIVE SYNTHESIS OF ALKENOL-TYPE PHEROMONES

Bruno Schaub, Gottfried Blaser and M. Schlosser *
Institut de Chimie organique de l'Université
Rue de la Barre 2, CH-1005 Lausanne (Switzerland)

Summary: In less than 2 hours, (Z)-alkenols of 97 – 98% stereoisomeric purity may be prepared and isolated (!) if a new type of "instant-ylids" is used.

The instant-ylid method [1] relies on the surprising inertness of sodium amide (pK of ammonia ∿ 40 towards phosphonium salts (pK ∿ 20) as long as the two components are mixed in the form of dry powders. Upon addition of an ethereal solvent, however, the ylid is quantitatively generated after a few minutes of stirring. Functional groups of moderate polarity are tolerated : instant-ylid mixtures of chloromethyl, methoxymethyl, methylmercaptomethyl and 2-picolylmethyl-triphenylphosphonium halides are commercially available, hence suitable for storage. The same approach, however, applied to hydroxy- or amino-bearing phosphonium salts could produce serious hazards since such functional groups are endowed with a particular high "kinetic acidity".

We now have overcome this obstacle by coating the sodium amide particles with paraffin [2]. Solid mixtures composed of ω-hydroxy-alkyl-triphenylphosphonium bromide (1 equiv.) and paraffin-coated sodium amide (2 equiv.) can be safely stored. Upon addition of tetrahydrofuran, they immediately set free the corresponding ylid 1 (a triphenylphosphonio-ω-sodiooxido-alkylid) which may then be employed in Wittig reactions with aldehydes or ketones affording sodium alkenolates 2 and, after hydrolysis, alkenols 3 .

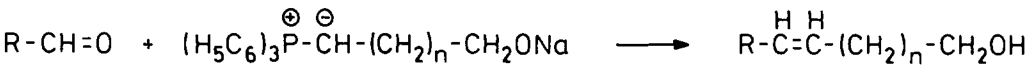


$$(H_5C_6)_3\overset{\oplus}{P}\text{-}\overset{\ominus}{C}H\text{-}(CH_2)_n\text{-}ONa \xrightarrow{R'(R)C=O} R'(R)C{=}CH\text{-}(CH_2)_n\text{-}CH_2ONa \longrightarrow R'(R)C{=}CH\text{-}(CH_2)_n\text{-}CH_2OH$$

1 **2** **3**

Up to now, hydroxy groups in ylid precursors have generally been protected in form of acetal functions. The present method not only saves this protection and the subsequent deprotection step but, in addition, tremendously simplifies the isolation of products. In contrast to paraffin (used for the coating of the sodium amide) and triphenylphosphine oxide(the inevitable by-product of carbonyl olefination reactions), sodium alcoholates 2 are insoluble in hydrocarbon solvents. Thus, all other products may simply be washed out with toluene or dichloromethane and the remaining alcoholates 2 neutralized to give the desired alkenols 3 . In a number of examples studied (see table) the final products were obtained in excellent yields, and typical (*Z/E*) ratios in the range of 97 : 3 to 98 : 2 were determined by gas chromatography (using carbowax 20M columns) or nmr spectroscopy (integrating the allyl decoupled olefinic signals [3]).

Table. Straight-chain (*Z*)-alkenols 3a - 3h obtained after reaction of aldehydes with "instant ylid" mixtures of ω-hydroxyalkyl-triphenylphosphonium bromides and sodium amide in tetrahydrofuran



$$R\text{-}CH{=}O + (H_5C_6)_3\overset{\oplus}{P}\text{-}\overset{\ominus}{C}H\text{-}(CH_2)_n\text{-}CH_2ONa \longrightarrow R\text{-}\overset{H}{C}{=}\overset{H}{C}\text{-}(CH_2)_n\text{-}CH_2OH$$

1 **3**

aldehyde : cross formula	phosph.salt: mp [°C] a)	ylid n+2	product b)	yield	bp [°C]/ mmHg c)	n_D^{20}
$C_{10}H_{20}O$	208 - 210	4	3a	72%	88 - $90/10^{-6}$	1.4582
$C_7H_{14}O$	182 - 184	5	3b	67%	88 - $92/10^{-4}$	1.4576
$C_8H_{16}O$	153 - 154	6	3c	73%	87 - $90/10^{-6}$	1.4578
$C_9H_{18}O$	142 - 144	7	3d	69%	101 - $103/10^{-4}$	1.4604
C_4H_8O	132 - 134	8	3e	84%	88 - $90/10^{-3}$	1.4577
C_4H_8O	65 - 67	9	3f	73%	89 - $91/10^{-6}$	1.4577
C_4H_8O	72 - 74 d)	10	3g	72%	93 - $96/10^{-6}$	1.4591
$C_5H_{10}O$	118 - 120	11	3h	70%	116 - $118/10^{-3}$	1.4612

a) Purity checked by elemental analyses and 360 MHz ^1H-nmr. The early members of these series of phosphonium salts (n+2 = 4 - 7) show reproducibility of the melting range while the higher homologs (n+2 = 8 - 11) melt under decomposition.

b) All compounds gave satisfactory elemental analyses (± 0.3%) and showed correct spectra.

c) Reduced pressure maintained with a rotatory pump (∿ 10^{-3} or 10^{-4} mmHg) or a diffusion pump (≲ 10^{-6} mmHg, "Klebevakuum").

d) From acetone; when crystallized from ethyl acetate, a solvent containing inclusive compound, mp 90 - 92°C (dec.) forms.

Numerous (*Z*)-alkenols exhibit biological activity as pheromones if not as cofactors or antagonists thereof [4]. The corresponding acetates are even more wide spread as chemical signals or mimics of such. For instance, (*Z*)-7-hexadecenyl acetate may be used to replace the natural sex attractant "gossyplure" for catching male pink ballworm moths (*Pectonophora gossypiella)* [5]. The aldehyde obtained upon oxidation of **3h** is the principal constituent of the tobacco budworm (*Heliothis virescens*) pheromone [6] and, in addition, appears to inhibit the proliferation of the corn earworm (*Heliothis zea*) [7]. Instant-ylids considerably facilitate the synthesis of such compounds. It should be emphasized that the paraffin-coated sodium amide offers just the comfort of allowing the large-scale preparation of an ylid precursor ready for use whenever it may be needed. If, however, only a single reaction is planned, it is more advantageous to generate the ylid by mixing the phosphonium salt and sodium amide powder immediately in the presence of the ethereal solvent [1].

A final hint concerns the quality of the ω-hydroxyalkyl-phosphonium salts. It should be perfect, since side products cannot be easily eliminated. For example, literature [9] specifies a "melting point" of 110°C for 8-hydroxyoctyl-triphenylphosphonium bromide. When we repeated its preparation by heating triphenylphosphine with 8-bromo-1-octanol neat or in acetonitrile or dimethylformamide, we always isolated a glassy material which contained some 30% of octamethylene-bis(triphenylphosphonium) dibromide . If, however, the quarternization was accomplished in refluxing ethanol, 81% of pure mono-phosphonium salt was obtained after 24 h; mp 132 - 134°C (from acetone).

Working procedure (typical example): Using rigorously dried (< 100 ppm H_2O) ammonia and sodium, approximately 100 g of sodium amide are prepared and all unreacted ammonia is removed by exhaustive pumping (10^{-5} mmHg) [8]. Under nitrogen, 2.1 mol (80 g) of the powdered material are added to 160 g of molten paraffin (solidification range 54 - 56°C; Fluka AG, order number 76230) kept at 65°C in a round bottom flask. After 10 min of magnetic stirring the suspension is cooled down in a dry-ice bath, the waxy product removed and, after addition of 20 g of sand, crushed in a mortar. Mixing with 1.0 mol (460 g) 6-hydroxyhexyl-triphenylphosphonium bromide in a rotatory evaporator gives the storable, ready-to-use instant-ylid reagent. In a three-necked flask, 25 mmol (approx. 67 mL; 17.5 g) of this reagent and 100 mL of tetrahydrofuran (or *tert*-butyl methyl ether) are vigorously stirred 30 min at 25°C. The evolving ammonia is carried away by a nitrogen stream which is allowed to escape through a drying tube ($CaCl_2$). At -80°C, 25 mmol of octanal are added. Shortly (about 15 min) after the reaction mixture has reached 25°C, it is diluted with 100 mL of pentane and centrifuged (10 min 2'800 rpm), the supernatant liquid [10] discarded and the sediment thoroughly suspended with 100 mL of a pentane/dichloromethane-mixture (5 : 1 by volume). After another centrifugation the residue is extracted a second time with 100 mL of the pentane/dichloromethane-mixture and, now essentially free from other products, collected after a final centrifugation. Water (10 mL) and ether (50 mL) are added, the ether layer is dried ($CaSO_4$) and evaporated. The residue distills at 87 - 90°C/10^{-6} mmHg; 3.9 g (73%) (*Z*)-6-tetradecen-1-ol. Lower members ($\leqslant C_{13}$) of the homologous alkenolate series are less soluble and hence 50 mL quantities of a 3 : 1 pentane/dichloromethane mixture suffice for each washing operation.

Acknowledgment. Financial help was provided by the Schweizerische Nationalfonds zur Förderung der wissenschaftlichen Forschung (grant no 2.635.0-82).

[1] M. Schlosser & B. Schaub, *Chimia* 1984 , *36*, 396.

[2] For details see the working procedure. Alternatively, a polymer blend may be used to cover the sodium amide grains and protect them against reaction (example : to a slurry of 30 g of sodium amide in 300 mL of pentane, in which 47 g of butadiene, 42 g of styrene and 6 g of divinylbenzene had been dissolved, 6 mL of a 1.5 N solution of *tert*-butyllithium in hexane is added. The polymerization is complete after roughly 90 min at 0°C. The coated sodium amide is collected by filtration and adherent solvent is removed under reduced pressure).

[3] A.M. Moiseenkov, B. Schaub, C. Margot & M. Schlosser, preceding communication.

[4] Reviews : C.A. Henrick, *Tetrahedron* 1977, *33*, 1845; R. Rossi, *Synthesis* 1977 , 817; J.M. Brand, J.C. Young & R.M. Silverstein in *L Zechmeister* "Progress in the Chemistry of Organic Natural Products" (1979), Vol. *37*, 1, Springer Verlag, Wien.

[5] N. Green M. Jacobson & J.C. Keller, *Experientia* 1969 , *25*, 682.

[6] W.L. Roelofs, A.S. Hill, R.T. Cardé & T. C. Baker, *Life Sci.* 1974 , *14*, 1555; J.H. Tumlinson, D.E. Hendricks, E.R. Mitchell, R.E. Doolittle & M.M. Brennan, *J. Chem. Ecol.* 1975 , *1*, 203.

[7] A.A. Sekul, A.N. Sparks, M. Beroza & B.A. Bierl, *J. Econ. Entomol.* 1975 , *68*, 603.

[8] Commercial sodium amide may be used instead, provided it is of sufficient quality (< 10% NaOH content). Addition of small amounts (2 - 20%) of potassium amide (or other potassium bases) to the sodium amide generally helps to accelerate the ylid formation.

[9] R.M. Waters, D.J. Voaden & J.D. Warthen, *Org. Prep. Proc. Int.* 1978 , *10*, 5.

[10] Sedimentation may replace centrifugation : after waiting 30 min, the alcoholate precipitate has deposited well enough on the bottom of a beaker to allow decantation of the supernatant liquid.

(Received in Germany 8 October 1984)