Heterocycles from Carbohydrate Precursors. Part 40.[1] Kinetic and Thermodynamic Products of Ketalation of 1-*C*-Substituted L-*threo*-Glycerol: A Regioselective Formation of 1,3-Dioxolanes[1]

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The mode of ketalation of some L-*threo*-glycerols has been studied. The kinetic product has an α-terminal (dioxolane) ring. The formation of β (dioxane) ring was also detected. The thermodynamic product has an α-*threo*-(dioxolane) ring. The regioselectivity of the reaction and the structures of the products have been studied.

The acetalation and ketalation of polyol hydroxy groups in order to afford them partial protection[2] is controlled by variable factors[2-11] such as the stereochemical relation of the hydroxy groups,[3] and the reversibility of the reaction.[4] Although the formation of dioxolane rings is almost preferred for ketals, the formation of dioxane rings has been also reported.[12,13] The isopropylidenation[14] of (**1**) under acid-catalysed conditions was reported[15] to give the α-terminal dioxolane (**12**), whose structure was revised[1] to the αT-dioxolane (**4**). In the present work, the details of the isopropylidenation of (**1**) and its analogues have been investigated.

The pattern of the course of acetonation of (**1**), under kinetic and thermodynamic controlled conditions, was found to be considerably different. Thus, as described before[14,15] with sulphuric acid as catalyst and monitoring of the reaction by t.l.c., it was found that two products (R_F 0.5 and 0.6) were formed immediately; the former not only predominated but its proportion increased with time till equilibration was attained. These two products were correctly (see later) believed to have structures (**4**) and (**12**) respectively. When the concentration of the sulphuric acid catalyst was decreased, the ratio of the products was found to be initially in the order (**12**) > (**4**) > (**22**): with time the proportion of (**4**) increased and after equilibration (24 h), (**22**) disappeared. The ratio of (**12**):(**4**) was then similar to that using more concentrated acid. Since, each pathway of the reaction, under such experimental condition, is expected to be reversible and a true equilibrium is established, the composition of the products is quite independent of the mechanism of reaction,[16] determined solely by the relative thermodynamic stabilities of (**12**) and (**4**).

In order to impose a considerable degree of kinetic control[7-10] on the products of the isopropylidenation of (**1**), the reaction pathways should be irreversible whereby the composition of the products will be dependent on the relative speed along the pathways, which are determined by entropy changes and by the stereochemistry of the transition states concerned.[17] This was achieved by the reaction of compound (**1**) with acetone using zinc chloride[18] or copper(II) sulphate as a catalyst. In both cases, initially compound (**12**) was first formed with a smaller amount of (**22**): with time a little of compound (**4**) was also formed. When the reaction mixture was kept overnight, compound (**22**) disappeared from the reaction: this was catalysed by zinc chloride. When compound (**12**) was subjected to acid-catalysed acetonation it rearranged into compound (**4**) and, after equilibration, the composition of the reaction mixture was similar to that for the similar acetonation of (**1**).

In order to explain the above results, the spatial disposition[4,19,20] of the oxygen atoms in the glycerolyl residue and the kinetic and energy changes involved in the formation of the acetal rings must be considered. The formation of compounds (**12**) and (**22**) arose as a result of the greater tendency of the primary hydroxy group[21] to participate in the formation of the hemiketal in the first stage of the reaction. Rapid cyclisation involving the nearest hydroxy group would then afford the first (or kinetic) product. The cyclisation can arise by rotation of C(2)–C(3) bond whereby the oxygen of the hemiketal may be brought in a relative position to C(1)–O or C(2)–O with a distance suitable for cyclisation to give either the terminal dioxolane (α-ring[4]) or dioxane (β-ring) respectively. However, the former cyclisation would be more favourable because one of the two methyl groups in the latter case was in an axial position.[22,23]

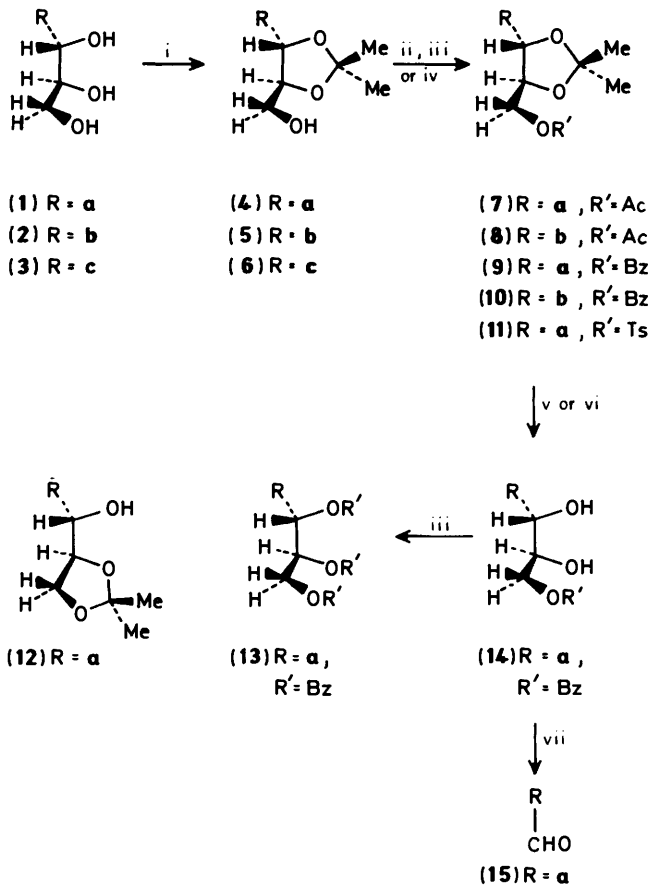
The rearrangement of the terminal α-ring of compound (**12**) to the α-*threo* (αT)-ring[24] of compound (**4**) could be explained as a reversible situation in which protonation of the oxygen atom of the ketal ring in compound (**12**) causes its opening to give an intermediate oxonium ion on C-2; this then undergoes cyclisation with 1–OH to give a dioxolane ring with more symmetrical substitution[19] than the terminal α-ring. Moreover, a driving force for this rearrangement is the presence of substituents on the α T-ring in a *trans* relationship. On the other hand, the terminal rings in the *erythro* analogues do not rearrange, under such condition, to the α-*erythro* (αC) rings because of the presence of substituents on the later ring in a *cis* disposition. However, such unfavourable αC-rings could only be formed when no other type of rings is possible, as in the case of *erythro*-1,2-diphenylethane-1,2-diol.[25]

The locations of the isopropylidene groups in both the thermodynamic and kinetic products were deduced by studying the deshielding effect experienced by the protons of the glycerolyl residues upon acylation. Thus, acetylation, benzoylation, and tosylation of compound (**4**) afforded the corresponding mono-*O*-acylated derivatives (**7**), (**9**), and (**11**) respectively, whose i.r. spectra showed the absence of hydroxy group absorption. The ^{1}H n.m.r. spectral analysis (Table 1) of the mono-*O*-acylated derivatives showed that the chemical shifts of the signals for 3-H (δ 3.9) and 3′-H (δ 3.8) of (**4**) were markedly affected by the acylation and shifted downfield to δ 4.20—4.60; in contrast, the signals of the two methine protons 1-H (δ 4.95—5.17) and 2-H (δ 4.8—5.0) on the glycerolyl side chain suffered no appreciable change. Moreover, comparison of the chemical shifts with that of the tri-*O*-acylated derivative (**13**) confirmed the assignment. This indicated that the ketal ring occupied the two secondary hydroxy groups.

O-Deisopropylidenation of compound (**9**) with aqueous acetic acid or aqueous trifluoroacetic acid afforded 3-(3-*O*-benzoyl-L-*threo*-glycerol-1-yl)-1-phenylpyrazole-4,5-dione 4-phenylhydrazone (**14**), whose i.r. spectrum showed bands at 1 720 cm^{-1} (Bz) and 3 450 cm^{-1} (OH); its ^{1}H n.m.r. spectrum

Table 1. ^{1}H N.m.r. chemical shifts (δ) and coupling constants (in Hz) for the 1,2-isopropylidene derivatives

Compd.	1-H (all d)	2-H (all m)	3-H (all q)	3'-H (all q)	OH (all br s)	Ac (all s)	CMe_2 (all s)	NH (all br s)	Ar	$J_{1,2}$	$J_{2,3}$	$J_{2,3'}$	$J_{3,3'}$
(4)	5.06	4.7	3.90	3.75	1.9		1.57 1.62	13.8	7.3 m 7.9 q	7.5	3.0	4.5	11.5
(5)	5.10	4.7	3.90	3.70	2.0		1.57 1.60	13.6	7.4 m 7.8 q	8.0	3.0	4.5	11.5
(7)	4.95	4.8	4.40	4.20		2.06	1.56 1.62	13.8	7.3 m 7.8 q	7.5	3.8	5.5	12.0
(8)	4.96	4.8	4.43	4.20		2.06	1.55 1.58	13.8	7.4 m 7.9 q	7.5	3.8	4.0	11.5
(9)	5.17	5.0	4.6 m				1.58 1.66	13.9	7.4 m 8.0 m	8.0			
(10)	5.08	4.9	4.6 m				1.56 1.62	13.8	7.4 m 7.9 m	8.0			
(11)	4.96	4.8	4.3 m				1.46 1.53	13.8	7.3 m 7.8 m	7.5			
(13)	6.73	6.3	4.83	4.70				13.6	7.3 m 7.9 m	6.8	3.8	5.3	12.0
(14)	5.06		4.6 m		2.5			13.7	7.3 m 8.6 m				



a; R = 4,5-dioxo-1-phenyl-4-phenylhydrazono-4,5-dihydropyrazolin-3-yl

b; R = 1-(*p*-bromophenyl)-4-(*p*-bromophenylhydrazono)(4,5-dioxo-4,5-dihydropyrazol-3-yl

c; R = 1-(*p*-chlorophenyl)-4-(*p*-chlorophenylhydrazono)-4,5-dioxo-4,5-dihydropyrazol-3-yl

Scheme 1. *Reagents:* i, Me_2CO–H^+; ii, Ac_2O–C_5H_5N; iii, BzCl–C_5H_5N; iv, TsCl–C_5H_5N; v, AcOH–H_2O; vi, CF_3CO_2H–H_2O; vii, $NaIO_4$

showed comparable chemical shifts for monobenzoylated glycerolyl protons. The identity of the compound was further established by its per-*O*-benzoylation to give the corresponding tribenzoate (**13**), and its periodate oxidation to give compound (**15**). Consequently, the isopropylidenation product was assigned the structure 3-(1,2-*O*-isopropylidene-L-*threo*-glycerol-1-yl)-1-phenylpyrazole-4,5-dione 4-phenylhydrazone (**4**) and the acyl derivatives must, therefore, be on C-3.

Extension of the isopropylidenation reaction to the L-*threo*-glycerol-1-yl derivatives (**2**) and (**3**), gave compounds (**5**) and (**6**) respectively. Acetylation and benzoylation of (**5**) afforded the corresponding mono-*O*-acyl derivatives (**8**) and (**10**) respectively.

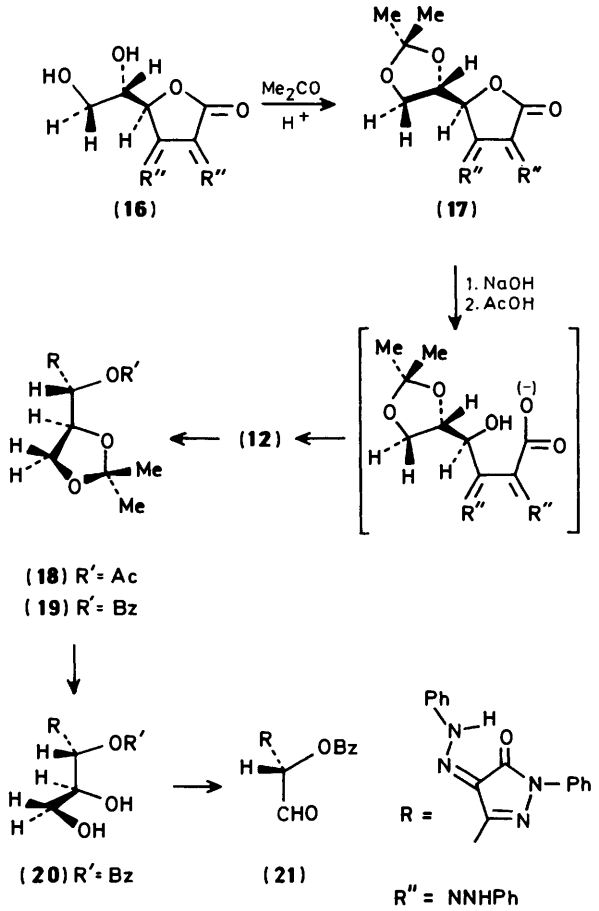
Acetylation and benzoylation of compound (**12**) gave compounds (**18**) and (**19**) respectively the ^{1}H n.m.r. spectra (Table 2) of which showed a downfield shift of the doublet due to 1-H, of the glycerolyl side chain, upon acylation [from δ 4.80 for (**12**) to δ 6.02 for (**18**)]; this indicated that acylation occurred at O-1. Since the C-2 methine proton (δ 4.5) and C-3 methylene protons (δ 4.1) were virtually unchanged, ketalisation had occurred at C-2 and C-3.

The acid hydrolysis of compound (**19**) afforded the 1-*O*-benzoyl derivative (**20**), whose peracylation afforded the tri-*O*-acyl derivative (**13**); its periodate oxidation gave the aldehyde (**21**) and not (**15**) confirming the structure of (**12**). This structure was unequivocally confirmed by its similarity to the product of rearrangement of the 5,6-isopropylidene compound (**17**), the O-1 of which is temporarily protected in a lactone ring and amenable for deprotection by the action of alkali, a condition suitable for the isopropylidene group to have survived, to give (**12**) after neutralisation. The structure of such a rearranged product was based on the mode of its preparation as well as by following the changes in the chemical shifts in the ^{1}H n.m.r. spectra.

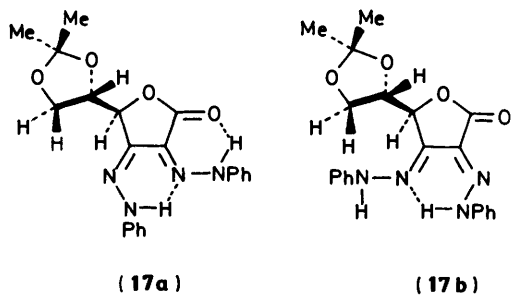
Acetonation of compound (**16**) gave the product (**17**) in two crystalline forms (**17a**) and (**17b**), whose i.r. spectra showed carbonyl lactone absorption at 1 735 and 1 750 cm^{-1}, respectively. The difference may be attributed to differences in the hydrogen bonding between the two hydrazone residues and the carbonyl group. Their ^{1}H n.m.r. spectra were identical, showing the isopropylidene group (δ 1.35 and 1.43), the 6,6'-H (δ 4.2), the 5-H (δ 4.4), the 4-H (δ 5.07), the aromatic protons (δ 7.2) and the 2 NH (δ 10.83 and 11.83). The deshielding effect on 4-H, confirmed that (**17**) is present in a 1,4-lactone ring structure and consequently the isopropylidene ring is on C-5 and C-6.

Table 2. ^{1}H N.m.r. chemical shifts (δ) and coupling constants (in Hz) for the 2,3-isopropylidene derivatives

Compd.	1-H (all d)	2-H (all m)	3-H (all q)	3'-H (all q)	OH (all br s)	Ac (all s)	CMe_2 (all s)	NH (all br s)	Ar	$J_{1,2}$	$J_{2,3}$	$J_{2,3'}$	$J_{3,3'}$
(12)	4.80	4.7	4.18	4.01	3.2		1.40 1.50	13.8	7.3 m 7.9 q	5.0	6.0	7.0	10.5
(18)	6.02	4.8	4.10	3.90		2.18	1.42 1.49	13.7	7.3 m 7.8 q	8.0	6.0	6.0	9.0
(19)	6.36	4.9	4.20	4.10			1.41 1.50	13.8	7.4 m 8.0 m 8.3 m				
(20)	6.43	4.6	3.8 m		2.0			13.7	7.3 m 8.0 m	5.4			

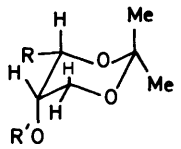


Scheme 2.



Scheme 3.

The structure of compound (**22**) was confirmed by acetylation to give (**23**), whose ^{1}H n.m.r. spectrum indicated that since 2-H experiences a downfield shift, the isopropylidene ring should be on C-1 and C-3.



(**22**) R' = H, R = α from Scheme 1
(**23**) R' = Ac

From the aforementioned data, it can be concluded that isopropylidenation of 1-C-substituted L-*threo*-glycerol under kinetic control gave the corresponding isopropylidene compound possessing an α-terminal dioxalane ring, which is the kinetic product, in addition to a smaller percentage of the isopropylidene compound possessing a dioxane ring. The kinetic product could be rearranged to the more favoured isopropylidene compound possessing an α-*threo* dioxolane ring, which is the major product under the thermodynamic-controlled isopropylidenation, and consequently the derivatives prepared from it should possess an α-*threo* dioxolane ring and not an α-terminal ring.[15]

Experimental

M.p.s were determined using Kofler block or a Meltemp apparatus and are uncorrected. I.r. spectra were recorded on a Unicam SP 200 and SP 1025 spectrophotometers. ^{1}H N.m.r. spectra were measured with Varian XL-100-15, EM-390 and Joel-100 spectrometers (for solutions in $CDCl_3$). Chemical shifts refer to an internal standard of tetramethylsilane (δ 0.00). T.l.c. was performed on pre-coated plastic plates (0.25 mm) of silica gel 60F-254 (E. Merck, Darmstadt, G.F.R.), using the solvent system ethyl acetate–hexane (3:5). Elemental analyses were performed at the microanalytical laboratory, Cairo University.

3-(1,2-O-*Isopropylidene*-L-threo-*glycerol*-1-*yl*)-1-*phenylpyrazole*-4,5-*dione* 4-*Phenylhydrazone* (**4**).—This compound was prepared by the isopropylidenation of compound (**1**) using a similar procedure to that described before;[15] the structure of the isolated product was not, however, (**12**) as previously formulated. T.l.c. of the mixture showed the presence of two products (R_F 0.5 and 0.6). The slower-migrating component (**4**) was the product isolated from the mixture by fractional crystallisation from ethanol. The fast-migrating component was obtained by evaporating the mother liquor and subjecting the

residue to column chromatography; it was eluted with ethyl acetate–hexane (3:5). The eluate enriched with the fast-migrating product (R_F 0.6) was evaporated and the residue recrystallised from ethanol to give orange needles of compound (**12**), m.p. (169—171 °C); identification was from ^{1}H n.m.r. evidence as well as by acetylation of the product to give (**18**).

Rearrangement of 3-(2,3-O-*Isopropylidene*-L-threo-*glycerol*-1-*yl*)-1-*phenylpyrazole*-4,5-*dione* 4-*Phenylhydrazone* (**12**).—A suspension of compound (**12**) (0.5 g) in dry acetone (15 ml) and 96% sulphuric acid (0.5 ml) was stirred for 6 h, and then kept overnight at room temperature. The resulting mixture was neutralised with anhydrous sodium carbonate and then filtered; the filtrate was evaporated to give a viscous syrup which was crystallised from ethanol to give orange needles (80%), m.p. 170—171 °C identified (i.r. and n.m.r.) as compound (**4**).

3-(3-O-*Acetyl*-1,2-O-*isopropylidene*-L-threo-*glycerol*-1-*yl*)-1-*phenylpyrazole*-4,5-*dione* 4-*Phenylhydrazone* (**7**).—A cold solution of compound (**4**) (0.5 g) in dry pyridine (5 ml) was treated with acetic anhydride (5 ml). The mixture was kept overnight at room temperature and then poured onto crushed ice; the product (91%) was filtered off, washed with water, dried, and recrystallised from ethanol to give orange needles, m.p. 154—155 °C (Found: C, 63.3; H, 5.5; N, 13.3. $C_{23}H_{24}N_4O_5$ requires C, 63.3; H, 5.5; N, 12.8%); $\nu_{max.}$(KBr) 3 050 (NH), 1 740 (OAc), and 1 660 cm^{-1} (OCN).

3-(3-O-*Benzoyl*-1,2-O-*isopropylidene*-L-threo-*glycerol*-1-*yl*)-1-*phenylpyrazole*-4,5-*dione* 4-*Phenylhydrazone* (**9**) and 3-(1,2-O-*Isopropylidene*-3-O-*tosyl*-L-threo-*glycerol*-1-*phenylpyrazole*-4,5-*dione* 4-*Phenylhydrazone* (**11**).—These compounds described previously,[15] were incorrectly formulated as derivatives of (**12**) instead of the correct structure (**4**): (**9**), m.p. 153—155 °C; (**11**), m.p. 166—167 °C.

3-(3-O-*Benzoyl*-L-threo-*glycerol*-1-*yl*)-1-*phenylpyrazole*-4,5-*dione* 4-*phenylhydrazone* (**14**).—A suspension of compound (**9**) (0.5 g) in aqueous 90% trifluoroacetic acid (10 ml) was kept for 15 min at room temperature. The mixture was diluted with cold water and the product (90%) was collected, successively washed with water and ethanol, dried, and recrystallised from ethanol to give compound (**14**) as orange needles, m.p. 156—157 °C alone or mixed with the product obtained by the hydrolysis of compound (**9**) with aqueous acetic acid.

Conventional benzoylation of compound (**14**) gave 1-phenyl-3-(1,2,3-tri-*O*-benzoyl-L-*threo*-glycerol-1-yl)pyrazole-4,5-dione 4-phenylhydrazone (**13**),[26] m.p. 154—156 °C.

3-*Formyl*-1-*phenylpyrazole*-4,5-*dione* 4-*Phenylhydrazone* (**15**).—A suspension of compound (**14**) (0.5 g) in distilled water (40 ml) was treated with a solution of sodium metaperiodate (0.3 g) in distilled water (10 ml). The mixture was processed as usual to give compound (**15**) as yellow–orange needles, m.p. 140—141 °C, unchanged on admixture with an authentic sample of compound (**15**) (lit.,[26] m.p. 139—141 °C) (Found: C, 65.5; H, 4.5. Calc. for $C_{16}H_{12}N_4O_2$ C, 65.8; H, 4.1%); $\nu_{max.}$(KBr) 1 705 (CHO) and 1 660 cm^{-1} (OCN).

1-p-*Bromophenyl*-3-(1,2-O-*isopropylidene*-L-threo-*glycerol*-1-*yl*)*pyrazole*-4,5-*dione* 4-p-*Bromophenylhydrazone* (**5**).—This compound was prepared by the isopropylidenation of compound (**2**), as described before,[15] but with revision of the structure to that of (**5**), m.p. 186—188 °C.

1-p-*Chlorophenyl*-3-(1,2-O-*isopropylidene*-L-threo-*glycerol*-1-*yl*)*pyrazole*-4,5-*dione* 4-(p-*Chlorophenylhydrazone*) (**6**).—The procedure was essentially that employed for the preparation of compound (**4**). The product (70%) was recrystallised from ethanol to give compound (**6**) as orange needles, m.p. 179—180 °C (Found: C, 54.7; H, 4.0; N, 12.5. $C_{21}H_{20}Cl_2N_4O_4$ requires C, 54.4; H, 4.4; N, 12.1%); $\nu_{max.}$(KBr) 3 360 (OH), 3 200 (NH), and 1660 cm^{-1} (OCN).

3-(3-O-*Acetyl*-1,2-O-*isopropylidene*-L-threo-*glycerol*-1-*yl*)-1-(p-*bromophenyl*)*pyrazole*-4,5-*dione* 4-p-*Bromophenylhydrazone* (**8**).—Conventional acetylation of compound (**5**) (0.2 g) with acetic anhydride (2 ml) and pyridine (5 ml) and recrystallisation of the product (85%) from ethanol gave compound (**8**) as orange needles, m.p. 170—171 °C (Found: C, 46.8; H, 4.0; N, 9.0. $C_{23}H_{22}Br_2N_4O_5$ requires C, 46.5; H, 3.7; N, 9.4%); $\nu_{max.}$(KBr) 1 740 (OAc) and 1 665 cm^{-1} (OCN).

1-(p-*Bromophenyl*)-3-(3-O-*benzoyl*-1,2-O-*isopropylidene*-L-threo-*glycerol*-1-*yl*)*pyrazole*-4,5-*dione* 4-(p-*Bromophenylhydrazone*) (**10**).—Benzoylation of compound (**5**) (0.2 g) with benzoyl chloride (1 ml) and pyridine (5 ml) and recrystallisation of the product (64%) from ethanol gave compound (**10**) as yellow–orange needles, m.p. 124—126 °C (Found: C, 51.2; H, 4.0. $C_{28}H_{24}Br_2N_4O_5$ requires C, 51.0; H, 3.7%); $\nu_{max.}$(KBr) 1 730 (OBz) and 1 660 cm^{-1} (OCN).

5,6-O-*Isopropylidene*-L-threo-2,3-*hexodiulosono*-1,4-*lactone* 2,3-*Bis*(*phenylhydrazone*) (**17**).—To a stirred suspension of the bis(phenylhydrazone)[14] (**16**) (4.0 g) in cold dry acetone (120 ml) was added 96% sulphuric acid (2 ml) dropwise during 20 min, while the temperature of the reaction mixture was maintained at 5—10 °C. The mixture was kept overnight after which the product (30%) was filtered off and recrystallised from acetone–ethanol to give red-orange needles of compound (**17a**), m.p. 195—196 °C (Found: C, 64.1; H, 5.6; N, 14.2. $C_{21}H_{22}N_4O_4$ requires C, 63.9; H, 5.6; N, 14.2%); $\nu_{max.}$(KBr) 3 200 (NH) and 1 735 cm^{-1} (OCO); δ($CDCl_3$): 1.37 and 1.45 (6 H, 2 s, 2 Me), 4.2 (2 H, m, 6,6′-H), 4.45 (1 H, m, 5-H), 5.07 (1 H, d, $J_{4,5}$ 4.5 Hz, 4-H), 7.2 (10 H, m, ArH), and 10.87 and 11.87 (2 H, 2 s, 2 NH).

The above filtrate was neutralised with anhydrous sodium carbonate and evaporated under reduced pressure to give a syrup which was recrystallised from ethanol to give compound (**17b**) (45%) as red needles, m.p. 185—186 °C (Found: C, 64.4; H, 5.3; N, 14.2. $C_{21}H_{22}N_4O_4$ requires C, 63.9; H, 5.6; N, 14.2%); $\nu_{max.}$(KBr) 3 250 (NH) and 1 750 cm^{-1} (OCO). Both products had identical ^{1}H n.m.r. spectra.

3-(2,3-O-*Isopropylidene*-L-threo-*glycerol*-1-*yl*)-1-*phenylpyrazole*-4,5-*dione* 4-*Phenylhydrazone* (**12**).—A suspension of either the orange or the red form of compound (**17**) (1.0 g) in water (200 ml) was heated with 2M aqueous sodium hydroxide (100 ml) until dissolution was complete. The mixture was cooled to *ca.* 5 °C and neutralised by dropwise addition of acetic acid. The product (85%) was at once filtered off, washed repeatedly with water, dried, and recrystallised from acetone–ethanol to afford orange needles, m.p. 170—171 °C; R_F 0.6 (Found: C, 64.1; H, 5.7; N, 14.0. $C_{21}H_{22}N_4O_4$ requires C, 63.9; H, 5.6; N, 14.2%); $\nu_{max.}$(KBr) 3 475 (OH) and 1 660 cm^{-1} (OCN).

3-(1-O-*Acetyl*-2,3-O-*isopropylidene*-L-threo-*glycerol*-1-*yl*)-1-*phenylpyrazole*-4,5-*dione* 4-*Phenylhydrazone* (**18**).—A cold solution of compound (**12**) (0.5 g) in dry pyridine (5 ml) was acetylated as in the preparation of compound (**7**) and the product (91%) was recrystallised from acetone–ethanol to give compound (**18**) as orange needles, m.p. 140—141 °C (Found: C, 63.1; H, 5.4; N, 12.7. $C_{23}H_{24}N_4O_5$ requires C, 63.3; H, 5.5; N, 12.8%); $\nu_{max.}$(KBr), 1 740 (OAc) and 1 660 cm^{-1} (OCN).

3-(1-O-*Benzoyl*-2,3-O-*isopropylidene*-L-threo-*glycerol*-1-*yl*)-1-*phenylpyrazole*-4,5-*dione* 4-*Phenylhydrazone* (**19**).—A cold

solution of compound (**12**) (2.0 g) in dry pyridine (10 ml) was benzoylated as in the preparation of compound (**11**) and the product (82%) was recrystallised from acetone–ethanol to give compound (**19**) as orange needles, m.p. 158—159 °C (Found: C, 67.7; H, 5.1; N, 11.2. $C_{28}H_{26}N_4O_5$ requires C, 67.5; H, 5.3; N, 11.2%); $\nu_{max.}$(KBr) 1 720 (OBz) and 1 665 cm^{-1} (OCN).

3-(1-O-*Benzoyl*-L-threo-*glycerol*-1-*yl*)-1-*phenylpyrazole*-4,5-*dione* 4-*Phenylhydrazone* (**20**).—The procedure used was essentially that employed for the preparation of compound (**14**), using compound (**19**). The product (80%) was recrystallised from ethanol to give (**20**) as orange needles, m.p. 186—188 °C (Found: C, 65.85; H, 5.0; N, 12.5. $C_{25}H_{22}N_4O_5$ requires C, 65.5; H, 4.8; N, 12.2%); $\nu_{max.}$(KBr), 3 230 (NH), 1 710 (OBz), and 1 660 cm^{-1} (OCN).

(1-*Phenyl*-4,5-*dioxo*-4-*phenylhydrazono*-4,5-*dihydropyrazol*-3-*yl*)-O-*benzoylglycolaldehyde*.—(**21**) A solution of compound (**20**) (0.3 g) in ethanol (100 ml) was treated with a solution of sodium metaperiodate (0.18 g) in distilled water (3 ml) with occasional shaking for 2 h. The mixture was diluted with water and kept overnight at room temperature. The product (34%) was collected, washed with water, dried, and recrystallised from ethanol to afford orange needles, m.p. 158—161 °C (Found: C, 67.7; H, 4.8. $C_{24}H_{18}N_4O_4$ requires C, 67.7; H, 4.3%); $\nu_{max.}$(KBr) 1 715—1 730 (OBz and CHO), and 1 665 cm^{-1} (OCN).

Isopropylidenation of Compound (**1**) *using Kinetic Control*.—(*a*) To a cold solution of zinc chloride (0.1 g) in acetone (40 ml) was added compound (**1**) (0.5 g). The mixture was stirred for 2 h. T.l.c. showed in addition to some starting material, one major product (**12**) (R_F 0.6) and lesser amounts of (**4**) (R_F 0.5) and (**22**) (R_F 0.4). The mixture was kept at room temperature overnight and then neutralised with ammonia and evaporated under reduced pressure. The residue was chromatographed on silica gel. Elution with ethyl acetate–hexane (3:5, v/v) gave compound (**12**) (40%), m.p. 169—171 °C, identified by comparison [^{1}H n.m.r. and giving the acetate (**18**)] with authentic material. The second fraction was chromatographically and spectroscopically identical with compound (**4**) (10%).

(*b*) To a solution of compound (**1**) (1.0 g) in a mixture of *N*,*N*-dimethylformamide (5 ml) and acetone (30 ml) was added anhydrous copper(II) sulphate (3.0 g). The mixture was stirred for 24 h at room temperature. T.l.c. showed in addition to some starting material, one major product (**12**) (R_F 0.6) and small proportions of (**4**) (R_F 0.5) and (**22**) (R_F 0.4). The mixture was filtered and the solid washed with acetone. Solid sodium hydrogen carbonate was added, and the filtrate was evaporated under reduced pressure. The residue was chromatographed on silica gel. Elution with ethyl acetate–hexane (3:5, v/v) gave compound (**12**) (30%), m.p. 170—171 °C identified by comparison (t.l.c. and ^{1}H n.m.r.) with authentic material. The next fractions were enriched with (**4**) (5%) (t.l.c., and ^{1}H n.m.r.). Further elution gave fractions enriched with (**22**), which upon evaporation under reduced pressure gave a residue (10%) whose conventional acetylation with acetic anhydride and pyridine afforded the acetate (**23**) (70%) (Found: C, 64.4; H, 5.4; N, 13.0. $C_{23}H_{24}N_4O_5$ requires C, 63.3; H, 5.5; N, 12.8%); δ($CDCl_3$) 1.60 and 1.63 (6 H, 2 s, 2 Me), 2.00 (3 H, s, OAc), 4.00 and 4.30 (2 H, 2 m, 3′-, 3-H), 5.23 (1 H, m, 2-H), 5.40 (1 H, d, $J_{1,2}$ 2.5 Hz, 1-H), 7.30 and 7.85 (10 H, 2 m, Ar), and 13.7 (1 H, br s, NH).

References

1 Part 39, E. S. H. El Ashry, Y. El Kilany and A. Mousaad, *J. Carbohydr. Chem.*, in press. For preliminary results E. S. H. El Ashry, Y. El Kilany, and F. Singab, XI International Carbohydrate Symposium, 1982, I-57; *Carbohydr. Res.*, 1983, **118**, c10.
2 A. B. Foster in 'Carbohydrate Chemistry and Biochemistry,' W. Pigman and D. Horton (eds.), Academic Press, New York, 1972, vol. 1 A, p. 391.
3 J. A. Mills, *Adv. Carbohydr. Chem.*, 1955, **10**, 1.
4 S. A. Barker and E. J. Bourne, *J. Chem. Soc.*, 1952, 905.
5 A. N. de Belder, *Adv. Carbohydr. Chem.*, 1965, **20**, 219.
6 B. Capon, *Chem. Rev.*, 1969, **69**, 407.
7 R. F. Brady, Jr., *Adv. Carbohydr. Chem. Biochem.*, 1971, **26**, 197.
8 A. N. de Belder, *Adv. Carbohydr. Chem. Biochem.*, 1977, **34**, 179.
9 D. M. Clode, *Chem. Rev.*, 1979, **79**, 491.
10 J. Gelas and D. Horton, *Heterocycles*, 1981, **16**, 1587.
11 E. S. H. El Ashry, *J. Chem. Soc., Chem. Commun.*, 1986, 1024.
12 K. W. Buck, A. B. Foster, R. H. Rees, J. M. Webber, and J. Lehmann, *Carbohydr. Res.*, 1965, **1**, 329.
13 J. G. Buchanan, S. J. Moorhouse, and R. H. Wightman, *J. Chem. Soc. Perkin Trans. 1*, 1981, 2258; J. G. Buchanan, M. E. Chacon Fuertes, A. R. Edgar, S. J. Moorhouse, D. I. Rawson, and R. H. Wightman, *Tetrahedron Lett.*, 1980, **21**, 1795.
14 H. Ohle, *Chem. Ber.*, 1934, **67**, 1750.
15 E. S. H. El Ashry, Y. El Kilany, and F. Singab, *Carbohydr. Res.*, 1980, **82**, 25.
16 R. H. De Wolfe, K. M. Ivanetich, and N. F. Perry, *J. Org. Chem.*, 1969, **34**, 848; P. M. Collins, *Tetrahedron*, 1965, **21**, 1809; E. H. Cordes and H. G. Bull, *Chem. Rev.*, 1974, **74**, 581.
17 J. A. Mills, *Chem. Ind.* (*London*), 1954, 633.
18 S. H. Dorcheus and D. G. Williams, *J. Org. Chem.*, 1963, **28**, 775; E. D. Hughes, *Q. Rev. Chem. Soc.*, 1948, **2**, 107.
19 S. A. Barker, E. J. Bourne, and D. H. Whiffen, *J. Chem. Soc.*, 1952, 3865.
20 S. J. Angyal and R. J. Beveridge, *Carbohydr. Res.*, 1978, **65**, 229; S. J. Angyal, D. Greeves, and J. A. Mills, *Aust. J. Chem.*, 1974, **27**, 1447; P. L. Durette and D. Horton, *Adv. Carbohydr. Chem. Biochem.*, 1971, **26**, 49.
21 A. H. Haines, *Adv. Carbohydr. Chem. Biochem.*, 1976, **33**, 11.
22 H. C. Brown, J. H. Brewster, and H. Checter, *J. Am. Chem. Soc.*, 1954, **76**, 467.
23 J. C. McCoubrey and A. R. Ubbelohde, *Q. Rev. Chem. Soc.*, 1951, **5**, 364.
24 L. Hough in a footnote in ref. 12 suggested that α-*threo* be used instead of the equivalent symbol αT of Barker and Bourne's terminology in ref. 4.
25 P. H. Hermans, *Z. Phys. Chem.*, 1924, **113**, 337.
26 H. El Khadem and E. S. H. El Ashry, *J. Chem. Soc.*, 1968, 2248.

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