Heterocycles from Carbohydrate Precursors. Part 41. Mode of Formation of 1,3-Dioxolanes and 1,3-Dioxanes from 1-*C*-Substituted Glycerols during their Benzylidenation[1]

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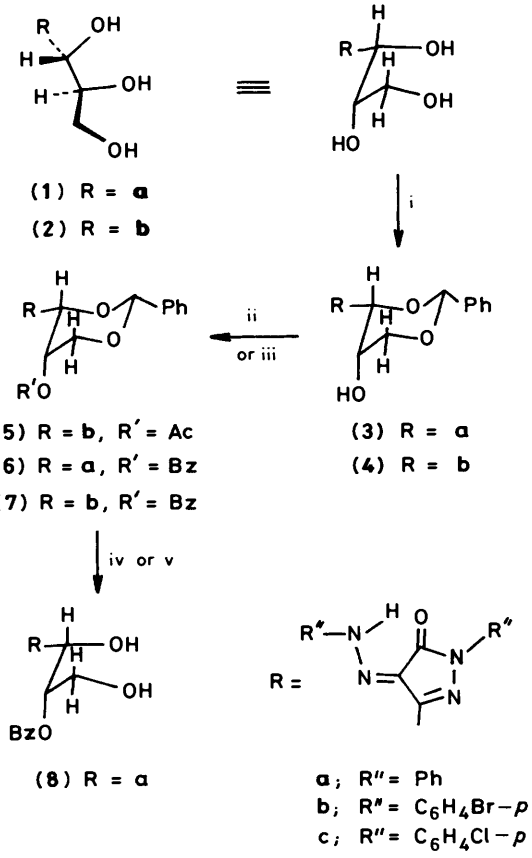
The benzylidenation of 1-*C*-substituted L-*threo*- and D-*erythro*-glycerols has been studied. The correlation of the stereochemical configuration of the glycerolyl part with the formation and location of either the dioxolane or dioxane rings is discussed. The structures have been deduced by a combination of both physical and chemical methods.

The regioselectivity of the isopropylidenation of 1-*C*-substituted L-*threo*- and D-*erythro*-glycerols has been reported.[1,2] It has been found that the structure of the products depend upon the method of their preparation as well as the stereochemical disposition of the hydroxy groups.[1-3] Owing to the synthetic value of the acetals, we describe in this paper the mode of benzylidenation of the 1-*C*-substituted L-*threo* and D-*erythro*-glycerols.

Examination of the structure of 1-*C*-substituted glycerolyls indicated the presence of three possible locations for a



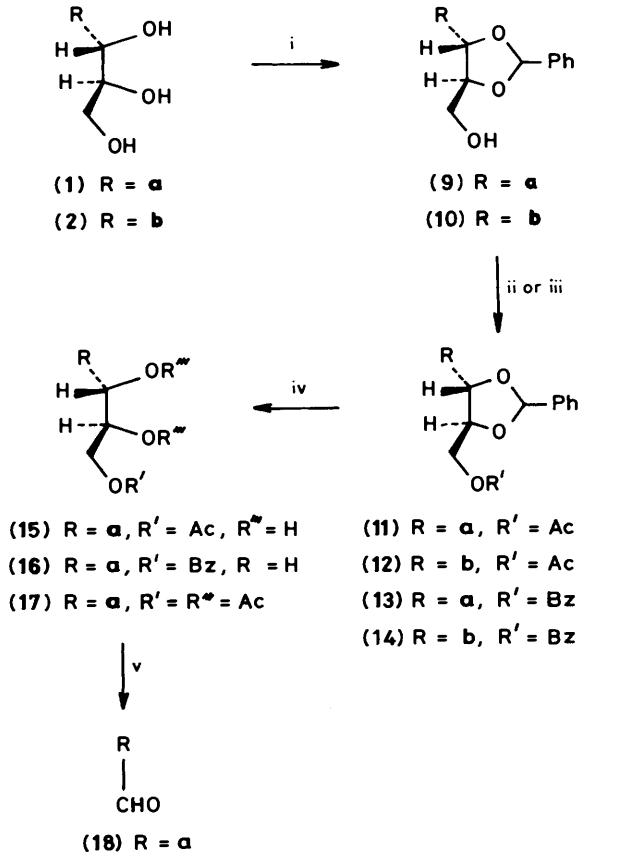
Scheme 1. i, $PhCHO–ZnCl_2$; ii, $Ac_2O–C_5H_5N$; iii, $BzCl–C_5H_5N$; iv, $AcOH–H_2O$; v, $TFA–H_2O$.

benzylidene group to be formed upon benzylidenation; two of them are of the 1,3-dioxolane type and the third is of the 1,3-dioxane type. When the L-*threo*-glycerols (**1**) and (**2**) were treated with benzaldehyde and zinc chloride as a catalyst, it was found that the major isolated product in each case was that having a β-terminal ring[4-6] (dioxane) and the products were formulated as (**3**) and (**4**), respectively. The ^1H n.m.r. spectrum of the crude product from (**1**) indicated that the major product was the dioxane (**3**) in addition to smaller amounts of the dioxolanes possessing α-*threo* and α-terminal rings. On the other hand, an α-terminal ring (dioxolane) as in (**29**) was formed when the D-*erythro* analogue (**28**) was subjected to the same condition. When the reaction was carried out in dimethyl sulphoxide and with sulphuric acid as catalyst the location of the acetal ring was reversed. Thus, the *threo* isomers (**1**) and (**2**) gave compounds (**9**) and (**10**) respectively, possessing α-*threo* rings[4-6] (dioxolanes), whereas the *erythro* analogue (**28**) gave compound (**32**) possessing a β-terminal ring[4-6] (dioxane). The third possible benzylidene acetal from the D-*erythro* glycerol should possess an α-*erythro* ring, but owing to the unfavourable steric disposition of substituents on the ring could not be formed. The α-terminal ring from the L-*threo* analogue could be prepared by constructing the benzylidene ring on a precursor having suitable protection on the 1-hydroxy group as in (**19**) and (**20**), where the hydroxy group is masked intramolecularly as a lactone ring. Thus, compounds (**21**) and (**22**) were prepared and, after deprotection under conditions where the dioxolane ring remained intact gave compounds (**23**) and (**24**) respectively. This rearrangement was promoted by opening of the lactone ring followed by re-heterocyclisation with the nitrogen of the hydrazone on C-3 instead of the oxygen to regenerate the starting precursors (**21**) and (**22**). A similar sequence of reactions on the D-*erythro* analogue of (**19**) afforded the benzylidene compound (**29**).

From the above reaction sequence we concluded that cyclisation of the oxonium ion intermediate, which is formed preferentially from the primary hydroxy group,[3] with the C-1 hydroxy group in the L-*threo* isomer occurred more readily than with the corresponding D-*erythro* isomer. This may arise because hydrogen bonding is possible only in the dioxane product from the L-*threo* isomer, and the conformation of the product influences the probability of its formation[7] in the cyclisation reaction.[3,8,9] However, the presence of the hydroxy group in an axial orientation probably decreased its thermodynamic stability leading to ready transformation to the corresponding product having an α-*threo* ring. However, the 2,3-acetal from the D-*erythro* analogue has unfavourable unsymmetrical substitution on the dioxolane ring, which may result in its transformation into the more stabilised 1,3-dioxane ring, where its bulky substituents are equatorially disposed rather than into the 1,2-acetal where its substituents would be 4,5-*cis*.

The situation is different in the L-*threo* analogue where its 1,2-acetal possesses 4,5-*trans* substituents and a more symmetrical substitution than that in the 2,3-acetal.

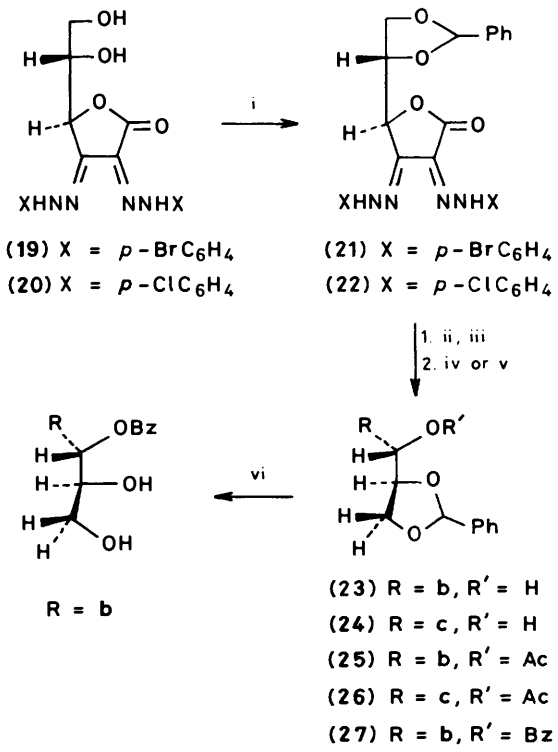
The structure of the various benzylidenes was deduced by a combination of chemical and spectroscopic methods. Acetylation and benzoylation of compounds (**3**) and (**4**) gave the corresponding mono-*O*-acylated derivatives (**5**)—(**7**). Debenzylidenation of compound (**6**) gave the mono-*O*-benzoyl diol (**8**), which since it failed to react with periodate indicated the presence of the two hydroxy groups at the 1,3-positions of the glycerolyl residue; the benzylidene group should, therefore, be located on them. The ^{1}H n.m.r. spectrum of compound (**6**) showed a pronounced downfield shift (δ 4.06 to 5.45) for 2-H upon benzoylation of compound (**3**) whereas the other protons suffered less of a shift. This indicated that the benzoyloxy group was at C-2. The *p*-bromophenyl analogue (**4**) also showed a similar shift for 2-H to that described for compound (**3**). Acetylation and benzoylation of compounds (**9**) and (**10**) afforded the mono-*O*-acylated derivatives (**11**)—(**14**) which showed a pronounced downfield shift for the terminal methylene protons compared with those for the parent hydroxy compounds (**9**) and (**10**); this indicated their attachment to the



Scheme 2. i, PhCHO–H$^+$; ii, Ac_2O–C_5H_5N; iii, BzCl–C_5H_5N; iv, AcOH–H_2O; v, $NaIO_4$

acyloxy group. Comparison of the results with those for the tri-*O*-acylated derivative (**17**) confirmed this. The chemical shifts for the other two methine protons (1-H and 2-H) of the glycerolyl side chains of compounds (**11**)—(**14**) differed little from those of their nonacylated precursors; this indicated that the benzylidene group bridged the two secondary hydroxy groups. Furthermore, debenzylidenation of compound (**11**) with aqueous acetic acid or aqueous trifluoroacetic acid afforded compound (**15**) whose peracetylation gave the tri-*O*-acetyl derivative (**17**); similarly, compound (**13**) gave compound (**16**), whose periodate oxidation gave the aldehyde (**18**).

The structures of compounds (**21**) and (**22**) were confirmed by ^{1}H n.m.r. spectroscopy which showed the 4-H doublet at lower field (δ 5.13—5.17), a result of the lactone carbonyl deshielding effect on it. These results confirm that the compound has a 1,4-lactone ring with the benzylidene group bridging the 5- and 6-hydroxy groups. The two NH signals appeared at δ 10.72—10.75 and 11.80—11.82 indicating their involvement in hydrogen bonding; the latter bond is the stronger as evidenced by its slower disappearance upon deuteriation. Hydrogen bonding between the NH and the lactone carbonyl explains the low value of the lactone carbonyl i.r. absorption.



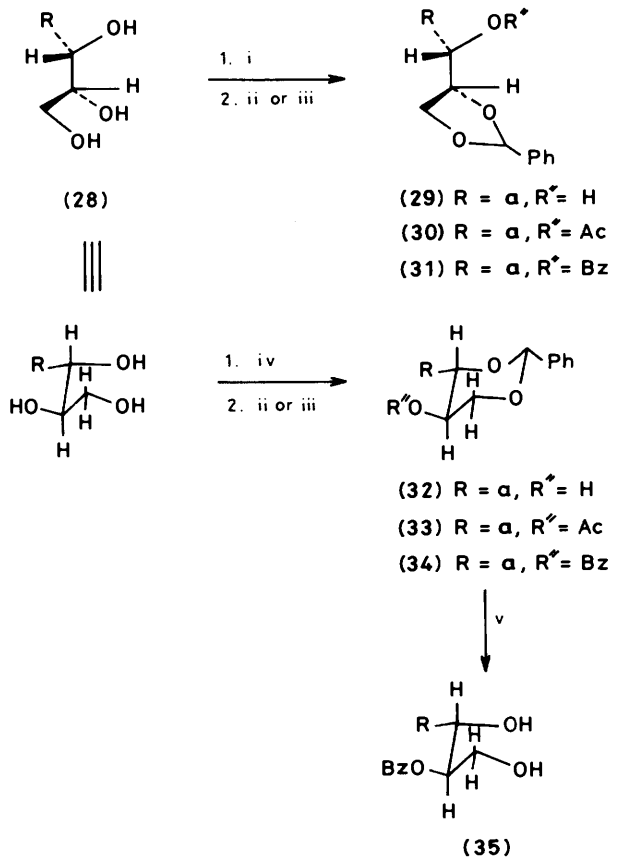
Scheme 3. i, PhCHO–$ZnCl_2$; ii, NaOH; iii, AcOH; iv, Ac_2O–C_5H_5N; v, BzCl–C_5H_5N; vi, AcOH–H_2O.

Rearrangement of the bishydrazones (**21**) and (**22**) into (**23**) and (**24**) respectively, was confirmed by disappearance of lactone carbonyl and NH absorption in the i.r. region and appearance of OCN group absorption.

The position of the benzylidene bridge in compounds (**23**) and (**24**) was based on the mode of the preparation of the latter, it being assumed that there was no migration of the former during the rearrangement. This supposition was confirmed by studying the ^{1}H n.m.r. spectra of their acylated derivatives (**25**)—(**27**) the 1-H shift of which was downfield; this showed that the acyloxy group was at C-1 and, consequently, the benzylidene group bridged the 2- and 3-hydroxy groups. Moreover, acid hydrolysis of compound (**27**) afforded 3-(1-*O*-benzoyl-L-*threo*-glycerol-1-yl)-1-(*p*-bromophenyl)pyrazole-4,5-dione 4-(*p*-bromophenylhydrazone).

The location of the benzylidene group in compounds (**29**) and (**32**) from the D-*erythro* analogue was similarly deduced from the 1-H and 2-H n.m.r. shift which occurred upon acylation.

The comformation of compounds (**32**)—(**34**) were such that



Scheme 4. i, $PhCHO–ZnCl_2$; ii, $Ac_2O–C_5H_5N$; iii, $BzCl–C_5H_5N$; iv, $PhCHO–H^+$; v, $AcOH–H_2O$.

all the substituents were equatorially disposed. Alternative conformations were ruled out for the acylated derivatives on the grounds that $J_{1,2}$ and $J_{2,3}$ are 10.5 Hz, an indication of the presence of triaxially oriented protons. The parent compound (**32**) has a smaller value for $J_{1,2}$ (7.5 Hz) indicating that other conformations may be present.

Experimental

M.p.s were determined on a Meltemp apparatus and are uncorrected. I.r. spectra were recorded with a Unicam SP 1025 spectrophotometer. ^1H N.m.r. spectra were determined with an EM-390 spectrometer using tetramethylsilane (TMS) as the standard and chemical shifts are given on the δ scale. T.l.c. was performed on Bakerflex silica gel 1B-F (2.5—7.5 cm) plates; the solvent was ethyl acetate–hexane (2:3). Microanalyses were performed in the Chemistry Department, Faculty of Science, Cairo University, Cairo, Egypt.

3-(1,3-O-*Benzylidene*-L-threo-*glycerol*-1-*yl*)-1-*phenylpyrazole*-4,5-*dione* 4-*Phenylhydrazone* (**3**).—A mixture of powdered fused zinc chloride (4.0 g) and benzaldehyde (20 ml) was vigorously stirred for 15—20 min; compound (**1**)[10] (2.0 g) was then added, and stirring was continued for 30 min, during which time the latter dissolved. The mixture was poured onto crushed ice (1 kg), and the product was collected and then taken up in methanol and poured onto a fresh portion of crushed ice. This process was repeated and then repeated using crushed ice with light petroleum (b.p. 40—60 °C). The resulting orange product was filtered off, successively washed with water and ethanol, and dried (80%). It was recrystallised from acetone–ethanol to provide orange needles, m.p. 195 °C; R_F 0.6 (Found: C, 67.5; H, 5.0; N, 13.2. $C_{25}H_{22}N_4O_4$ requires C, 67.9; H, 5.0; N, 12.7%); $\nu_{max.}$(KBr) 3 475 (OH), 1 670 (OCN), and 1 600 cm^{-1} (C=N); δ($CDCl_3$) 3.67 (br s, 1 H, OH), 4.06 (m, 1 H, 2-H), 4.3 (m, 2 H, 3-, 3'-H), 5.30 (s, 1 H, 1-H), 5.80 (s, 1 H, PhCH), 7.4 (m, 13 H, ArH), 7.9 (dd, 2 H, *J* 7.5 Hz, *J* < 1 Hz, *o*-H of 1-*N*-phenyl ring), and 13.74 (br s, 1 H, NH); the hydroxy and imino proton singlets disappeared upon deuteriation.

The 2-*O*-benzoate (**6**) crystallised from acetone–ethanol as orange needles, m.p. 158—160 °C (Found: C, 70.1; H, 4.6; N, 10.4. $C_{32}H_{26}N_4O_5$ requires C, 70.3; H, 4.8; N, 10.3%; $\nu_{max.}$(KBr) 1 730 (OBz), 1 670 (OCN), and 1 600 cm^{-1} (C=N); δ($CDCl_3$) 4.5 (m, 2 H, 3-, 3'-H), 5.45 (m, 2 H, 1-, 2-H), 5.87 (s, 1 H, PhCH), 7.35, 7.76, and 8.06 (2 m and d, 20 H, ArH), and 13.75 (br s, 1 H, NH); the latter disappeared upon deuteriation.

3-(1,3-O-*Benzylidene*-L-threo-*glycerol*-1-*yl*)-1-(p-*bromophenyl*)*pyrazole*-4,5-*dione* 4-(p-*Bromophenylhydrazone*) (**4**).—Compound (**2**) (2.0 g) was treated as for compound (**1**) to yield the product (83%) as orange needles (from acetone–ethanol), m.p. 225—226 °C; R_F 0.56 (Found: C, 49.7; H, 3.2; N, 9.5. $C_{25}H_{20}Br_2N_4O_4$ requires C, 50.0; H, 3.4; N, 9.3%); $\nu_{max.}$(KBr) 3 440 (OH), 1 670 (OCN), and 1 590 cm^{-1} (C=N); δ($CDCl_3$) 3.4 (br s, 1 H, OH), 4.03 (m, 1 H, 2-H), 4.3 (m, 2 H, 3-, 3'-H), 5.27 (s, 1 H, 1-H), 5.77 (s, 1 H, PhCH), 7.4 (m, 11 H, ArH), 7.8 (d, 2 H, *J* 9 Hz *o*-H of 1-*N*-phenyl ring), and 13.5 (br s, 1 H, NH); the hydroxy and imino proton singlets disappeared upon deuteriation.

The 2-*O*-acetate (**5**) (78%) has m.p. 215—216 °C (Found: C, 50.3; H, 3.7; N, 8.4; $C_{27}H_{22}Br_2N_4O_5$ requires C, 50.5; H, 3.5; N, 8.7%); $\nu_{max.}$(KBr) 1 740 (OAc), 1 665 (OCN), and 1 590 cm^{-1} (C=N); δ($CDCl_3$) 2.03 (s, 3 H, $COCH_3$), 4.37 (br s, 2 H, 3-, 3'-H), 5.3 (d, 2 H, 1-, 2-H), 5.80 (s, 1 H, PhCH), 7.4 (m, 11 H, ArH), 7.8 (d, 2 H, *J* 7.5 Hz, *o*-H of 1-*N*-*p*-bromophenyl ring) and 13.7 (br s, 1 H, NH); the latter disappeared upon deuteriation.

The 2-*O*-benzoate (**7**) (87%) has m.p. 208—210 °C; R_F 0.69 (Found: C, 54.2; H, 3.4; N, 7.5. $C_{32}H_{24}Br_2N_4O_5$ requires C, 54.5; H, 3.4; N, 7.9%); $\nu_{max.}$(KBr) 1 730 (OBz), 1 670 (OCN), and 1 590 cm^{-1} (C=N); δ($CDCl_3$) 4.35 (m, 2 H, 3-, 3'-H), 5.30 (m, 2 H, 1-, 2-H), 5.73 and 5.83 (2 s, 1 H, PhCH), 7.50 (m, 18 H, ArH), and 13.6 (br s, 1 H, NH); the latter disappeared upon deuteriation.

3-(2-O-*Benzoyl*-L-threo-*glycerol*-1-*yl*)-1-*phenylpyrazole*-4,5-*dione* 4-*Phenylhydrazone* (**8**).—(*a*) A suspension of compound (**6**) (0.5 g) in water (10 ml) and aqueous 75% acetic acid (50 ml) was heated until dissolution was complete and then kept for 24 h at room temperature. The mixture was diluted with cold water and the product (71%) was filtered off, washed repeatedly with water, and dried. It crystallised from ethanol as orange needles, m.p. 160—161 °C (Found: C, 65.3; H, 4.6; N, 12.0. $C_{25}H_{22}N_4O_5$ requires C, 65.5; H, 4.8; N, 12.2%); $\nu_{max.}$(KBr) 3 440 (OH), 1 700 (OBz), 1 660 (OCN), and 1 590 cm^{-1} (C=N); δ($CDCl_3$) 1.67, 3.49 (2 br s, 2 H, 2 OH), 4.09 (d, 2 H, $J_{2,3}$ 6 Hz, 3-, 3'-H), 5.34 (d, 1 H, 1-H), 5.59 (m, 1 H, 2-H), 7.3—7.88 (m, 15 H, ArH), and 13.63 (br s, 1 H, NH); the two hydroxy and imino proton singlets disappeared upon deuteriation.

(*b*) A solution of compound (**6**) (0.5 g) in 90% aqueous trifluoroacetic acid (10 ml) was kept for 15 min at room temperature. The mixture was diluted with cold water and the product (90%) was filtered off, washed repeatedly with water, and dried. It recrystallised from ethanol as orange needles, m.p. 160—161 °C alone or in admixture with the product from (*a*). Both products had identical i.r. and ^1H-n.m.r. spectra.

3-(1,2-O-*Benzylidene*-L-threo-*glycerol*-1-*yl*)-1-*phenylpyrazole*-4,5-*dione* 4-*Phenylhydrazone* (**9**).—A mixture of compound (**1**) (0.5 g), dry benzaldehyde (2.5 ml), and dimethyl sulphoxide (10 ml) containing concentrated sulphuric acid (3

drops) was set aside for 4 days at room temperature with occasional shaking. The reaction mixture was poured onto crushed ice and the mixture was shaken with light petroleum (b.p. 40—60 °C) (100 ml). The product was filtered off, washed with ice–water, light petroleum, and ethanol and dried; it crystallised from acetone–ethanol as orange needles (81%), m.p. 194—195 °C; R_F 0.53 (Found: C, 67.9; H, 4.8; N, 12.7. $C_{25}H_{22}N_4O_4$ requires C, 67.9; H, 5.0; N, 12.7%); $\nu_{max.}$(KBr) 3 460 (OH), 1 670 (OCN), and 1 600 cm^{-1} (C=N); δ($CDCl_3$): 1.8 (br s, 1 H, OH), 3.87 (q, 1 H, $J_{2,3'}$ 4.5 Hz, $J_{3,3'}$ 12 Hz, 3'-H), 4.07 (q, 1 H, $J_{2,3}$ 3 Hz, 3-H), 4.9 (m, 1 H, 2-H), 5.3 (d, 1 H, $J_{1,2}$ 6 Hz, 1-H), 6.17, 6.30 (2 s, 1 H, PhCH), 7.4 (m, 13 H, ArH), 7.95 (dd, 2 H, J 7.5 Hz, J < Hz, *o*-H of *N*-phenyl ring), and 13.80 (br s, 1 H, NH); the hydroxy and imino proton singlets disappeared upon deuteriation.

The 3-*O*-acetate (**11**) (73%) had m.p. 159—161 °C; R_F 0.67 (Found: C, 67.1; H, 5.2; N, 11.5. $C_{27}H_{24}N_4O_5$ requires C, 66.9; H, 5.0; N, 11.6%); $\nu_{max.}$(KBr) 3 080 (NH), 1 755 (OAc), 1 665 (OCN), and 1 600 cm^{-1} (C=N); δ($CDCl_3$) 2.03 (s, 3 H, $COCH_3$), 4.33 (q, 1 H, $J_{2,3'}$ 5.3 Hz, $J_{3,3'}$ 12 Hz, 3'-H), 4.5 (q, 1 H, $J_{2,3}$ 3.7 Hz, 3-H), 5.0 (m, 2 H, 2-H), 5.10 (d, 1 H, $J_{1,2}$ 6 Hz, 1-H), 6.27 (s, 1 H, PhCH), 7.4 (m, 13 H, ArH), 7.95 (dd, 2 H, J 7.5 Hz, J < 1 Hz, *o*-H of the *N*-phenyl ring), and 13.70 (br s, 1 H, NH); the latter disappeared upon deuteriation.

The 3-*O*-benzoate (**13**) had m.p. 185—187 °C (Found: C, 70.1; H, 4.9; N, 10.0. $C_{32}H_{26}N_4O_5$ requires C, 70.3; H, 4.8; N, 10.3%); $\nu_{max.}$(KBr) 3 080 (NH), 1 730 (OBz), 1 665 (OCN), and 1 600 cm^{-1} (C=N); δ($CDCl_3$) 4.70 (d, 2 H, 3-, 3'-H), 5.13 (m, 1 H, 2-H), 5.33 (d, 1 H, $J_{1,2}$ 6 Hz, 1-H), 6.33 (s, 1 H, PhCH), 7.4 and 8.0 (2 m, 20 H, ArH), and 13.80 (br s, 1 H, NH); the latter disappeared upon deuteriation.

3-(1,2-O-*Benzylidene*-L-threo-*glycerol*-1-*yl*)-1-(p-*bromophenyl*)*pyrazole*-4,5-*dione* 4-(p-*Bromophenylhydrazone*) (**10**).—Compound (**2**) (0.5 g) was treated as for compound (**1**) to yield the title compound (**10**) (77%). It crystallised from acetone–ethanol as orange needles, m.p. 124—125 °C (Found: C, 49.7; H, 3.6; N, 9.3; $C_{25}H_{20}Br_2N_4O_4$ requires C, 50.0; H, 3.4; N, 9.3%); $\nu_{max.}$(KBr) 3 440 (OH), 1 670 (OCN), and 1 600 cm^{-1} (C=N); δ($CDCl_3$) 1.70 (br s, 1 H, OH), 3.83 (q, 1 H, $J_{2,3'}$ 5.3 Hz, $J_{3,3'}$ 12 Hz, 3'-H), 4.03 (q, 1 H, $J_{2,3}$ 3.2 Hz, 3-H), 4.85 (m, 1 H, 2-H), 5.27 (d, 1 H, $J_{1,2}$ 6 Hz, 1-H), 6.17 and 6.25 (2 s, 1 H, PhCH), 7.50 and 7.87 (2 s, 13 H, ArH) and 13.60 (br s, 1 H, NH); the latter disappeared upon deuteriation.

The 3-*O*-acetate (**12**) (78%) crystallised from acetone–ethanol as orange needles, m.p. 123—125 °C (Found: C, 50.9; H, 3.3; N, 8.9. $C_{27}H_{22}Br_2N_4O_4$ requires C, 50.5; H, 3.4; N, 8.7%); $\nu_{max.}$(KBr) 1 750 (OAc), 1 670 (OCN), and 1 590 cm^{-1} (C=N); δ($CDCl_3$) 2.18 (s, 3 H, $COCH_3$), 4.33 (2 q, 2 H, 3-, 3'-H), 5.04 (m, 1 H, 2-H), 5.37 (d, 1 H, $J_{1,2}$ 6 Hz, 1-H) 6.14, 6.25 (2 s, 1 H, PhCH), 7.4 (m, 11 H, ArH), 7.8 (dd, 2 H, J 7.5 Hz, J < 1 Hz, *o*-H of the *N*-*p*-bromophenyl ring), and 13.7 (br s, 1 H, NH); the latter disappeared upon deuteriation.

The 3-*O*-benzoate (**14**) (85%) crystallised from acetone–ethanol as orange needles, m.p. 100—101 °C (Found: C, 54.4; H, 3.4; N, 7.7. $C_{32}H_{24}Br_2N_4O_5$ requires C, 54.5; H, 3.4; N, 7.9%); $\nu_{max.}$(KBr) 1 725 (OBz), 1 670 (OCN), and 1 590 cm^{-1} (C=N); δ($CDCl_3$) 3.91 (m, 2 H, 3-, 3'-H), 4.77 (m, 1 H, 2-H), 5.25 (d, 1 H, $J_{1,2}$ 6 Hz, 1-H), 6.17 (s, 1 H, PhCH), 7.4 and 7.8 (2 m, 18 H, aromatic protons) and 13.56 (br s, 1 H, NH); the latter disappeared upon deuteriation.

3-(3-O-*Acetyl*-L-threo-*glycerol*-1-*yl*)-1-*phenylpyrazole*-4,5-*dione* 4-*Phenylhydrazone* (**15**).—(a) Compound (**11**) (0.5 g) was hydrolysed with aqeuous 75% acetic acid as for compound (**8**) and recrystallisation of the product (75%) from ethanol gave the title compound (**15**) as orange needles, m.p. 136—138 °C (Found: C, 60.8; H, 6.2; N, 14.4. $C_{20}H_{20}N_4O_5$ requires C, 60.6; H, 6.1: N, 14.1%); $\nu_{max.}$(KBr) 3 440 (OH), 1 730 (OAc), and 1 665 cm^{-1} (C=N); δ($CDCl_3$–D_2O) 2.07 (s, 3 H, $COCH_3$), 3.9 (m, 1 H, 2-H), 4.33 (m, 2 H, 3-, 3'-H), 4.97 (m, 1 H, 1-H), and 7.4 and 7.88 (2 m, 10 H, ArH).

3-(3-O-*Benzoyl*-L-threo-*glycerol*-1-*yl*)-1-*phenylpyrazole*-4,5-*dione* 4-*Phenylhydrazone* (**16**).—A suspension compound (**13**) (0.5 g) in water (10 ml) was heated with aqueous 75% acetic acid (50 ml) as before. The product (75%) crystallised from ethanol as orange needles, m.p. 155—156 °C, R_F 0.32; identical with an authentic sample.

3-*Formyl*-1-*phenylpyrazole*-4,5-*dione* 4-*Phenylhydrazone* (**18**).—A suspension of compound (**15**) (0.5 g) in distilled water (40 ml) was treated with a solution of sodium metaperiodate (0.3 g) in distilled water (10 ml) and left overnight at room temperature with occasional shaking. The product crystallised from ethanol as yellow–orange needles, m.p. and mixed m.p. 139—140 °C (lit.,[10] m.p. 139—141 °C); it was identical with an authentic sample.

5,6-O-*Benzylidene*-L-threo-2,3-*hexodiulosono*-1,4-*lactone* 2,3-*Bis*(p-*bromophenylhydrazone*) (**21**).—Compound (**19**)[11] (2.0 g) was treated with benzaldehyde (20 ml) and zinc chloride (4.0 g) as for compound (**3**) and recrystallisation of the product (86%) from chloroform–methanol gave the title compound (**21**) as red crystals, m.p. 213—214 °C; R_F 0.6 (Found: C, 49.8; H, 3.6; N, 9.0. $C_{25}H_{20}Br_2N_4O_4$ requires C, 50.0; H, 3.4; N, 9.3%); $\nu_{max.}$(KBr) 3 270 (NH), 1 730 (CO_2), and 1 590 cm^{-1} (C=N); δ($CDCl_3$) 4.3 (m, 3 H, 5-, 6-, 6'-H), 5.13 (d, 1 H, $J_{4,5}$ 3.5 Hz, 4-H), 5.78 and 5.88 (2 s, 1 H, PhCH), 7.2 (m, 13 H, ArH), and 10.75 and 11.82 (2 s, 2 H, 2 NH); the two singlets of the imino proton disappeared upon deuteriation, the former more slowly than the latter.

5,6-O-*Benzylidene*-L-threo-2,3-*hexodiulosono*-1,4-*lactone* 2,3-*Bis*(p-*chlorophenylhydrazone*) (**22**).—Treatment of compound (**20**)[11] with dry benzaldehyde (20 ml) and zinc chloride (4.0 g) as before and recrystallisaton of the product (83%) from chloroform–methanol gave the title compound (**22**) as red crystals, m.p. 217—218 °C; R_F 0.7 (Found: C, 58.8; H, 4.0; Cl, 13.5; N, 10.6. $C_{25}H_{20}Cl_2N_4O_4$ requires C, 58.7; H, 3.9; Cl, 13.8; N, 11.0%); $\nu_{max.}$(KBr) 3 240 (NH), 1 730 (CO_2), and 1 595 cm^{-1} (C=N); δ($CDCl_3$) 4.4 (m, 3 H, 5-, 6-, 6'-H), 5.17 (d, 1 H, $J_{4,5}$ 3.7 Hz, 4-H), 5.73 and 5.83 (2 s, 1 H, PhCH), 7.3 (m, 13 H, ArH), and 10.72 and 11.80 (2 s, 2 H, 2 NH); the two singlets of the imino protons disappeared upon deuteriation, the former more slowly than the latter.

3-(2,3-O-*Benzylidene*-L-threo-*glycerol*-1-*yl*)-1-(p-*bromophenyl*)*pyrazole*-4,5-*dione* 4-(p-*Bromophenylhydrazone*) (**23**).—A solution of compound (**21**) (1.0 g) in acetone (100 ml) was stirred at 70—80 °C with 2M potassium hydroxide solution (200 ml) for 6 h and then kept overnight at room temperature. The resulting solution was cooled to 5 °C, and glacial acetic acid was added to pH 7, the temperature being kept < 10 °C. The product (80%) was collected immediately, washed with water and then cold ethanol, dried, and crystallised from acetone–ethanol to the title compound (**23**) as orange needles, m.p. 94—95 °C; R_F 0.46 (Found: C, 50.2; H, 3.5; N, 9.0. $C_{25}H_{20}Br_2N_4O_4$ requires C, 50.0; H, 3.4; N, 9.3%); $\nu_{max.}$(KBr) 3 420 (OH), 1 665 (OCN), and 1 590 cm^{-1} (C=N); δ($CDCl_3$) 3.2 (br s, 1 H, OH), 4.17 (m, 2 H, 3-, 3'-H), 4.73 (m, 1 H, 2-H), 4.9 (m, 1 H, $J_{1,2}$ 3.7 Hz, 1-H), 5.83 and 6.0 (2 s, 1 H, PhCH), 7.4 (m, 11 H, ArH), 7.78 (d, 2 H, J 8 Hz, *o*-H of *N*-*p*-bromophenyl ring), and 13.5 (br s, 1 H, NH); the hydroxy and imino proton singlet disappeared upon deuteriation.

The 1-*O*-acetate (**25**) (87%) crystallised from ethanol as orange needles, m.p. 85—87 °C (Found: C, 50.7; H, 3.8; N, 8.6.

$C_{27}H_{22}Br_2N_4O_5$ requires C, 50.5; H, 3.5; N, 8.7%); $\nu_{max.}$(KBr) 3 080 (NH), 1 750 (OAc), 1 670 (OCN), and 1 600 cm^{-1} (C=N); $\delta(CDCl_3)$ 2.15 and 2.18 (2 s, 3 H, $COCH_3$), 4.2 (m, 2 H, 3-, 3'-H), 4.8 (m, 1 H, 2-H), 5.80 and 5.95 (2 s, 1 H, PhCH), 6.14 (t, 1 H, $J_{1,2}$ 7.5 Hz, 1-H), 7.2 (m, 11 H, ArH), 7.84 (d, 2 H, *J* 7.5 Hz, *o*-H of the *N*-*p*-bromophenyl ring), and 13.5 (br s, 1 H, NH); the latter singlet disappeared upon deuteriation.

The 1-*O*-benzoate (**27**) (86%) crystallised from acetone–ethanol as orange needles, m.p. 96—97 °C; R_F 0.6 (Found: C, 54.3; H, 3.2; N, 7.7 $C_{32}H_{24}Br_2N_4O_5$ requires C, 54.5; H, 3.4; N, 7.9%); $\nu_{max.}$(KBr) 1 730 (OBz), 1 670 (OCN), and 1 590 cm^{-1} (C=N); $\delta(CDCl_3)$ 4.39 (m, 2 H, 3-, 3'-H), 5.11 (m, 1 H, 2-H), 5.87 and 5.92 (2 s, 1 H, PhCH), 6.39 (m, 1 H, 1-H), 7.59 (m, 11 H, ArH), 8.12 (d, 2 H, *J* 7.5 Hz, *o*-H of the *N*-*p*-bromophenyl ring), and 13.59 (br s, 1 H, NH); the latter singlet disappeared upon deuteriation.

3-(2,3-O-*Benzylidene*-L-threo-*glycerol*-1-*yl*)-1-(p-*chlorophenyl*)*pyrazole*-4,5-*dione* 4-(p-*Chlorophenylhydrazone*) (**24**).—A solution of compound (**22**) (1.0 g) in acetone (100 ml) was treated as for compound (**23**) and the product (75%) was crystallised from acetone–ethanol to give the title compound (**24**) as orange needles, m.p. 84—85 °C; R_F 0.57 (Found: C, 58.5; H, 3.8; N, 11.0. $C_{25}H_{20}Cl_2N_4O_4$ requires C, 58.7; H, 3.9; N, 10.9%); $\nu_{max.}$(KBr) 3 440 (OH), 3 000 (NH), 1 670 (OCN), and 1 600 cm^{-1} (C=N); $\delta(CDCl_3)$ 4.22 (m, 2 H, 3-, 3'-H), 4.75 (m, 1 H, 2-H), 4.9 (m, 1 H, 1-H), 5.77 and 5.84 (2 s, 1 H, PhCH), 7.3 (m, 11 H, ArH), 7.85 (d, 2 H, *J* 8.4 Hz, *o*-H of *N*-*p*-chlorophenyl ring), and 13.54 (br s, 1 H, NH).

The 1-*O*-acetate (**26**) (84%) crystallised from acetone–ethanol as orange needles, m.p. 89—90 °C (Found: C, 58.9; H, 3.8; N, 10.3. $C_{27}H_{22}Cl_2N_4O_5$ requires C, 58.6; H, 4.0; N, 10.1%); $\nu_{max.}$(KBr) 1 750 (OAc), 1 670 (OCN), and 1 590 cm^{-1} (C=N); $\delta(CDCl_3)$ 2.0 and 2.1 (2 s, 3 H, $COCH_3$), 4.24 (m, 2 H, 3-, 3'-H), 4.88 (m, 1 H, 2-H), 5.77 and 5.93 (2 s, 1 H, PhCH), 6.12 (t, 1 H, $J_{1,2}$ 7.5 Hz, 1-H), 7.26 (m, 11 H, ArH), 7.82 (d, 2 H, *J* 9 Hz, *o*-H of the *N*-*p*-bromophenyl ring), and 13.54 (br s, 1 H, NH); the latter singlet disappeared upon deuteriation.

3-(2,3-O-*Benzylidene*-D-erythro-*glycerol*-1-*yl*)-1-*phenylpyrazole*-4,5-*dione* 4-*Phenylhydrazone* (**29**).—Treatment of compound (**28**) with benzaldehyde and zinc chloride as in the preparation of compound (**23**), and recrystallisation of the product (84%) from acetone–ethanol gave the title compound (**29**) as orange needles, m.p. 194—196 °C (lit.,[12] m.p. 196—198 °C); R_F 0.57 (Found: C, 67.9; H, 5.3; N, 12.8. $C_{25}H_{22}N_4O_4$ requires C, 67.9; H, 5.0; N, 12.7%). It has i.r. and ^1H n.m.r. spectra identical with an authentic sample.[12]

The 1-*O*-acetate (**30**) (84%) had m.p. 154—155 °C; R_F 0.7 (Found: C, 66.8; H, 4.9; N, 11.5. $C_{27}H_{24}N_4O_5$ requires C, 66.9; H, 5.0; N, 11.6%); $\nu_{max.}$(KBr) 1 750 (OAc), 1 675 (OCN), and 1 600 cm^{-1} (C=N); $\delta(CDCl_3)$ 2.07 and 2.2 (2 s, 3 H, $COCH_3$), 4.34 (m, 2 H, 3-, 3'-H), 4.9 (m, 1 H, 2-H), 5.8 and 6.0 (2 s, 1 H, PhCH), 6.27 and 6.35 (2 d, 1 H, $J_{1,2}$ 5.3 Hz, 1-H), 7.4 (m, 13 H, ArH), 7.96 (d, 2 H, *J* 7.5 Hz, *o*-H of 1-*N*-phenyl ring), and 13.7 (br s, 1 H, NH); the latter disappeared upon deuteriation.

The 1-*O*-benzoate (**31**) had m.p. 181—183 °C (lit.,[12] m.p. 182—184 °C); R_F 0.77 (Found: C, 70.1; H, 4.5; N, 10.2. $C_{32}H_{26}N_4O_5$ requires C, 70.3; H, 4.8; N, 10.3%). It had i.r. and ^1H-n.m.r. spectra identical with an authentic sample.[12]

3-(1,3-O-*Benzylidene*-D-erythro-*glycerol*-1-*yl*)-1-*phenylpyrazole*-4,5-*dione* 4-*Phenylhydrazone* (**32**).—Reaction of compound (**28**) (0.5 g) with dry benzaldehyde (2.5 ml) in dimethyl sulphoxide (10 ml) containing concentrated sulphuric acid (3 drops) as for compound (**9**) and recrystallisation of the product (89%) from acetone–ethanol gave the title compound (**32**) as orange needles, m.p. 180—182 °C; R_F 0.48 (Found: C, 68.1; H, 4.6; N, 12.5. $C_{25}H_{22}N_4O_4$ requires C, 67.9; H, 5.0; N, 12.7%); $\nu_{max.}$(KBr) 3 450 (OH), 1 670 (OCN), and 1 600 cm^{-1} (C=N); $\delta(CDCl_3)$ 1.6 (br s, 1 H, OH), 3.8 (t, 1 H, $J_{2,3'} = J_{3,3'}$ = 10.5 Hz, 3'-H), 4.5 (m, 2 H, 2-, 3-H), 4.83 (d, 1 H, $J_{1,2}$ 7.5 Hz, 1-H), 5.7 (s, 1 H, PhCH), 7.4 (m, 13 H, ArH), 7.89 (d, 2 H, *J* 7.5 Hz, *o*-H of 1-*N*-phenyl ring), and 13.8 (br s, 1 H, NH); the hydroxy and imino proton singlets disappeared upon deuteriation.

The 2-*O*-acetate (**33**) (88%) had m.p. 243—245 °C; R_F 0.52 (Found: C, 67.3; H, 4.7; N, 11.2. $C_{27}H_{24}N_4O_5$ requires C, 66.9; H, 5.0; N, 11.6%); $\nu_{max.}$(KBr) 3 080 (NH), 1 745 (OAc), 1 665 (OCN), and 1 600 cm^{-1} (C=N); $\delta(CDCl_3)$ 2.0 (s, 3 H, $COCH_3$), 3.78 (t, 1 H, $J_{2,3} = J_{3,3'}$ = 10.5 Hz, 3'-H), 4.54 (q, 1 H, $J_{2,3}$ 5.3 Hz, 3-H), 5.01 (d, 1 H, $J_{1,2}$ 10 Hz, 1-H), 5.70 (s, 1 H, PhCH), 5.75 (m, 1 H, 2-H), 7.33 (m, 13 H, ArH), 7.94 (d, 2 H, *J* 7.5 Hz, *o*-H of 1-*N*-phenyl ring), and 13.75 (br s, 1 H, NH); the latter disappeared upon deuteriation.

The 2-*O*-benzoate (**34**) (83%) had m.p. 220 °C; R_F 0.58 (Found: C, 70.2; H, 4.8; N, 10.0. $C_{32}H_{26}N_4O_5$ requires C, 70.3; H, 4.8; N, 10.3%); $\nu_{max.}$(KBr) 3 080 (NH), 1 725 (OBz), 1 670 (OCN), and 1 600 cm^{-1} (C=N); $\delta(CDCl_3)$ 3.89 (t, 1 H, $J_{2,3'} = J_{3,3'}$ = 10.5 Hz, 3'-H), 4.78 (q, 1 H, $J_{2,3}$ 5.3 Hz, 3-H), 5.0 (d, 1 H, 1-H), 5.75 (s, 1 H, PhCH), 5.90 (m, 1 H, 2-H), 7.45 and 7.90 (m and t, 20 H, ArH), and 13.8 (br s, 1 H, NH); the latter disappeared upon deuteriation.

3-(2-O-*Benzoyl*-D-erythro-*glycerol*-1-*yl*)-1-*phenylpyrazole*-4,5-*dione* 4-*Phenylhydrazone* (**35**).—Hydrolysis of compound (**34**) (0.5 g) with aqueous 75% acetic acid (50 ml), as for compound (**8**) gave the title compound (**35**) (75%). It crystallised from ethanol as orange needles, m.p. 155—156 °C, R_F 0.16 (Found: C, 65.2; H, 4.8; N, 11.8. $C_{25}H_{22}N_4O_5$ requires C, 65.5; H, 4.8; N, 12.2%); $\nu_{max.}$(KBr) 3 440 (OH), 1 710 (OBz), 1 660 (OCN), and 1 600 cm^{-1} (C=N); $\delta(CDCl_3)$ 3.34 (br s, 2 H, 2 OH), 4.12 (d, 2 H, 3-, 3'-H), 5.31 (d, 1 H, 1-H), 5.62 (m, 1 H, 2-H), 7.27 and 7.89 (2 m, 15 H, ArH), and 13.56 (br s, 1 H, NH); the hydroxy and imino proton singlets disappeared upon deuteriation.

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