CHEMISTRY LETTERS, pp.701-704, 1974. Published by the Chemical Society of Japan

SYNTHESES OF FURANS AND PYRROLES FROM ACYCLIC 1,3-DIENES VIA 3,6-DIHYDRO-1,2-DIOXINS

Kiyosi KONDO and Masakatsu MATSUMOTO
Sagami Chemical Research Center, Nishi-Ohnuma 4-4-1,
Sagamihara, Kanagawa 229

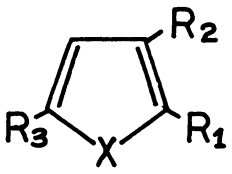
Base-catalyzed isomerization of 3,6-dihydro-1,2-dioxins followed by dehydration and the isomerization in the presence of primary amines provide useful, high yield routes to furans and pyrroles, respectively.

Recently we have described that the photosensitized oxygenation of simple acyclic 1,3-dienes gave 3,6-dihydro-1,2-dioxins in good yields.[1] Some special 1,2-dioxins are known to be dehydrated to furans; the 1,4-endo-peroxide of 1,1'-dicyclohexenyl was converted to 2,3,4,5-dicyclohexenofuran under alkaline condition.[2] 2,5-Diphenylfuran was obtained from 3,6-diphenyl-3,6-dihydro-1,2-dioxin by the treatment with 1% sulfuric acid in acetic acid.[3] Recently, pyrolysis or isomerization on basic alumina was also reported as an effective method for the transformation.[4] However, Yields and reaction conditions seemed to be hardly satisfactory in view of our aim of applying the method for the syntheses of natural products. We have now established a generally applicable and facile condition for the transformation of 1,2-dioxins to the corresponding furans as well as the use of the same intermediates for the syntheses of pyrroles.

Treatment of 3,6-diphenyl-3,6-dihydro-1,2-dioxin in ethanol with a catalytic amount of KOH for 10 min at room temperature, followed by pouring the reaction mixture into a dilute aqueous H_2SO_4 resulted in the formation of 2,5-diphenylfuran in quantitative yield. Under the same reaction conditions, 3-phenyl-, 4-phenyl-, and 3,4-diphenyl-3,6-dihydro-1,2-dioxins were quantitatively dehydrated to the corresponding furans as shown in Table 1. As the alkylfurans are generally unstable in aqueous acid, following modification is recommended for the dehydration of

1,2-dioxins bearing alkyl substituents. The 1,2-dioxin was treated either with a catalytic amount of KOH in Et_2O-MeOH (4:1) or with Bu^tOLi in THF at -78°C. The resulting mixture was carefully acidified by the dropwise addition of H_2SO_4 in MeOH or THF at -78°C and the excess acid was finally quenched with solid $NaHCO_3$ at the same temperature. According to this procedure, 3-methyl-, 3-t-butyl-, 2-methyl- and 2,5-dimethylfurans were prepared in 78-92% yields from the corresponding 1,2-dioxins.

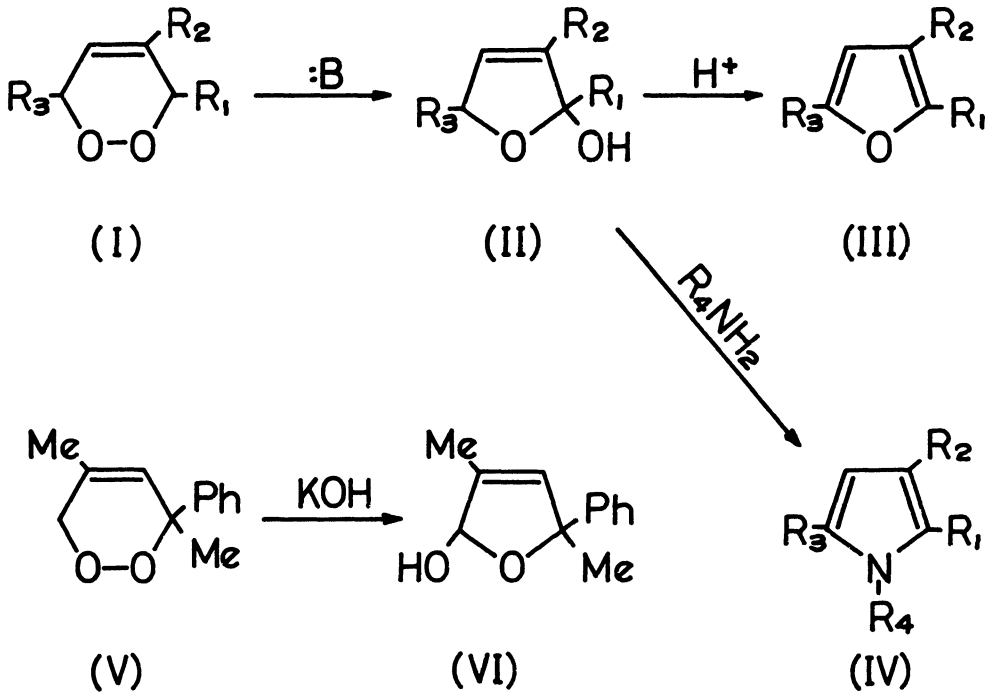
Table 1 Furans and Pyrroles from 1,2-Dioxins.



R_1	R_2	R_3	X	Yield(%)
Ph	H	Ph	O	100
Ph	H	H	O	100
H	Ph	H	O	100
Ph	Ph	H	O	100
Me	H	H	O	78
H	Me	H	O	89
Me	H	Me	O	79
H	Bu^t	H	O	92
H	Me	H	NPh	68
H	Bu^t	H	NPh	64
H	Ph	H	NPh	56
Ph	Ph	H	NPh	61
H	Bu^t	H	NCH_2Ph	47
H	Ph	H	NCH_2Ph	49
Ph	Ph	H	NCH_2Ph	69
Ph	H	Ph	NEt	69
H	Bu^t	H	NH	93
H	Ph	H	NH	91
Ph	H	Ph	NH	83

When the treatment of 1,2-dioxins with strong base was conducted in the presence of primary amine, we could obtain N-substituted pyrroles directly. For example, heating of an equimolar mixture of 4-methyl-1,2-dioxin and aniline in EtOH in the presence of KOH for 10 hr produced 3-methyl-1-phenylpyrrole (m.p. 60.5-61.5°C) in 68% yield. Similarly, 4-t-butyl- and 3,4-diphenyl-1,2-dioxins were transformed into the corresponding N-phenylpyrroles. Alkylamines, aralkylamines, and even more ammonia itself are the possible nitrogen sources for this pyrrole syntheses. Thus, for example, introduction of dry ammonia to the refluxing solution of 4-t-butyl-1,2-dioxin in EtOH containing a trace amount of KOH afforded 3-t-butylpyrrole. The yields are also summarized in Table 1.

The results cited above and the previously reported results on the isomerization of endo-peroxide to keto-alcohol[2] suggest that unsaturated lactol (II) will be the primary product of the base-catalyzed reaction of 1,2-dioxin (I). The dehydrative aromatization of (II) under acidic conditions will afford furans (III). On the other hand, base-catalyzed isomerization of (II) to unsaturated keto-alcohol followed by condensation with amines may produce pyrroles (IV). Insight as to the nature



of the relatively unstable lactol (II) was obtained from the reaction of a 3,3-disubstituted 1,2-dioxin. Thus 3,5-dimethyl-3-phenyl-3,6-dihydro-1,2-dioxin (V) was quantitatively isomerized to the lactol (VI) upon treatment with KOH in MeOH for 10 min at room temperature. The nmr spectrum of the isolated lactol (VI) indicated that the product was a mixture of two diastereoisomers (ca. 1:1).

REFERENCES

1) K. Kondo and M. Matsumoto, Chem. Commun., 1332 (1972).

2) K. Gollnick and G. O. Schenck, "1,4-Cycloaddition Reactions", ed. by J. Hamer, Academic Press, New York, (1967), p296.

3) G. Rio and J. Berthelot, Bull. Soc. Chim. France, 1664 (1969).

4) E. Demole, C. Demole, and D. Berthet, Helv. Chim. Acta, 56, 265 (1973).

(Received May 2, 1974)