323. *The Rearrangement of Allyl Ethers in the Purine Series, with Some Remarks on the Hydrogenation of Allyl Ethers.*

By Ernst Bergmann and Heinz Heimhold.

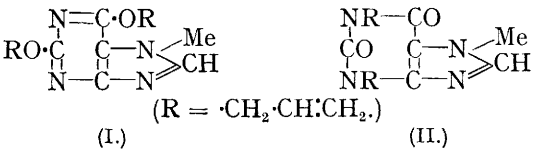
In the preceding paper enolic allyl ethers were reported to be rearranged less smoothly than phenolic derivatives into the isomeric *C*-allyl derivatives. The question whether heterocyclic allyl ethers behave like the phenol derivatives has not been fully investigated, the only data available being that 2-allyloxyquinolone and 4-allyloxyquinaldine are rearranged into *N*-allylquinolone and 4-hydroxy-3-allylquinaldine, respectively (Tschitschibabin and Jeletzky, *Ber.*, 1924, **57**, 1158; Mander-Jones and Trikojus, *J. Amer. Chem. Soc.*, 1932, **54**, 2570).

In the course of synthetic experiments in the purine series, we prepared the 2 : 6-*diallyloxy*-7-*methylpurine* (I; see below) by interaction of 2 : 6-dichloro-7-methylpurine and sodium allyloxide. On heating, it is isomerised, and it is concluded that isomerisation is due to a migration of the allyl group from oxygen to nitrogen because allylamine can be detected by its characteristic odour. 1 : 3-*Diallyl*-7-*methylxanthine* (II) has a markedly higher m. p. than its isomeride (I).

The proof of structure (I) is based on the following considerations: Fission of the *O*-benzyl linkage by means of hydrogen in the presence of a catalyst has been recorded by M. Bergmann (*Ber.*, 1932, **65**, 1192, 1201, 1692, and later work; see also Fischer, *ibid.*, pp. 337, 345; Freudenberg, Duerr, and Hochstetter, *Ber.*, 1928, **61**, 1735; Rosenmund and Zetzsche, *Ber.*, 1921, **54**, 2038; compare van Duzee and Adkins, *J. Amer. Chem. Soc.*, 1935, **57**, 147). Since the allyl and the benzyl group have very similar chemical properties (the comparison extends to pharmacological effects: *Ber.*, 1918, **51**, 79; 1921, **54**, 2081; 1922, **55**, 3536; 1923, **56**, 538; 1926, **59**, 1081; 1927, **60**, 2551), we have tested the stability of the *O*-allyl linkage towards hydrogen; phenyl allyl ether, on treatment with hydrogen in propyl-alcoholic solution, gives 75% of phenyl propyl ether and 25% of free phenol. An analogous reaction was applied to compound (I); the hydrogenation took place very smoothly and gave heteroxanthine (III). The isomeric 1 : 3-diallyl-7-methylxanthine is not converted into heteroxanthine.

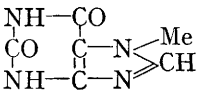
The migration of the allyl group in the rearrangement of phenolic allyl ethers is accompanied by a displacement of the double bond and of the "outer-valency" in the group. The same is true for the rearrangement in the purine series. The interaction of 2 : 6-dichloro-7-methylpurine and the sodium derivative of Δ^{β}-hexen-δ-ol, $CH_3 \cdot CH{:}CH \cdot CH(OH) \cdot Et$, gave a product (IV), which underwent rearrangement when distilled in a vacuum, and since

the new product on ozonisation afforded propaldehyde and propionic acid it must have the structure (V), showing that the rearrangement was not merely a migration of the hexenyl group. The reaction is completely analogous to the corresponding rearrangement in the benzene series.

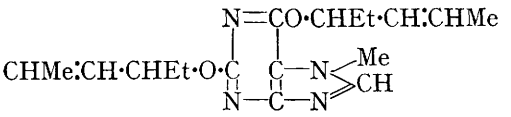


(R = ·CH_2·CH:CH_2.)

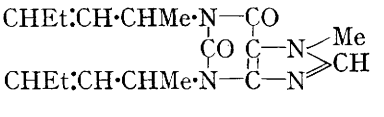
(I.) (II.)



(III.)



(IV.)



(V.)

Further proof that the product obtained after distillation is not (IV) is afforded by the fact that on hydrogenation it gives no trace of heteroxanthine.

The splitting of the C–O bond occurs in preference to hydrogenation of the double bond of the allyl group, as may be deduced from the fact that 2 : 6-*dipropoxy*-7-*methylpurine* is not attacked by hydrogen.

Experimental.

2 : 6-*Diallyloxy*-7-*methylpurine* (I).—A solution of sodium (0·23 g.) in allyl alcohol (25 g.) was heated with 2 : 6-dichloro-7-methylpurine (1 g.; Fischer, *Ber.*, 1897, **30**, 2400) in a sealed tube at 100° for 3 hours. The sodium chloride was filtered off, washed with alcohol, the filtrate evaporated in a vacuum, and the residue recrystallised from ligroin; needles, m. p. 111—112° (Found: N, 22·5. $C_{12}H_{14}O_2N_4$ requires N, 22·8%).

Hydrogenation. This compound (0·75 g.) was hydrogenated for 3 hours in boiling propyl alcohol (60 c.c.) in presence of palladised barium sulphate. The filtered solution gave a precipitate on cooling; by repeatedly extracting the insoluble part of the reaction product (containing the catalyst) with the mother-liquor and combining the precipitates, pure heteroxanthine (0·23 g.) (III) was obtained, decomp. 360° (Found: C, 43·1; H, 3·7; N, 33·4. Calc. for $C_6H_6O_2N_4$: C, 43·3; H, 3·6; N, 33·7%).

1 : 3-*Diallyl*-7-*methylxanthine* (II).—0·1 G. of the diallyl ether (I) was heated at 150° for 2 hours; the liquid solidified while hot, and on cooling, the mass, which exhibited the typical smell of allylamine, was triturated with alcohol and recrystallised from the same solvent; shining crystals, m. p. 277—278° (Found: C, 58·3; H, 5·8; N, 22·6. $C_{12}H_{14}O_2N_4$ requires C, 58·5; H, 5·7; N, 22·8%).

1 : 3-*Di*-(α-*methyl*-Δ^{β}-*pentenyl*)-7-*methylxanthine* (V).—2 : 6-Dichloro-7-methylpurine (2 g.) was added to a solution of sodium (0·45 g.) in Δ^2-hexen-4-ol (20 g.) (Reif, *Ber.*, 1906, **39**, 1603; 1908, **41**, 2739; Kyriakides, *J. Amer. Chem. Soc.*, 1914, **36**, 663), and heated to 165° for 4 hours in a sealed tube with continuous shaking. After cooling, the mass was diluted with 3 vols. of water and extracted with ether. After evaporation of the ether, the excess of hexenol was distilled off from the mixture, which had an aminic smell. The residue distilled at 215—225°/12 mm. as a thick, yellow syrup (Found: C, 65·3; H, 8·0; N, 16·6. $C_{18}H_{26}O_2N_4$ requires C, 65·5; H, 7·9; N, 17·0%). Experiments with cinnamyl alcohol or geraniol did not give crystallisable products.

On ozonisation of (V) in carbon tetrachloride solution, the ozonide was precipitated, and when the reaction mass was heated with 5 vols. of water, the smell of propionaldehyde appeared. The acid liquid was made alkaline, the solvent and the neutral volatile products removed with steam, and the residue acidified and again distilled with steam. The distillate was neutralised, evaporated to dryness, the residue dissolved in water, and lead acetate solution added. The precipitate was identified as basic lead propionate (see Beilstein, 1920, Vol. II, p. 268).

Hydrogenation of Phenyl Allyl Ether.—The ether (10 g.; Claisen, *Annalen*, 1919, **418**, 78) was hydrogenated for 8 hours in boiling propyl alcohol (35 c.c.) in presence of palladised barium sulphate (2 g.). The filtered solution was evaporated, and the residue shaken with 30% sodium hydroxide (25 c.c.). The insoluble matter was extracted with ether, and purified by distillation, phenyl propyl ether (5 g.), b. p. 69°/14 mm. (Found: C, 79·8; H, 8·4. Calc. for $C_9H_{12}O$: C, 79·4;

H, 8·8%), being obtained. The alkaline solution was acidified, the phenol (2 g.) extracted with ether, and identified by conversion into phenyl carbanilate (Leuckart, *J. pr. Chem.*, 1890, **41**, 318), needles, m. p. 123—124°, from alcohol.

2 : 6-*Dipropoxy*-7-*methylpurine*.—2 : 6-Dichloro-7-methylpurine (1·32 g.; Fischer, *Ber.*, 1897, **30**, 2400) was added to a solution of sodium (0·3 g.) in propyl alcohol (35 c.c.) and heated for 12 hours at 130—140° in a sealed tube with continuous shaking. The solution was filtered, evaporated in a vacuum, and the residue diluted with water and extracted with ether. The product was isolated as an oil, which crystallised on standing. Trituration with light petroleum gave 0·66 g. of the required substance, which was recrystallised from the same solvent containing some ethyl acetate; m. p. 92° (Found : C, 57·3; H, 7·2. $C_{12}H_{18}O_2N_4$ requires C, 57·6; H, 7·2%). The *substance* was not altered by treatment with palladium and hydrogen.

The above experiments were carried out in the laboratory of the Friedrich Wilhelm University, Berlin.

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