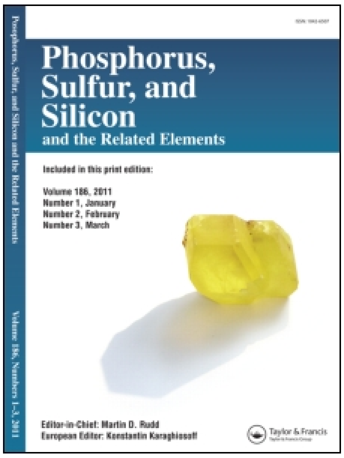


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

Novel Synthetic Aspects of the Staudinger Reaction

Andrzej Zwierzak[a]; Anna Koziara[a]
[a] Institute of Organic Chemistry, Technical University, Poland

To cite this Article Zwierzak, Andrzej and Koziara, Anna(1987) 'Novel Synthetic Aspects of the Staudinger Reaction', Phosphorus, Sulfur, and Silicon and the Related Elements, 30: 1, 331 — 334

To link to this Article: DOI: 10.1080/03086648708080588

URL: http://dx.doi.org/10.1080/03086648708080588

Phosphorus and Sulfur, 1987, Vol. 30, pp. 331–334
Photocopying permitted by license only

NOVEL SYNTHETIC ASPECTS OF THE STAUDINGER REACTION

ANDRZEJ ZWIERZAK AND ANNA KOZIARA
Institute of Organic Chemistry, Technical University,
Żwirki 36, 90-924 Lodz 40, Poland.

Abstract New applications of the Staudinger reaction for the preparation of amines are discussed.

It is well documented that an azido group can be considered as a convenient precursor of an amino function. Despite its wide applicability the transformation of azides into primary amines is subject, however, to interference by other functional groups. Such difficulties can be often overcome by the reduction of azides via the corresponding iminophosphoranes, usually referred to as Staudinger reaction[1]. In spite of its synthetic potential this reaction was employed for preparative purposes only occasionally[2]. The phosphite-azide coupling method, the less popular variant of the Staudinger reaction, was suggested as a useful approach to pure N-methylanilines from the respective phenyl azides[3] and employed for transforming some 5´-azidonucleosides into the corresponding phosphoroamidates and amines[4]. The reduction of organic azides via triphenylphosphinimines[2] suffers from several drawbacks: (i)the formation as well as the decomposition of triphenylphosphinimines is relatively slow and often takes place under drastic conditions; (ii) inconvenient application of pure azides is recommended; (iii) partial deprotection of triphenylphosphinimines is not possible.

Simple and convenient transformation of alkyl halides into the corresponding primary amines is the subject of this communication. We propose the one-pot procedure involving: (i) azidation of an alkyl bromide (1) under solid-liquid PTC conditions; (ii) the Staudinger reaction of crude azide (2) with triethyl phosphite; (iii) two-step deprotection of the iminophosphorane (3) by means of gaseous hydrogen chloride:

$$\underset{(1)}{\mathrm{R\text{-}Br}} \xrightarrow[\mathrm{C_6H_6/DMF\ (1:1),\ 80^\circ,\ 6\text{-}12\ h}]{\mathrm{NaN_3/Bu_4\overset{+}{N}\ \overset{-}{Br}\ /5\text{-}10\ mol\text{-}\%}} \left[\ \underset{(2)}{\mathrm{R\text{-}N_3}} \xrightarrow[20\text{-}30^\circ]{\mathrm{(EtO)_3P}}\right.$$

$$\left.\longrightarrow \underset{(3)}{\mathrm{R\text{-}N{=}P(OEt)_3}} \xrightarrow{\mathrm{HCl/C_6H_6}} \underset{(4)}{\mathrm{R\text{-}NH\text{-}P(O)(OEt)_2}}\ \right] \xrightarrow{\mathrm{HCl}}$$

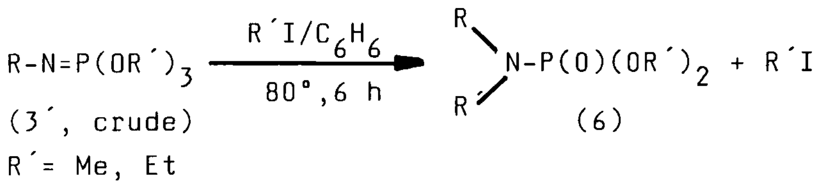
$$\longrightarrow \underset{(5)}{\left[\mathrm{R\text{-}\overset{+}{N}H_3}\right]}\mathrm{\overset{-}{Cl}}$$

Solid-liquid PTC system using benzene-DMF (1:1) as solvent and tetrabutylammonium bromide as catalyst was generally found the most suitable for azidation. Liquid-liquid PTC system consisting of aqueous sodium azide and neat alkyl bromide[5] is the method of choice for azidation of cycloalkyl bromides. Overall yields of amine hydrochlorides are high (60-80%) for primary bromides and still reasonable (50-70%) for secondary substrates. The presence of C-C unsaturation and /or carboalkoxyl group in the halide molecule does not interfere and these functions remain totally unaffected.

The hitherto unknown direct approach to t-alkylamines from the corresponding t-alkyl chlorides is also feasible by the above mentioned procedure. Azidation is in this case performed in benzene or dichloromethane by means of trimethylsilyl azide (20% excess) in the presence of 25 mol-% of tin tetrachloride as catalyst. Under the optimized conditions (6 days at 15-20°) competing elimination is markedly suppressed and t-alkylamine hydrochlorides are obtained under standard treatment of crude azides in workable (25-45%) overall yields.

The general amination procedure is readily adjustable for the preparation of diethyl N-alkylphosphoroamidates which can be considered as "phosphoryl protected" amine derivatives and which are valuable starting materials for the preparation of secondary amines by an alkylative approach[6]. The protection of P-N bond against cleavage is possible when crude iminophosphoranes (3) are refluxed in benzene (1 h) with one molar equivalent of water. Distillation of the product in vacuo affords pure phosphoroamidates (4) in 50-80% overall yield.

Crude iminophosphoranes (3′) prepared by the Staudinger reaction with trimethyl or triethyl phosphite can be easily and quantitatively transformed into N,N-disubstituted phosphoroamidates (6) when refluxed in benzene with an excess of methyl or ethyl iodide respectively:



(3′, crude)

R′= Me, Et

(6)

The use of higher alkyl iodides is not recommended because it results in partial elimination of hydrogen iodide and the phosphoroamidates (6) thus formed are contaminated with considerable amounts of the corresponding dialkyl N-alkylphosphoroamidates. Conventional deprotection of (6) affords secondary amine hydrochlorides in 60-95% overall yield.

REFERENCES

1. Yu. Gololobov, I. N. Zhmurova, and L. F. Kasukhin, Tetrahedron, 37, 437 (1981).
2. L. Horner and A. Gross, Liebigs Ann. Chem. 591, 117 (1955); W. S. Mungall, G. L. Greene, G. A. Heavner, and R.L. Letsinger, J. Org. Chem., 40, 1659 (1975); K. Baum, P. T. Berkovitz, V. Grakauskas, and T. G. Archibald, J. Org. Chem., 48, 2953 (1983); M. Vaultier, N. Knouzi, and R. Carrie, Tetrahedron Lett., 24, 763 (1983).
3. V. A. Gilyarov, R. V. Kudryavtsev, and M. I. Kabachnik, Zh. Obshch. Khim., 36, 708 (1966).
4. W. Freist, K. Schattka, F. Cramer, and B. Jastorff, Chem. Ber., 105, 991 (1972).
5. W. P. Reeves and M. L. Bahr, Synthesis, 823 (1976).
6. A. Zwierzak, Synthesis, 332 (1984).