Tetrahedron. 1964, Vol. 20, pp. 2091 to 2096. Pergamon Press Ltd. Printed in Northern Ireland

THE REACTION BETWEEN 2,3-DIHYDROFURAN AND DIHALOCARBENES

AN ATTEMPTED 2H-PYRAN SYNTHESIS

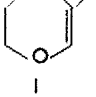
J. C. Anderson, D. G. Lindsay and C. B. Reese
University Chemical Laboratory, Cambridge, England

(*Received* 28 *May* 1964)

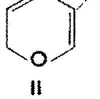
Abstract—2,3-Dihydrofuran (III) reacts with dichlorocarbene to give the expected adduct (IV), which readily isomerizes to 2,3-dichloro-5,6-dihydro-2H-pyran (V). When either IV or V is heated in quinoline solution, the aldehyde (VIII) is obtained. When V is exposed to atmospheric moisture, the bis-dihydropyranyl ether (IX) is formed. The t-butyl ether (XII) is obtained when 2,3-dihydrofuran is treated with bromoform and potassium t-butoxide at 0°.

The use of halocyclopropane intermediates[1] in the synthesis of certain homocyclic and heterocyclic systems, of which some are not otherwise readily accessible, is now well established. Although this method was first illustrated over eighty years ago,[2] by the preparation of 3-chloropyridine from pyrrole, it has only been used extensively since the fundamental studies on dihalocarbenes[3] by Hine, Doering and others.

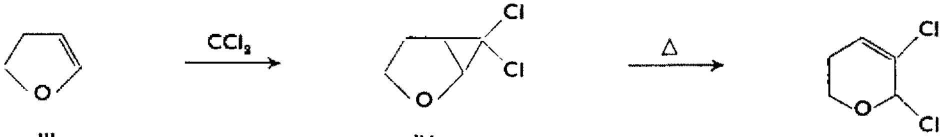
This synthetic approach was well exemplified by the two-step conversions of 2,3-dihydropyran into 2,3-dihydrooxepine (I; R = H) and 2,3-dihydro-6-chlorooxepine (I; R = Cl), reported by Schweizer and Parham.[4] At that time, neither of the parent heterocyclic systems, 2H- and 4H-pyran was known, and it seemed to us that it might be possible to synthesize 2H-pyran (II; R = H) from 2,3-dihydrofuran in a similar way. Apart from the intrinsic interest in obtaining 2H-pyran, the latter seemed likely to be a suitable starting material for a synthesis of oxepine by this halocyclopropane route. Recently, two different preparations of 4H-pyran have been reported.[5,6]



I



II



III IV V

---

[1] W. E. Parham and E. E. Schweizer, *Organic Reactions* Vol. 13; pp. 55–90. J. Wiley, New York (1963).

[2] G. L. Ciamician and M. Dennstedt, *Ber. Dtsch. Chem. Ges.* **14,** 1153 (1881).

[3] For reviews on carbenes see: W. Kirmse, *Angew. Chem.* **73,** 161 (1961); *Ibid.* **71,** 537 (1959); E. Chinoporos, *Chem. Rev.* **63,** 235 (1963); J. Hine, *Physical Organic Chemistry* (2nd Edition) Chap. 24. McGraw-Hill, New York (1962).

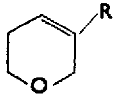
[4] E. E. Schweizer and W. E. Parham, *J. Amer. Chem. Soc.* **82,** 4085 (1960).

[5] J. Strating, J. H. Keijer, E. Molenaar and L. Brandsma, *Angew. Chem.* **74,** 465 (1962).

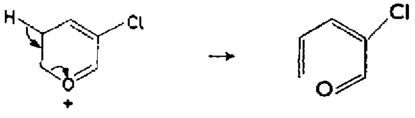
[6] S. Masamune and N. T. Castellucci, *J. Amer. Chem. Soc.* **84,** 2452 (1962).

As dichlorocarbene is more readily generated than chlorocarbene and as the use of the former avoids stereochemical complications, it was decided in the first place to attempt the synthesis of 5-chloro-2H-pyran (II; $R = Cl$). 2,3-Dihydrofuran (III), prepared[7] by the base-catalysed isomerization of commercially-available 2,5-dihydrofuran, was treated with dichlorocarbene, generated by the action of sodium methoxide on ethyl trichloroacetate.[8] The expected adduct 6,6-dichloro-2-oxabicyclo[3.1.0]-hexane (IV), the structure of which was confirmed by IR and NMR spectroscopy, was distilled from the products in 58% yield, but only if care was taken to keep the heating-bath temperature below 60°. If the bath temperature was allowed to rise above 60°, an exothermic reaction took place and no bicylic adduct (IV) was obtained, but a less volatile isomer instead. This isomerization reaction also occurred when pure IV was heated at 60°.

By analogy with the recently described thermal rearrangement of 6,6-dibromobicyclo[3.1.0]hexane to 2,3-dibromocyclohexene[9] and the related isomerization reactions of the dihalocarbene adducts of norbornylene,[10] this isomer of IV was assigned the structure 2,3-dichloro-5,6-dihydro-2H-pyran (V). Its IR spectrum, which showed a strong band at 1650 cm^{-1}, and NMR spectrum were in accord with this structure. When V was treated with lithium aluminium hydride in ether solution, it was converted into 3-chloro-5,6-dihydro-2H-pyran (VI; $R = Cl$) which, apart from the olefinic proton region, had an NMR spectrum very similar to that of 5,6-dihydro-2H-pyran[11] (VI; $R = H$).



VI



VII VIII

As IV and V were possible precursors of 5-chloro-2H-pyran (II; $R = Cl$), a solution of each in excess quinoline was heated at 120° under reduced pressure according to the procedure of Schweizer and Parham.[4] However, in both cases a pale yellow liquid, which showed strong absorption in the IR at 1695 cm^{-1}, was obtained. This material, which was isomeric with 5-chloro-2H-pyran (II; $R = Cl$), had a low intensity absorption band at 337 mμ; it readily formed a 2,4-dinitrophenylhydrazone with strong absorption at 382 mμ. Its NMR spectrum showed clearly that it was not a 2H-pyran derivative and it was assigned the structure, 2-chloro-penta-2,4-dien-1-al (VIII). The 2,4-dinitrophenylhydrazone[12] of penta-2,4-dien-1-al has a strong absorption band at 383 mμ.

It is possible that 5-chloro-2H-pyran (II; $R = Cl$) is an intermediate in the formation of the aldehyde (VIII), as the 2H-pyran system may be unstable with respect to its open-chain valence tautomer under the reaction conditions. An analogy for such

---

[7] R. Paul, H. Fluchaire and G. Collardeau, *Bull. Soc. Chim. Fr.* 668 (1950).

[8] W. E. Parham and E. E. Schweizer, *J. Org. Chem.* **24**, 1733 (1959).

[9] J. Sonnenberg and S. Winstein, *J. Org. Chem.* **27**, 748 (1962).

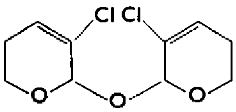
[10] C. W. Jefford, *Proc. Chem. Soc.* 64 (1963); R. C. De Selms and C. H. Combs, *J. Org. Chem.* **28**, 2206 (1963); E. Bergman, *Ibid.* **28**, 2210 (1963).

[11] S. Olsen, *Acta Chem. Scand.* **5**, 1168 (1951).

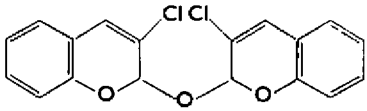
[12] E. L. Pippen and M. Nonaka, *J. Org. Chem.* **23**, 1580 (1958).

a rearrangement is the irreversible isomerization[13] of allyl vinyl ether to penta-4-en-1-al at 250°. However, with either IV or V as the starting material, the conjugate acid (VII) of 5-chloro-2H-pyran is a possible reaction intermediate. This oxonium ion (VII) could collapse (in the manner indicated) to give the aldehyde (VIII) directly.

From the outcome of the reaction between 2,3-dihydrofuran (III) and dibromocarbene (see below), it seemed likely that 2,3-dichloro-5,6-dihydro-2H-pyran (V) would undergo nucleophilic substitution at C(2) rather than base catalysed elimination. For this reason the approach to a 2H-pyran synthesis starting from 2,3-dihydrofuran was discontinued and the reaction between the latter compound and chlorocarbene was not investigated.

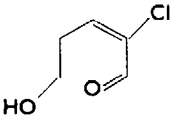


IX

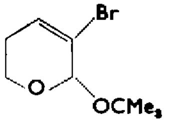


X

During this study we observed that when 2,3-dichloro-5,6-dihydro-2H-pyran (V) was exposed to atmospheric moisture, hydrogen chloride was evolved and a crystalline product with the molecular formula $C_{10}H_{12}Cl_2O_3$ was deposited. This compound has been assigned the structure (IX) on the basis of its NMR spectrum and its reaction with aqueous acid (see below). This observation became especially interesting when, very recently, Parham *et al.*[14] described the reaction between benzofuran and dichlorocarbene. These workers were able to isolate a product only after their reaction mixture had been treated with water; they formulated this compound as bis[3-chloro-2(3-chromenyl)] ether (X) which corresponds to bis[3-chloro-2(5,6-dihydro-2H-pyranyl)] ether (IX). Furthermore, the isolation and characterization of compounds IV and V support the reaction scheme suggested by Parham *et al.*[14] When IX was treated with hot dilute aqueous acid, it was converted into a single volatile product (as indicated by gas chromatography) which showed strong absorption in the IR at 1700 cm^{-1}. This hydrolysis product was characterized as its 2,4-dinitrophenylhydrazone, which had the elemental analysis and absorption spectrum expected for such a derivative of 2-chloropenta-2-en-1-al-5-ol (XI). A corresponding product was reported[14] in the benzofuran series.



XI



XII

In an attempt to prepare 6,6-dibromo-2-oxabicyclo[3.1.0]hexane, 2,3-dihydrofuran (III) was treated with bromoform and potassium t-butoxide in t-butanol at 0°. However, no dibromocarbene adduct was isolated from the products but only 2-t-butoxy-3-bromo-5,6-dihydro-2H-pyran (XII). Gas chromatographic analysis of the cold reaction mixture showed the presence of the latter compound but gave no

---

[13] E. Vogel, *Angew. Chem. internat. Edit.* 2, 6 (1963).

[14] W. E. Parham, C. G. Fritz, R. W. Soeder and R. M. Dodson, *J. Org. Chem.* 28, 557 (1963).

indication of the expected adduct, which had presumably rearranged even at 0°. No reaction occurred between 6,6-dichloro-2-oxabicyclo [3.1.0] hexane (IV) and potassium t-butoxide in t-butanol at room temperature. Apart from the additional high field singlet ascribed to the resonance of the t-butyl protons, the NMR spectrum of XII was closely similar to that of IX. This is in accord with the proposed structures.

EXPERIMENTAL

M.ps are uncorrected. IR spectra were measured on a Perkin-Elmer Infracord or a Perkin-Elmer model 21 spectrophotometer. UV spectra were measured on a Cary model 14 M-50 recording spectrophotometer. NMR spectra of 10% solutions in CCl_4 were run at 40 Mc/s with tetramethylsilane as internal standard.

2,3-*Dihydrofuran* (III)

2,5-Dihydrofuran (114 g) and 1·25M potassium t-butoxide in t-butanol (80 ml) were heated together in sealed tubes at 180°, according to the method of Paul *et al.*[7] The products were carefully fractionated to yield III (58 g, 51%), b.p. 54–55° and 2,5-dihydrofuran (24 g, 21%), b.p. 65–67°. These fractions were gas chromatographically homogeneous.

6,6-*Dichloro-2-oxabicyclo*[3.1.0]*hexane* (IV)

To a stirred, ice-cold suspension of freshly prepared sodium methoxide (8·4 g) in a solution of III (9·4 g, distilled from $LiAlH_4$) and dry pentane (100 ml) under N_2, redistilled ethyl trichloroacetate (27·5 g) was added rapidly. A vigorous reaction, which caused pentane to boil, occurred immediately. The reaction mixture was stirred for a further 3 hr, then filtered and the residue washed with pet. ether (b.p. 40–60°). The filtrate and washings were evaporated at 30°/15 mm and the residue distilled at 1·5 mm, with a bath temp of 55°. 6,6-*Dichloro-2-oxabicyclo*[3.1.0]*hexane* (IV) (11 g, 58%) distilled as a colourless liquid, b.p. 34–38°/1·5 mm (41–43°/2 mm) and was collected in an acetone–dry ice cooled trap. (Found: C, 39·5; H, 3·9. $C_5H_6Cl_2O$ requires: C, 39·3; H, 3·9%). The compound has no appreciable IR absorption in the region 1500–2000 cm^{-1}. NMR spectrum: 6·0τ, a multiplet, weight 3, assigned to C(1) and C(3) protons; 7·65τ, a multiplet, weight 3, assigned to C(4) and C(5) protons.

Thermal rearrangement of 6,6-*dichloro-2-oxabicyclo*[3.1.0]*hexane* (IV)

(a) The above preparation of IV was repeated with sodium methoxide (7·5 g), 2,3-dihydrofuran (8·5 g), pentane (90 ml) and ethyl trichloroacetate (25 g). The products were worked up as before except that the final distillation was conducted at 18 mm. 2,3-*Dichloro*-5,6-*dihydro*-2H-*pyran* (V; 8·6 g, 46%) distilled as a colourless liquid b.p. 70–80°/18 mm; 76–78°/14 mm on redistillation. Found: (C, 39·7; H, 4·0. $C_5H_6Cl_2O$ requires: C, 39·3; H, 3·9%). ν_{max} 1645 cm^{-1}; NMR spectrum: 3·35τ, a singlet, assigned to C(2) proton; 5·85τ, a multiplet, assigned to C(6) protons; 7·6τ, a multiplet, assigned to C(5) protons.

(b) Compound IV (16 g) was heated at 60°, and its rearrangement followed by gas chromatography. It was found to be complete after 15 min, when the resulting V was distilled, yield 14·7 g (90%), b.p. 76–78°/14 mm.

3-*Chloro*-5,6-*dihydro*-2H-*pyran* (VI; R = Cl)

A solution of V (4·3 g) in anhydrous ether (10 ml) was treated with a suspension of $LiAlH_4$ (0·5 g) in ether (10 ml) at a rate which maintained the solvent under gentle reflux. Then the reaction mixture was externally heated for a further 40 min, methyl formate (5 ml) added to destroy the excess $LiAlH_4$, followed by dil. H_2SO_4 (2N, 5 ml). The organic layer was separated from the aqueous layer, dried ($MgSO_4$), and distilled. 3-*Chloro*-5,6-*dihydro*-2H-*pyran* (VI; R = Cl; 1·5 g, 45%) was collected as a colourless liquid, b.p. 136–138°/760 mm. (Found: C, 50·5; H, 6·2; Cl, 28·3. C_6H_7ClO requires: C, 50·6; H, 6·0; Cl, 29·9%), ν_{max} 1654 cm^{-1}. NMR spectrum: 4·1τ, a multiplet, weight 1, assigned to C(4) proton; 6·0τ, a multiplet, weight 2, assigned to C(2) protons; 6·3τ, a triplet, weight 2, assigned to C(6) protons; 7·75τ, a multiplet, weight 2, assigned to C(5) protons. Except for the resonances of the olefinic protons, the latter spectrum resembled that of VI (R = H): 4·24τ, a multiplet, wt 2, assigned to C(3) and C(4) protons; 5·97τ, a multiplet, wt 2, assigned to C(2) protons; 6·3τ, a triplet, wt 2, assigned to C(6) protons; 7·9τ, a multiplet, wt 2, assigned to C(5) protons.

2-*Chloropenta*-2,4-*dien*-1-*al* (VIII)

(a) Compound IV (3 g) was dissolved in redistilled quinoline (10 g). The solution, contained in a distillation apparatus, was heated under red. press. in an atm of N_2 with the heating-bath temp initially at 90°. When this temp was increased to 120°, 2-*chloropenta*-2,4-*dien*-1-*al* (VIII) distilled as a pale yellow liquid, b.p. 67–68°/19 mm, yield 0·75 g, 33%, (Found: C, 51·4; H, 4·2; Cl, 30·4. C_5H_5ClO requires: C, 51·5; H, 4·3; Cl, 30·4%); ν_{max} 1695 cm^{-1}; λ_{max}^{EtOH} 271, 337 mμ (log ε 4·25, 2·0). NMR spectrum: 0·55τ, a singlet, wt 1, assigned to aldehydic proton; 2·9τ, a multiplet, wt 2, assigned to C(3) and C(4) protons; 4·1τ, a double triplet, wt 2, assigned to C(5) protons.

(b) When V (3 g) was dissolved in quinoline (10 g) and the solution heated as above, VIII (1 g, 44%), b.p. 69–70°/24 mm was obtained.

The 2,4-*dinitrophenylhydrazone of* 2-*chloropenta*-2,4-*dien*-1-*al* (VIII)

This derivative was obtained from VIII in the usual manner and crystallized from chloroform–ethanol as red needles, m.p. 168–170° with dec. (Found: C, 44·7; H, 3·5; N, 19·0. $C_{11}H_9ClN_4O_4$ requires: C, 44·5; H, 3·1; N, 18·9%). λ_{max}^{EtOH} 382, 296, 265, 246 mμ (log ε 4·56, 4·09, 4·22, 4·20). The 2,4-dinitrophenylhydrazone[12] of penta-2,4-dien-1-al has $\lambda_{max}^{CHCl_3}$ 383 mμ (log ε 4·56).

Bis[3-*chloro*-2(5,6-*dihydro*-2H-*pyranyl*)] *ether* (IX)

Compound V (11·8 g) was evenly distributed between 4 uncovered Petrie dishes (4″ diameter), which were placed in a draught of air for 24 hr. The evolution of HCl was detected and a gummy crystalline mass was deposited. This material was recrystallized from ethanol to give colourless needles of bis[3-*chloro*-2(5,6-*dihydro*-2H-*pyranyl*)] *ether* (IX; 3·5 g, 30%), m.p. 137–139°. (Found: C, 47·9; H, 5·0; Cl, 27·9; M.W., 248. $C_{10}H_{12}Cl_2O_3$ requires: C, 47·8; H, 4·8; Cl, 28·3%; M.W., 251), $\nu_{max}^{CHCl_3}$ 1665 cm^{-1}. NMR spectrum: 3·9τ, a quartet, wt 2, assigned to C(4) protons; 4·9τ, a singlet, wt 2, assigned to C(2) protons; 6·0τ, a multiplet, wt 4, assigned to C(6) protons; 7·8τ, a multiplet, wt. 4, assigned to C(5) protons.

Acidic hydrolysis of bis[3-*chloro*-2(5,6-*dihydro*-2H-*pyranyl*)] *ether* (IX)

A suspension of IX (0·1 g) in 3N HCl aq (12 ml) was heated under reflux for 10 min, after which time complete solution had been effected. The cooled solution was extracted with chloroform (3 × 10 ml) and the dried (Na_2SO_4) chloroform extract evaporated to a brownish-yellow oil, which gave a single peak on a gas chromatogram and which had ν_{max} 1700 cm^{-1}. The 2,4-*dinitrophenylhydrazone of* 2-*chloropenta*-2-*en*-1-*al*-5-*ol* (XI) was prepared from this oil in the normal manner, and crystallized from ethanol in orange needles, m.p. 181–182° with dec. (Found: C, 42·0; H, 3·4; N, 17·9. $C_{11}H_{11}ClN_4O_5$ requires: C, 42·0; H, 3·5; N, 17·8%). λ_{max}^{EtOH} 371, 253, 212 mμ (log ε 4.45, 4.17, 4.24). λ_{infl} 282 mμ (log ε 3·96).

Reaction between 2,3-*dihydrofuran* (III), *bromoform, and potassium* t-*butoxide in* t-*butanol*

To a stirred, ice-cold solution of 2,3-dihydrofuran (19·8 g) and bromoform (75·9 g) in dry t-butanol (50 ml) was added a 1·04M solution of potassium t-butoxide in t-butanol (450 ml) over a period of 6 hr. When all the base had been added, the mixture was stirred for a further hr. Water (500 ml) and pentane (500 ml) were added and the layers separated. The organic layer was washed with water (4 × 500 ml), dried ($MgSO_4$), filtered, and evaporated to an oil which, on distillation, gave 2-t-*butoxy*-3-*bromo*-5,6-*dihydro*-2H-*pyran* (XII; 16 g, 21%). b.p. 50–52°/0·2 mm. (Found: C, 46·4; H, 6·5; Br, 33·5. $C_9H_{15}BrO_2$ requires: C, 46·0; H, 6·4; Br, 34·0%). NMR spectrum: 3·8τ, a multiplet, wt 1, assigned to C(4) proton; 4·95τ, a singlet, wt 1, assigned to C(2) proton; 6·25τ, a multiplet, wt 2, assigned to C(6) protons; 7·9τ, a multiplet, wt 2, assigned to C(5) protons; 8·75τ, a singlet, wt 9, assigned to t-butyl protons.

When this experiment was repeated, the cold reaction mixture was shown, by gas chromatography, to contain XII as the latest volatile component and no product with the retention time expected for 6,6-dibromo-2-oxabicyclo[3.1.0]hexane.

Reaction between 6,6-dichloro-2-oxabicyclo[3.1.0]*hexane and potassium* t-*butoxide in* t-*butanol*

To a 6% solution of potassium t-butoxide in t-butanol (3 ml), IV (0·6 g) was added and the resulting solution maintained at room temp. Gas chromatographic analysis indicated that no measurable reaction had occurred after 23 min.

Acknowledgements—Two of us (J. C. A. and D. G. L.) thank the Department of Scientific and Industrial Research for the award of Research Studentships. One of us (D. G. L.) also thanks King's College, Cambridge, for the award of a Senior Studentship.