Tetrahedron Letters No. 23, pp 1965 - 1968, 1974. Pergamon Press. Printed in Great Britain.

A NOVEL VARIATION OF THE LOSSEN REARRANGEMENT

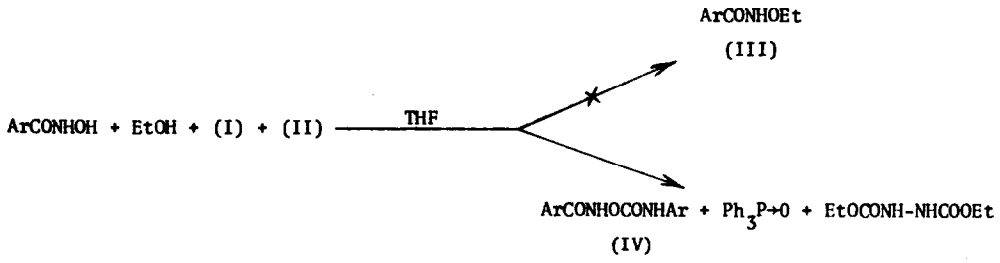
S. Bittner*, S. Grinberg and I. Kartoon

Department of Chemistry, Ben-Gurion University of the Negev, Beer Sheva, Israel

(Received in UK 10 April 1974; accepted for publication 24 April 1974)

It has been shown that reacting alcohols with carboxylic acids, hydrogen phosphate esters [1,2] and imides [3], in the presence of equimolar amounts of diethyl azodicarboxylate and triphenylphosphine, yields esters or N-alkylimides. These findings suggested the possibility of a direct route to O-alkylhydroxamates (III) through alkylation of hydroxamic acids with alcohols.

Various aromatic hydroxamic acids (1 mmole) were allowed to react with 1 mmole each of triphenylphosphine (I), ethanol and diethylazodicarboxylate (II) in tetrahydrofuran (THF) at room temperature. The hydroxamic acids reacted immediately, as indicated by TLC, and the disappearance of the red color with ferric chloride. However, the NMR spectrum of the products showed only aromatic protons, and no ethyl peaks were present. Infra-red data [ν_{max}(Nujol); 3255 (NH); 1760 and 1745 (C=O urethane); 1640 and 1555 (amide I and II bands)cm^{-1}] and elemental analyses proved that the compounds are products of a Lossen rearrangement, namely O-(N-phenylcarbamyl) hydroxamates (IV):



This variation of the Lossen rearrangement is coupled to a redox system, i.e., diethylazodicarboxylate is reduced to the hydrazo derivative and triphenylphosphine is oxidized to the phosphine oxide.

In some cases (IV) underwent a spontaneous second Lossen rearrangement [4] and only diarylurea (V) could be isolated:

$$\underset{}{\text{ArCONHOCONHAr}} \longrightarrow \underset{\text{(V)}}{\text{ArNHCONHAr}} + CO_2$$

Ethanol did not participate in the reaction and could be omitted in subsequent experimentation. The yields of IV or V were 70-85%.

TABLE

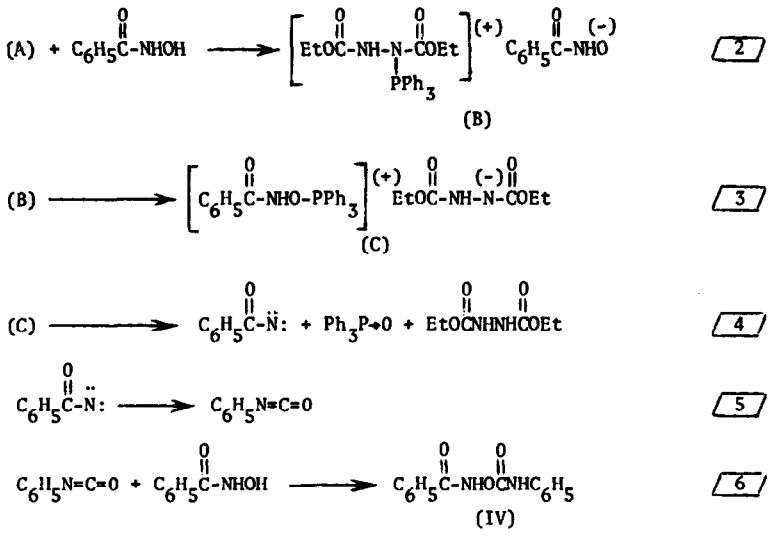
Hydroxamic Acid	Yield of Rearrangement Product[1] %
a. $C_6H_5CONHOH$	72
b. p-Cl-$C_6H_4CONHOH$	80
c. p-NO_2-$C_6H_4CONHOH$	85
d. o-Me-$C_6H_4CONHOH$	71[2]
e. p-Me-$C_6H_4CONHOH$	74[2]

(1) Satisfactory infrared, ultraviolet and NMR spectra as well as elemental analyses were obtained.

(2) Isolated as the diarylurea.

Mitsunobu *et al* [5] have suggested that alkoxyphosphonium salts are powerful alkyl donors reacting with various nucleophiles which act as alkyl group acceptors. Our studies suggested the following mechanism for the rearrangement:

$$Ph_3P + EtOC(=O)-N=N-C(=O)OEt \longrightarrow \underset{\text{(A)}}{EtOC(=O)-\overset{(-)}{N}-N(\overset{(+)}{P}Ph_3)-C(=O)OEt} \qquad (1)$$



An internal quaternary phosphonium salt (A) is formed which transforms to an external phosphonium salt (B) with the hydroxamate as an anion. Within this salt, the nucleophilic hydroxamate can be expected to react with the quaternary phosphorous to give a third phosphonium salt (C) with the diethylcarboxyhydrazoate as the anion. Salt (C) decomposes in a process comprising transfer of hydrogen, formation of triphenylphosphine oxide and migration of the phenylic group to the nitrogen. The isocyanate thus formed reacts with a second molecule of hydroxamic acid and yields the O-carbamyl N-acyl hydroxylamine (IV).

There is as yet no experimental proof of this mechanism or of the formation of the key intermediate - the triphenyl benzohydroxamyl phosphonium salt (C).

Three noteworthy features are manifest in this variation, and differ from the classic Lossen rearrangement:

1) The rearrangement is direct without the usual need for preliminary O-acylation of the hydroxamic acid [6].
2) Basic conditions which are usually necessary are not required in this variation. The rearrangement takes place under neutral conditions.
3) The reaction is spontaneous at room temperature and proceeds well in aprotic solvents.

Further studies using different hydroxylamine derivatives are now under way.

References

1. O. Mitsunobu and M. Yamada, Bull. Chem. Soc. Jap. 40, 2380 (1967).

2. O. Mitsunobu, K. Kato and J. Kimura, J. Amer. Chem. Soc., 91, 6510 (1969).

3. O. Mitsunobu, M. Wada and T. Sano, J. Amer. Chem. Soc. 94, 679 (1972).

4. Y. Knobler, N. Frydman and Hanna Eliasoff, Isr. J. Chem., 9, 165 (1971).

5. O. Mitsunobu and M. Egerchi, Bull. Chem. Soc. Jap. 44, 3427 (1971).

6. P.A.S. Smith, in "Open Chain Nitrogen Compounds", Volume II. W.A. Benjamin Inc., New York, 1966, p. 81-85.