

## ON RIBOSYLATION AND MOLECULAR STRUCTURE OF GLYOXYLIC ACID SEMICARBAZONE DERIVATIVES\*

P.FIEDLER, H.HŘEBABECKÝ and J.BERÁNEK

*Institute of Organic Chemistry and Biochemistry,  
Czechoslovak Academy of Sciences, 166 10 Prague 6*

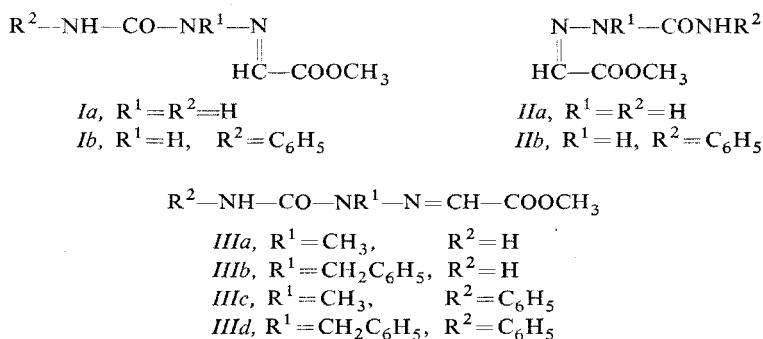
Received January 7th, 1975

Ribosylation of the mercury, silver or lithium salt of the semicarbazone *Ia* results in formation of a mixture of isomeric ribosyl derivatives *IV*, *VIa*, and *VIIa*. Ribosylation of 2-alkylsemicarbazones *IIIa* (*IIIb*) affords a mixture of the anomers *VIIb* and *VIIc* (*VIIc* and *VIIc*). Compound *V* is obtained from the 4-phenylsemicarbazone *Ib*. Isomerism of both amidic bonds and the N—N, C=N, and CH—CO bonds of the thus-obtained semicarbazones has been examined. On the basis of IR spectra, the 4-substituted derivatives were shown to display *trans* conformation on the N<sub>(4)</sub>—C<sub>(3)</sub> amidic bond while with all 2-unsubstituted substances, the conformation on the C<sub>(3)</sub>—N<sub>(2)</sub> bond was *cis*. Both in solutions and in the solid state, the (*Z*)-isomers on the C=N bond display a practically planar structure with an intramolecular hydrogen bond between the N<sub>(2)</sub>—H group and the ester carbonyl group. This observation unequivocally confirms the *s-trans* conformation on the N—N bond and the *s-cis* conformation on the CH—CO bond. The β and α anomers *VI* and *VII* (series *a*, *b*, *c*) can be distinguished by means of NMR, CD, and IR spectra.

In the preceding paper<sup>1</sup>, the isomerisation and alkylation of methyl glyoxylate semicarbazone has been examined. The resulting alkyl derivatives have been studied with respect to the influence of substituents on the course of the cyclisation leading to 6-azauracil derivatives. This reaction has also been investigated as model reaction for some glycosylations which are dealt with in this and the subsequent paper<sup>2</sup>. In the present paper, we wish to report on ribosylations of metal salts of the methyl glyoxylate semicarbazone *Ia*, 2-methylsemicarbazone *IIIa*, 2-benzylsemicarbazone *IIIb*, and 4-phenylsemicarbazone *Ib* and on examinations of the molecular structure of the thus-obtained substances. While the alkylation of methyl glyoxylate semicarbazone occurs exclusively at position 2, the condensation of various salts of the unsubstituted semicarbazone *Ia* results in a mixture of isomeric products ribosylated both at position 2 and 4. The present paper also reports on separation of the particular isomers and determination of their structure by means of physicochemical methods (IR, NMR, and CD spectra).

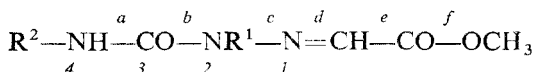
\* Part II in the series Analogues of Nucleosides; Part I: This Journal 40, 2364 (1975).

Condensation of the mercury, silver, and lithium salt of the semicarbazone *Ia* with 2,3,5-tri-*O*-benzoyl-*D*-ribofuranosyl bromide affords mixtures of isomeric ribosylsemicarbazones. By means of column chromatography on silica gel, the mixture was separated into three isomers which were assigned the isomeric structures *IV*, *Via*, and *VIIa* on the basis of spectral measurements. The chromatographically fastest isomer *Via* and the less mobile isomer *VIIa* represent the anomeric 4-ribosylsemicarbazones. The least chromatographically mobile isomer *IV* is identical with methyl glyoxylate 2-(2,3,5-tri-*O*-benzoyl- $\beta$ -*D*-ribofuranosyl)semicarbazone as prepared by the silylation method<sup>2</sup>. As it may be seen from Table I, the ratio of particular isomers in the reaction mixture is dependent on the metal in the salt.



Condensation of the 4-phenylsemicarbazone *Ib* mercuric salt with 2,3,5-tri-*O*-benzoyl-*D*-ribofuranosyl bromide affords the 4-phenyl-2-ribosylsemicarbazone *V*. The sodium salts of the 2-alkylsemicarbazones *IIIa* and *IIIb* cannot be prepared<sup>1</sup> in contrast to the corresponding mercuric salts. Condensation of these mercuric salts with 2,3,5-tri-*O*-benzoyl-*D*-ribofuranosyl bromide affords mixtures of  $\alpha$  and  $\beta$  anomers of the 2-alkyl-4-ribofuranosylsemicarbazones *VIb*, *VIIb* and *VIc*, *VIIc* which may be separated by column chromatography on silica gel. Approximately identical amounts of the two anomeric 4-ribofuranosyl derivatives *VIb*, *VIIb* are formed from the 2-methylsemicarbazone *IIIa*. In ribosylation of the 2-benzylsemicarbazone *IIIb*, the  $\alpha$ -anomer *VIIc* is obtained as the main product.

The molecular structure of semicarbazones of 1,2-dicarbonyl compounds has not been hitherto investigated. An attempt is therefore made in the present paper to assign on the basis of chemical and physicochemical properties particular spatial arrangements to 2- and 4-substituted methyl glyoxylate semicarbazones (for their preparation see this and the preceding paper<sup>1</sup>).



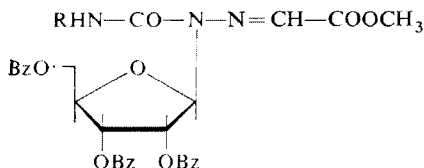
Without taking into consideration the conformational isomerism on the N-substituent and O-methyl bonds, there are six bonds (*a* to *f*) in the molecule of the  $N_{(4)}$ -monosubstituted methyl glyoxylate semicarbazone on which spatial isomerism may be involved.

*a*, the  $C_{(3)}-N_{(4)}$  amidic bond with potential *cis-trans* isomerism. This bond is fixed in the *trans* conformation by the presence of a bulky substituent, *e.g.*, a phenyl group, on the  $N_{(4)}$  nitrogen atom.

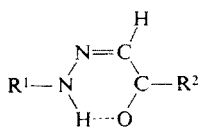
*b*, the  $C_{(3)}-N_{(2)}$  amidic bond; both amidic bonds form an urea system. The N,N'-dialkylureas occur in the *trans-trans* form only. The presence of the *trans-cis* isomer has not been hitherto established even in trace amount<sup>3-6</sup>. In semicarbazones, the situation is somewhat different. Probably due to repulsion of lone electron pairs on the carbonyl oxygen atom and the  $N_{(1)}$  nitrogen atom, the *cis* conformation on the  $C_{(3)}-N_{(2)}$  bond is highly favoured. In the case of  $N_{(4)},N_{(4)}$ -diethylsemicarbazones of aromatic aldehydes, the 2,3-*cis* isomer<sup>7</sup> of some derivatives moderately predominates over the *trans* isomer. A similar situation may be observed with N-acylhydrazones<sup>7,8</sup>.

*c*, the  $N_{(2)}-N_{(1)}$  bond with potential *s-trans* and *gauche* isomerism. Neither the *s-cis* isomer (under the assumption of a *cis* conformation on the  $C_{(3)}-N_{(2)}$  bond, *vide infra*) nor the complete rotation about the N—N bond are possible for steric reasons. None of the existing papers on the structure of semicarbazones deals with the potential isomerism on the N—N bond; the crystal structure of semicarbazones has not been hitherto examined. With N,N'-disubstituted hydrazine derivatives with pyramidal and trigonal hybridisation of nitrogen atoms (symmetrically disubstituted hydrazines<sup>9</sup>, azines<sup>10</sup>), the *gauche* form usually predominates; in this form, the planes of the two parts of the molecule are situated in an angle of 60–90°. The relations on the  $C_6H_5-N=C$  bond, *e.g.*, in benzalanilines, are similar<sup>11</sup>. With methyl glyoxylate semicarbazones, the existence of a nonplanar structure cannot be consequently *a priori* excluded. Raevskij and co-workers<sup>12</sup> examined conjugation between the amidic carbonyl group and the  $N=C$  bond in semicarbazones and thiosemicarbazones by means of the  $\nu(C=N)$  line intensity in Raman spectrum. Owing to the observed conjugation, an approximately planar structure has been ascribed<sup>12</sup> to thiosemicarbazones. This structure has also been confirmed by X-ray determinations of thiosemicarbazones<sup>13,14</sup>. With semicarbazones, the conjugation is much lower<sup>12</sup>. On the other hand, with (*Z*)-isomers of semicarbazones of  $\alpha$ -dicarbonyl compounds, the planar *s-trans* conformation on the N—N bond may be stabilised by intramolecular hydrogen bonds (conjugate chelation, formula VIII). Such a chelation is known in the case of the related phenylhydrazones of  $\alpha$ -dicarbonyl compounds<sup>15-20</sup>.

*d*,  $C=N$  bond. With 2-unsubstituted semicarbazones, the (*Z*)-isomer may form intramolecular hydrogen bonds (VIII); both the (*Z*)- and (*E*)-isomers may be isolated in contrast to semicarbazones of monocarbonyl compounds. The exclusive ability of the (*Z*)-isomers to cyclise with the formation of 6-azauracil derivatives makes possible the unequivocal determination of the



IV, R = H  
V, R =  $C_6H_5$



VIII

TABLE I  
Yields (%) of Isomeric Methyl Glyoxylate Ribofuranosylsemicarbazones

| Method                        | <i>IV</i> | <i>VIa</i> | <i>VIIa</i> |
|-------------------------------|-----------|------------|-------------|
| Mercuric salt                 | 14.5      | 2.5        | 11          |
| Silver salt                   | 3.5       | 21         | 2.5         |
| Lithium salt                  | 4         | 2.5        | 32          |
| Silyl derivative <sup>a</sup> | 31        | 0          | 0           |

<sup>a</sup> Ref. <sup>2</sup>.

TABLE II  
Chemical Shifts ( $\delta$  scale) of Sugar Protons in Methyl Glyoxylate Semicarbazone Ribosyl Derivatives

Chemical shifts expressed in p. p. m.; tetramethylsilane as internal standard. The spectra were measured in deuteriochloroform.

| Compound    | H <sub>1'</sub> | H <sub>2'</sub> | H <sub>3'</sub> | H <sub>4'</sub> | H <sub>5a'</sub> | H <sub>5b'</sub> |
|-------------|-----------------|-----------------|-----------------|-----------------|------------------|------------------|
| <i>IV</i>   | —               | m 5.90—6.40     | —               | —               | m 4.50—4.90      | —                |
| <i>V</i>    | —               | m 6.10—6.45     | —               | —               | m 4.55—4.90      | —                |
| <i>VIa</i>  | —               | m 5.70—6.10     | —               | —               | m 4.55—4.70      | —                |
| <i>VIb</i>  | —               | m 5.70—6.10     | —               | —               | m 4.50—4.70      | —                |
| <i>VIc</i>  | —               | m 5.70—6.15     | —               | —               | m 4.55—4.75      | —                |
| <i>VIIa</i> | d 6.26          | dd 5.40         | dd 4.94         | pentet 3.87     | dd 4.26          | dd 4.49          |
| <i>VIIb</i> | d 6.36          | dd 5.50         | dd 4.99         | pentet 3.94     | dd 4.34          | dd 4.55          |
| <i>VIIc</i> | d 6.40          | dd 5.54         | dd 5.05         | pentet 4.01     | dd 4.35          | dd 4.59          |

TABLE III  
Coupling Constants (H<sub>2</sub>) of  $\alpha$ -Ribofuranosyl Derivatives of Methyl Glyoxylate Semicarbazones

| Compound    | $J_{1'2'}$ | $J_{2'3'}$ | $J_{3'4'}$ | $J_{4'5a'}$ | $J_{4'5b'}$ | $J_{5a'5b'}$ |
|-------------|------------|------------|------------|-------------|-------------|--------------|
| <i>VIIa</i> | 4.2        | 5.5        | 9.0        | 4.5         | 3.5         | 12.0         |
| <i>VIIb</i> | 4.0        | 5.5        | 9.1        | 4.5         | 3.3         | 12.2         |
| <i>VIIc</i> | 4.0        | 5.5        | 9.0        | 4.8         | 3.5         | 12.0         |

configuration on the C=N bond. The hitherto reported cyclisations of methyl glyoxylate (*E*)-semicarbazones must be preceded by isomerisation to the (*Z*)-isomer<sup>1</sup>. The isomerisation does not occur under conditions of IR spectral measurements.

*e*, N=C—C=O bond with potential *s-cis-s-trans* or gauche isomerism. Methyl and ethyl esters of the simplest  $\alpha,\beta$ -unsaturated carboxylic acids occur as mixtures of the more stable *s-trans* isomers and "non-*s-trans*" isomers, probably *s-cis* isomers<sup>21,22</sup>. A similar situation may be expected with the (*E*)-isomers of methyl glyoxylate semicarbazone *Ia* and *Ib*. On the other hand with (*Z*)-isomers of compounds *IIa* and *IIb*, the stability of the *s-cis* conformation of bond *e* may be enhanced by the formation of intramolecular hydrogen bonds between the N<sub>(2)</sub>-H and C=O groups (*cf.* formula *VIII*). With the related glyoxal phenylhydrazone, the somewhat higher stability of the *s-cis* conformation of the (*Z*)-isomer possessing an intramolecular hydrogen bond is also indicated by energy calculation of the particular conformers by the extended Hückel method<sup>23</sup>. As inferred from IR (refs<sup>15,20</sup>) and NMR (refs<sup>18,19</sup>) spectral measurements, these hydrogen bonds are very weak with phenylhydrazones of  $\alpha$ -dicarbonyl compounds, the chelate cycle is not stabilised by resonance. The strength of these hydrogen bonds is much lower with phenylhydrazones of  $\alpha$ -keto esters than with phenylhydrazones of  $\alpha$ -diketones<sup>19</sup>. In the case of phenylhydrazones and also semicarbazones of  $\alpha$ -keto esters, an intramolecular hydrogen bond involving the ethereal oxygen atom is theoretically possible; such a bond which would not affect the generally more favourable transoid conformation of the N=C—C=O system, has not been hitherto observed.

*f*, O=C—O—CH<sub>3</sub> bond. Only the (*Z*)-conformer (C=O and O—CH<sub>3</sub> bonds are *cis*) has been observed with all hitherto investigated methyl esters of carboxylic acids<sup>24-28</sup>. The same conformation is also assumed with methyl esters of  $\alpha,\beta$ -unsaturated carboxylic acids<sup>21,22</sup>. The isomerism on this bond is not of importance in determinations of the whole structure of the present semicarbazones and has been mentioned for the sake of completeness only.

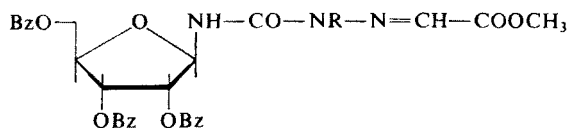
The IR (refs<sup>7,8,29-33</sup>) and NMR spectra (refs<sup>34,35</sup>) of various semicarbazones have been examined except for semicarbazones of  $\alpha$ -keto esters. The IR spectra of the present semicarbazones are shown in Tables IV—VIII. The low solubility of numerous substances did not permit the measurement of NMR spectra in nonpolar solvents.

On the basis of IR spectra, the conformation on both amidic bonds of the present semicarbazones has been determined. In chloroform solutions, the stretching vibration of the N<sub>(2)</sub>-H bond in (*E*)-isomers of 2-unsubstituted compounds *Ia*, *Ib*, *VIa*, and *VIIa* is situated in the range of 3342 to 3346 cm<sup>-1</sup>. In the same solvent, the IR spectra of the N<sub>(4)</sub>,N<sub>(4)</sub>-diethylsemicarbazones of aromatic aldehydes have been examined by Hadži and Jan<sup>7</sup> (the (*E*)-configuration on the C=N bond has been assumed in the case of these compounds) and found to exhibit two N<sub>(2)</sub>-H bands at 3335 cm<sup>-1</sup> and 3383 cm<sup>-1</sup> approximately of the same intensity; these bands have been ascribed to the *cis* and *trans* isomer on the N<sub>(2)</sub>-C<sub>(3)</sub> amidic bond. In our case, the *cis* isomer deeply predominates since a single band is observed with compounds *Ia*, *Ib*, *VIa*, and *VIIa*. Furthermore, all the three (*E*)-isomers of 4-substituted semicarbazones exhibit an additional very broad band of the intermolecularly bonded N<sub>(2)</sub>-H group centered at about 3020 cm<sup>-1</sup> and of the halfwidth between 200 and 300 cm<sup>-1</sup>; this band does not disappear in tetrachloromethane solution even at concentrations

of  $3 \cdot 10^{-4}$  M. Similar bands have been observed with lactams, *e.g.*, 2-pyridinone<sup>36</sup>, which form stable dimers. This finding confirms the *cis* conformation of the  $N_{(2)}-C_{(3)}$  amide bond of the (*E*)-isomers *Ib*, *Vla*, and *VIIa*. The formation of *cis* dimers has also been encountered with semicarbazones of aldehydes and ketones<sup>31</sup>. The (*Z*)-isomers of 2-unsubstituted semicarbazones *IIa* and *IIb* also exhibit a single band at  $3290$  to  $3297$   $\text{cm}^{-1}$  due to the intramolecularly bonded  $N_{(2)}-H$  group. The presence of an at least trace amount of the other isomer on the  $N_{(2)}-C_{(3)}$  amidic bond has not been detected by IR spectrum. Since the (*Z*)-isomers in contrast to the (*E*)-isomers are readily cyclised to 1,2,4-triazine-3,5-diones, it may be inferred that the single  $\nu(N_{(2)}-H)$  band present in IR spectrum corresponds to the *cis* conformation on the  $N_{(2)}-C_{(3)}$  bond. With 2-substituted semicarbazones, the  $\text{CO-NR}^1$ -*cis* conformation on the amidic 2,3-bond is sterically more advantageous than the *trans* conformation.

When the 2,3-amidic bond of 4-phenyl- and 4-(tribenzoylribofuranosyl)-semicarbazones is *cis*, only the *trans* conformation of the 3,4-amidic bond may be expected. Only in this conformation, the phenyl residue can be coplanar with the urea portion of the semicarbazone molecule. When compared with acetanilide<sup>37</sup>, the  $\nu(N_{(4)}-H)$  bands of glyoxylic acid 4-phenylsemicarbazones are considerably shifted to lower wavenumbers, *e.g.*, to  $3390$   $\text{cm}^{-1}$  in chloroform solutions. The  $N_{(4)}-H$  group of semicarbazones is obviously influenced by the neighbourhood of the lone electron pair on the  $N_{(1)}$  nitrogen atom.

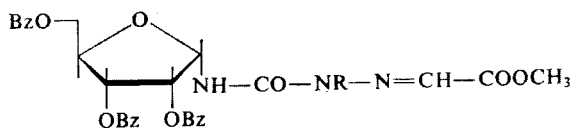
In condensations of metal salts of methyl glyoxylate semicarbazone and 2-alkylsemicarbazones with 2,3,5-tri-*O*-benzoyl-*D*-ribofuranosyl bromide, the resulting



*Vla*, R = H, (*E*)-isomer

*VIIb*, R = CH<sub>3</sub>

*VIIc*, R = CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>



*VIIIa*, R = H, (*E*)-isomer

*VIIIb*, R = CH<sub>3</sub>

*VIIIc*, R = CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>

TABLE IV  
IR Spectra of  $H_2NCONH-N=CHCOOCH_3$  ( $cm^{-1}$ )

| Band                           | Ia                             |                                |                      | Ia-d <sub>3</sub>                            |                                |  | IIa                  |  |                      | IIa-d <sub>3</sub>                         |  |  |
|--------------------------------|--------------------------------|--------------------------------|----------------------|--|--------------------------------|--|----------------------|--|----------------------|--|--|--|
|                                | CHCl <sub>3</sub> <sup>a</sup> | CDCl <sub>3</sub> <sup>b</sup> | KBr                  | CDCl <sub>3</sub> <sup>b</sup>               | fluorube<br>nujol <sup>c</sup> | CDCl <sub>3</sub> <sup>d</sup>             | KBr                  | CDCl <sub>3</sub> <sup>d</sup>             | KBr                  | CDCl <sub>3</sub> <sup>e</sup>             | CDCl <sub>3</sub> <sup>e</sup>             |  |
| $\nu_a(NH_2)$ , $\nu_a(ND_2)$  | 3 535w                         | 3 535vw                        | 3 423s               | { 2 653w <sup>a</sup><br>2 640w <sup>a</sup> | 2 564s                         | 3 539s <sup>f</sup>                        | 3 427m               | 3 539s <sup>f</sup>                        | 3 427m               | 2 654m <sup>g</sup>                        | 2 654m <sup>g</sup>                        |  |
| $\nu_s(NH_2)$ , $\nu_s(ND_2)$  | —                              | —                              | 3 300m, sh           | —  | —                              | —  | 3 307w, sh           | —  | 3 307w, sh           | —  | —  |  |
| $\nu(NH)$ , $\nu(ND)$          | 3 416w<br>3 346w               | 3 417vw<br>3 347vw             | 3 227m, br<br>3 253m | 2 488w <sup>a</sup><br>2 488w <sup>a</sup>   | 2 383s<br>2 406s               | 3 420m <sup>f</sup><br>3 297m <sup>f</sup> | 3 223m<br>3 275m     | 3 420m <sup>f</sup><br>3 297m <sup>f</sup> | 3 223m<br>3 275m     | 2 489s <sup>g</sup><br>2 442w <sup>g</sup> | 2 489s <sup>g</sup><br>2 442w <sup>g</sup> |  |
| $\nu(CO)$ of ester<br>amide-I  | h                              | h                              | —                    | h  | —                              | —  | 1 723w, sh           | —  | 1 723w, sh           | —  | —  |  |
| $\nu(CO)$ of ester<br>amide-I' | { 1 723s<br>—                  | { 1 719m, br<br>—              | 1 690s<br>1 723s     | —<br>1 704w, br                              | —<br>1 663s                    | 1 720m, sh<br>1 702s                       | 1 676s<br>1 699m, sh | 1 720m, sh<br>1 702s                       | 1 676s<br>1 699m, sh | —<br>1 697s                                | —<br>1 697s                                |  |
| $\nu(C=N)$                     | x                              | 1 603w                         | 1 585s               | 1 594vw                                      | 1 584m                         | 1 585w, sh                                 | 1 580m               | 1 585w, sh                                 | 1 580m               | 1 574w, br                                 | 1 574w, br                                 |  |
| $\beta_s(NH_2)$ (amide-II)     | x                              | 1 569w                         | 1 603m, sh           | —  | —                              | 1 564m                                     | 1 594m               | 1 564m                                     | 1 594m               | —  | —  |  |
| 1 550–1 050 $cm^{-1}$ region   | x                              | x                              | 1 507w               | x  | 1 501w                         | —  | —                    | —  | —                    | —  | —  |  |
| $\delta(CH_3)$                 | x                              | x                              | —                    | x  | 1 467m                         | 1 455w, sh                                 | 1 466m               | 1 455w, sh                                 | 1 466m               | 1 451w, sh                                 | 1 451w, sh                                 |  |
|                                | x                              | x                              | 1 438m               | 1 424w                                       | 1 432m                         | 1 437m                                     | 1 438m               | 1 437m                                     | 1 438m               | 1 424m                                     | 1 424m                                     |  |
|                                | x                              | x                              | 1 404m               | 1 413w, sh                                   | —                              | 1 401w                                     | 1 408w               | 1 401w                                     | 1 408w               | —  | —  |  |

TABLE IV  
(Continued)

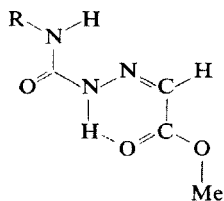
| Band             | Ia                             |                                |        | Ia-d <sub>3</sub>              |                              |                                | IIa        |                                |            | IIa-d <sub>3</sub>             |  |  |
|------------------|--------------------------------|--------------------------------|--------|--------------------------------|------------------------------|--------------------------------|------------|--------------------------------|------------|--------------------------------|--|--|
|                  | CHCl <sub>3</sub> <sup>a</sup> | CDCl <sub>3</sub> <sup>b</sup> | KBr    | CDCl <sub>3</sub> <sup>b</sup> | forube<br>nujol <sup>c</sup> | CDCl <sub>3</sub> <sup>d</sup> | KBr        | CDCl <sub>3</sub> <sup>d</sup> | KBr        | CDCl <sub>3</sub> <sup>e</sup> |  |  |
|                  | x                              | x                              | —      | x                              | 1 382m                       | —                              | —          | —                              | —          | —                              |  |  |
|                  | x                              | x                              | 1 350m | x                              | —                            | —                              | —          | —                              | —          | —                              |  |  |
|                  | x                              | 1 293w                         | —      | 1 293w                         | —                            | —                              | —          | —                              | —          | —                              |  |  |
|                  | x                              | —                              | 1 246m | —                              | 1 231m                       | 1 221s                         | 1 226s     | 1 217s                         | 1 217s     | 1 217s                         |  |  |
|                  | x                              | —                              | 1 199w | 1 183w                         | 1 168m                       | 1 187m                         | 1 195w, sh | 1 186w                         | 1 195w, sh | 1 186w                         |  |  |
|                  | x                              | 1 156w                         | 1 152s | —                              | 1 143w                       | 1 132w                         | 1 133m     | 1 142w                         | 1 133m     | 1 142w                         |  |  |
|                  | x                              | x                              | 1 091m | x                              | 1 065m                       | 1 085m, br                     | 1 083m     | 1 085m, br                     | 1 083m     | 1 058w                         |  |  |
| $\nu(\text{CH})$ | x                              | x                              | 911m   | x                              | 910m                         | 862m                           | 883w       | 862m                           | 883w       | 861w                           |  |  |

<sup>a</sup> Saturated solution, 1 cm (concentration of about 0.001M); <sup>b</sup> saturated solution, 2.6 mm; <sup>c</sup> 1 350 to 850 cm<sup>-1</sup> region; <sup>d</sup> saturated solution 0.1 mm; <sup>e</sup> concentration 0.15M, 0.1 mm; <sup>f</sup> in CHCl<sub>3</sub>, 0.003M, 1 cm; <sup>g</sup> concentration 0.002M, 1 cm; <sup>h</sup> the  $\nu(\text{CO})$  band considerably asymmetrical, probable wavenumber of the maximum of the minor component, 1 740 to 1 745 cm<sup>-1</sup>; <sup>x</sup> solvent absorption.

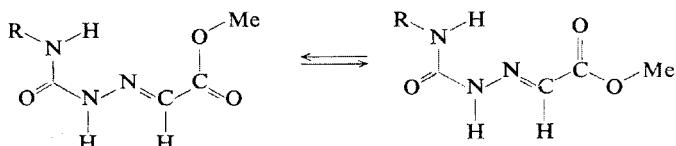


4-ribosyl derivatives are always obtained as mixtures of two isomers differing *inter alia* by IR, NMR, and CD spectra. The IR spectrum of one of the two isomers (in chloroform) was always strikingly similar to that of 2,3,5-tri-O-benzoyl- $\beta$ -D-ribofuranose (in the 950–1200  $\text{cm}^{-1}$  region). The other isomer always exhibited some additional bands such as at 982 ( $\pm 7$ ) m, 1034 m (sh), 1059 m, and 1084 (sh)  $\text{cm}^{-1}$ . The presence of the *trans*-amidic bands in both isomers excluded the highly improbable existence of a *trans-cis* isomerism on the  $\text{N}_{(4)}\text{-C}_{(3)}$  amidic bond. Resemblance between spectra of one of the isomers and 2,3,5-tri-O-benzoyl- $\beta$ -D-ribofuranose on the one hand and a moderate difference in the case of the other isomer suggests involvement of  $\beta$ - and  $\alpha$ -anomers. In the IR spectrum of  $\beta$ -anomers, the  $\nu(\text{N}_{(4)}\text{-H})$  values are by 11–16  $\text{cm}^{-1}$  lower and the amide-II band values are by 20–23  $\text{cm}^{-1}$  higher. As it may be inferred from inspection of Dreiding stereomodels of the two anomers, the formation of an intramolecular hydrogen bond with the carbonyl group of the benzoyl residue at position 2' is more advantageous in the case of  $\beta$ -anomers than with the carbonyl group of the benzoyl residue at position 3' of the  $\alpha$ -anomer with respect to the different ribofuranose ring conformation. It is highly probable that the  $\nu(\text{N}_{(4)}\text{-H})$  bands present in spectra of chloroform solutions of the two anomers at concentration of  $3 \cdot 10^{-3} \text{M}$  do not represent vibrations of free NH groups but of those bound by a weak intramolecular hydrogen bond. Their halfwidth is somewhat greater than that of free  $\nu(\text{N}_{(2)}\text{-H})$ . The IR spectra of the two anomers also differ in the  $\nu(\text{CH})$  region.

The CD spectra of compounds *VIa*, *VIb*, and *VIc* markedly differ from those of compounds *VIIa*, *VIIb*, and *VIIc*. The ribosylsemicarbazones *VIa*, *VIb*, and *VIc* exhibit a positive maximum of the optically active band of benzoyl groups at 231.5 to 235 nm and a negative maximum at 262.5–266 nm with an inflex at 255.5–259 nm. The CD curves of compounds *IV* and *V* exhibit a similar course. The CD spectrum of compound *IV* displays a positive maximum of the optically active band of benzoyl groups at 235 nm, a negative maximum at 256 nm, and a positive poorly intensive maximum at 294 nm. The CD curve of compound *V* exhibits a positive maximum at 223.5 nm corresponding to benzoyl groups and a negative maximum at 239.5 nm with an inflex at 257 nm. In CD spectra of compounds *VIIa*, *VIIb*, and *VIIc*, there is present a positive maximum of the optically active band of benzoyl groups at 235



IX



X

TABLE V  
IR Spectra of  $H_2NCONR^1-N=CHCOOCH_3$  ( $cm^{-1}$ )

| Band                          | IIIa                           |                                 | IIIa-d <sub>2</sub> |                                | IIIb                           |                                | IIIb-d <sub>2</sub>            |                                | IV |
|-------------------------------|--------------------------------|---------------------------------|---------------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|----|
|                               | CHCl <sub>3</sub> <sup>a</sup> | CH <sub>3</sub> CN <sup>b</sup> | KBr                 | CHCl <sub>3</sub> <sup>a</sup> | CHCl <sub>3</sub> <sup>c</sup> | CHCl <sub>3</sub> <sup>c</sup> | CHCl <sub>3</sub> <sup>c</sup> | CHCl <sub>3</sub> <sup>d</sup> |    |
| $\nu_a(NH_2)$ , $\nu_a(ND_2)$ | 3 536 <sup>e</sup>             | z                               | 3 464m              | 2 655m <sup>e</sup>            | 3 535 <sup>e</sup>             | 2 654w                         | 3 535 <sup>e</sup>             | 3 535 <sup>e</sup>             |    |
| $\nu_s(NH_2)$ , $\nu_s(ND_2)$ | 3 417m <sup>e</sup>            | z                               | { 3 296m<br>3 235m  | 2 503m <sup>e</sup>            | 3 417 <sup>e</sup>             | 2 493w                         | 3 416m <sup>e</sup>            | 3 416m <sup>e</sup>            |    |
| $\nu(CO)$ of ester            | 1 737s, sh                     | 1 740s                          | <sup>f</sup>        | 1 737m, sh                     | 1 736m, sh                     | 1 737m, sh                     | <sup>g</sup>                   | <sup>g</sup>                   |    |
| amide-I                       | 1 722vs                        | { 1 716vs                       | 1 704s, br          | —                              | { 1 712s                       | —                              | { 1 710s, sh                   | —                              |    |
| $\nu(CO)$ of ester            | 1 710vs                        | —                               | 1 722s              | { 1 707vs                      | —                              | { 1 709s                       | —                              | —                              |    |
| amide-I'                      | —                              | —                               | —                   | 1 694s, sh                     | 1 692m, sh                     | 1 692m, sh                     | 1 693m, sh                     | 1 691w, sh                     |    |
| $\nu(C=N)$                    | 1 591s                         | 1 588s                          | 1 589m, sh          | 1 591s                         | 1 593m                         | 1 593m                         | 1 604m <sup>h</sup>            | —                              |    |
| $\beta_s(NH_2)$ (amide II)    | 1 556s                         | 1 571s                          | 1 581s              | —                              | 1 556s                         | —                              | 1 557m                         | —                              |    |
| $\beta_s(ND_2)$               | —                              | —                               | —                   | 1 114m                         | —                              | 1 147m                         | —                              | —                              |    |
| $\gamma(CH)$                  | 885m                           | 889w                            | —                   | 886w                           | 891w                           | 891w                           | 906w, br                       | —                              |    |
|                               | 875w, sh                       | 872w                            | 877m                | 875w                           | 874w                           | 874w                           | 868w                           | —                              |    |

<sup>a</sup> 0.19m, 0.1 mm; <sup>b</sup> 0.17m, 0.1 mm; <sup>c</sup> 0.13m, 0.1 mm; <sup>d</sup> 0.076m, 0.1 mm; <sup>e</sup> 0.003m, 1 cm; <sup>f</sup> considerably asymmetrical  $\nu(CO)$  band, increased absorption at the higher wavenumbers; <sup>g</sup> interference of the  $\nu(CO)$  benzoate band at 1 727  $cm^{-1}$ , vs; <sup>h</sup> along with the vibration 8a of the phenyl group; z the region was not measured.

TABLE VI  
IR Spectra of  $C_6H_5NHCONH-N=CHCOOCH_3$  ( $cm^{-1}$ )

| Band                            | <i>Ib</i>      |                          |                     |                  |
|---------------------------------|----------------|--------------------------|---------------------|------------------|
|                                 | $C_2Cl_4^a$    | $CCl_4^b$                | $CHCl_3^c$          | $CH_3CN^d$       |
| $\nu(N^4H), \nu(N^4D)$          | <i>z</i>       | 3 394w <sup>h</sup>      | 3 395m <sup>i</sup> | 3 388w, br       |
| $\nu(N^2H), \nu(N^2D)$          | <i>z</i>       | 3 348w <sup>h</sup>      | 3 343m <sup>i</sup> | 3 274w, br       |
| $\nu(N^2H), \nu(N^2D)$ of dimer | <i>z</i>       | —                        | —                   | —                |
|                                 | <i>z</i>       | 3 020w, vbr <sup>h</sup> | 3 045m, vbr         | —                |
| $\nu(CO)$ of ester              | 1 751m, sh     | 1 746w, sh               | 1 737m, sh          | 1 745m           |
| amide-I<br>$\nu(CO)$ of ester   | } 1 733m, br } | } 1 730m, br }           | } 1 723s, sh }      | } 1 715s }       |
| amide-I'                        |                |                          |                     |                  |
| amide-I, amide-I' of dimer      | 1 704s         | 1 704m                   | 1 703s              | —                |
| } $\nu(C=N)$ }                  | —              | <i>x</i>                 | —                   | —                |
|                                 | 1 598m         | <i>x</i>                 | 1 597s              | 1 597m           |
|                                 | —              | <i>x</i>                 | —                   | —                |
| amide-II                        | 1 540s         | <i>x</i>                 | 1 539vs             | 1 539s           |
| 19a <sup>k</sup>                | 1 502w         | <i>x</i>                 | 1 504m              | <i>x</i>         |
| 1500—1350 $cm^{-1}$ region      | 1 481w, br     | <i>x</i>                 | 1 484w, sh          | <i>x</i>         |
|                                 | —              | —                        | —                   | <i>x</i>         |
| 19b <sup>k</sup>                | 1 449m         | 1 450w                   | 1 449m              | <i>x</i>         |
| $\delta(CH_3)$                  | 1 436w, sh     | 1 436w                   | 1 438m              | <i>x</i>         |
|                                 | —              | —                        | —                   | <i>x</i>         |
|                                 | <i>x</i>       | —                        | —                   | <i>x</i>         |
| 1280—1100 $cm^{-1}$ region      | 1 259m         | <i>x</i>                 | 1 265m              | 1 263m           |
|                                 | 1 242m         | <i>x</i>                 | 1 243m              | 1 239m           |
|                                 | —              | <i>x</i>                 | <i>x</i>            | —                |
|                                 | 1 190w         | <i>x</i>                 | 1 191w              | 1 189m           |
| amide-III                       | <i>x</i>       | 1 144m                   | 1 149vs             | 1 141s           |
| $\nu(CH) N=CH$                  | <i>x</i>       | 906vw, br                | 910w, br            | 919w, sh<br>909w |

<sup>a</sup> Saturated solution, 1 mm; <sup>b</sup> saturated solution, 2.6 mm; <sup>c</sup> 0.135M, 0.1 mm; <sup>d</sup> 0.088M, 0.1 mm; <sup>e</sup> 0.027M, 0.5 mm; <sup>f</sup> saturated solution, 0.5 mm; <sup>g</sup> 0.12M, 0.1 mm; <sup>h</sup> saturated solution, 1 cm; <sup>i</sup> 0.003M, 1 cm; <sup>j</sup> 0.005M, 1 cm; <sup>k</sup> vibrational modes of the phenyl group (Wilson numbering); *x*, *z* see Notes in Tables IV and V.

TABLE VI  
(Continued)

| KBr        | <i>Ib-d<sub>2</sub></i>        |                               | <i>Iib</i>                     |                                 |                            | <i>Iib-d<sub>2</sub></i>                     |  |
|------------|--------------------------------|-------------------------------|--------------------------------|---------------------------------|----------------------------|--|--|
|            | CHCl <sub>3</sub> <sup>e</sup> | CCl <sub>4</sub> <sup>f</sup> | CHCl <sub>3</sub> <sup>c</sup> | CH <sub>3</sub> CN <sup>g</sup> | KBr                        | CHCl <sub>3</sub> <sup>c</sup>               |  |
| 3 371s     | { 2 527w, sh<br>2 514w         | 3 403s <sup>i</sup>           | 3 395s <sup>i</sup>            | 3 351w                          | 3 327m                     | { 2 530s <sup>j</sup><br>2 513m <sup>j</sup> |  |
| 3 272s, br | 2 491w                         | 3 292m <sup>i</sup>           | 3 294m <sup>i</sup>            | 3 299w                          | 3 287m                     | 2 444w                                       |  |
| 3 167m, br | —                              | —                             | —                              | —                               | —                          | —  |  |
| —          | 2 320w, vbr                    | —                             | —                              | —                               | —                          | —  |  |
| —          | 1 739s, sh                     | —                             | —                              | —                               | 1 728w, sh                 | —  |  |
| 1 695s     | —                              | 1 733m                        | 1 723s, sh                     | ~1 720s, sh                     | 1 690s                     | —  |  |
| 1 730vs    | 1 721s, sh                     | { 1 712m<br>1 705m            | 1 704vs                        | 1 703s                          | 1 712m, sh                 | } 1 703vs                                    |  |
| —          | 1 709s                         | —                             | —                              | —                               | —                          |  |  |
| —          | 1 687s                         | —                             | —                              | —                               | —                          |  |  |
| —          | 1 601s                         | 1 604m                        | 1 604m, sh                     | 1 603m, sh                      | 1 604m, sh                 | 1 603m                                       |  |
| 1 596s     | 1 595s, sh                     | 1 598w, sh                    | 1 598m                         | 1 596m                          | 1 595m                     | —  |  |
| 1 585s     | —                              | —                             | 1 584m, sh                     | 1 583m, sh                      | 1 579m                     | 1 573w                                       |  |
| 1 537vs    | —                              | 1 536s                        | 1 538vs                        | 1 538s                          | 1 537s                     | —  |  |
| 1 504m     | 1 506s                         | 1 505w, sh                    | 1 505m, sh                     | 1 507m, sh                      | 1 506m                     | 1 505s                                       |  |
| 1 493m, sh | 1 486 m, sh                    | 1 482vw                       | 1 488w, sh                     | x                               | —                          | 1 486w                                       |  |
| —          | 1 471s                         | —                             | —                              | x                               | —                          | 1 465s                                       |  |
| 1 448s     | 1 451s                         | 1 447m                        | 1 449s                         | x                               | 1 449m                     | —  |  |
| 1 433m     | 1 434s                         | { 1 440m, sh<br>1 424vw, sh   | { 1 443m, sh<br>1 424w, sh     | x                               | { 1 440m, sh<br>1 426w, sh | —  |  |
| —          | 1 386s                         | —                             | —                              | x                               | —                          | 1 426vs                                      |  |
| 1 363m     | —                              | 1 371w                        | 1 372m                         | x                               | 1 376w                     | —  |  |
| 1 276s     | 1 260m                         | —                             | —                              | —                               | —                          | —  |  |
| 1 250m     | x                              | —                             | —                              | —                               | —                          | —  |  |
| —          | x                              | 1 204s                        | x                              | 1 212vs                         | 1 217s                     | x  |  |
| 1190s      | x                              | 1 185m                        | 1 187s                         | 1 188s                          | 1 182m                     | 1 187s                                       |  |
| 1 155vs    | —                              | 1 124s                        | 1 122vs                        | 1 123s                          | 1 125m                     | —  |  |
| 905s       | 909w, br                       | 854w                          | 861m                           | 864w                            | 865m                       | 861w   |  |

to 238 nm with an inflex at 256.5–264 nm and a negative maximum at 211–220 nm. As indicated by the course of CD spectra, pairs of anomeric compounds are involved in the case of methyl glyoxylate 4-ribofuranosylsemicarbazones.

The two groups of compounds also differ in the sign of the optical rotation  $[\alpha]_D$ . Compounds *IV*, *Via*, *Vib*, and *Vic* exhibit negative signs while the specific optical rotation values of compounds *VIIa*, *VIIb*, and *VIIc* are positive. Since the  $\beta$  configuration of compound *IV* has been unequivocally established by cyclisation to 6-azauridine<sup>2</sup>, related compounds *Via*, *Vib*, and *Vic* also possess this configuration; consequently, the configuration at the anomeric center of compounds *VIIa*, *VIIb*, and *VIIc* is  $\alpha$ .

The same conclusions may also be drawn from NMR spectra. The sugar protons of the ribosylsemicarbazones *IV*, *V*, *Via*, *Vib*, and *Vic* are poorly different in their chemical shifts and cannot be therefore distinguished; the particular coupling constants are also difficult to determine. The sugar protons form two multiplets. One of them ( $\delta$  5.70–6.45 p.p.m.) corresponds to the  $H_{1'}$ ,  $H_{2'}$ , and  $H_{3'}$  protons while the other one ( $\delta$  4.50–4.90 p.p.m.) is formed by the  $H_{4'}$  and  $H_{5'}$ . The NMR spectra of some other benzoylated  $\beta$ -D-ribofuranosyl derivatives, e.g., 1,2,3,5-tetra-O-benzoyl- $\beta$ -D-ribofuranose<sup>38</sup>, 1-O-acetyl-2,3,5-tri-O-benzoyl- $\beta$ -D-ribofuranose<sup>38</sup>, 2',2',2'-trichloroethyl 2,3,5-tri-O-benzoyl- $\beta$ -D-ribofuranoside<sup>39</sup>, and 2',3',5'-tri-O-benzoyl-5-azacytidine<sup>40</sup>, are of the same character.

In contrast to the NMR spectra of the  $\beta$ -anomers, the corresponding protons in the spectra of the  $\alpha$ -ribosides *VIIa*, *VIIb*, and *VIIc* are well resolved as shown in Table II. The  $H_{1'}$  protons form doublets, the  $H_{2'}$  and  $H_{3'}$  protons form doublets of doublets, and the  $H_{4'}$  proton exhibits pentets. The two  $H_{5'}$  protons occur as two doublets of doublets. For the corresponding coupling constants see Table III. Analogous spectra may be observed with some other benzoylated  $\alpha$ -D-ribofuranosyl derivatives such as 1,2,3,5-tetra-O-benzoyl- $\alpha$ -D-ribofuranose<sup>38</sup>, 2',2',2'-trichloroethyl 2,3,5-tri-O-benzoyl- $\alpha$ -D-ribofuranoside<sup>39</sup>, and 1-(2,3,5-tri-O-benzoyl- $\alpha$ -D-ribofuranosyl)-5-azacytosine<sup>40</sup>.

On comparison of IR spectra of the present semicarbazones in the  $\nu(C=O)$  region, the probable conformation of the  $N=C-C=O$  bonds was estimated. The carbonyl bands of methyl glyoxylate semicarbazones exhibit a complex structure; with tri-O-benzoylribofuranosyl derivatives, the presence of an intensive benzoate band at about  $1726\text{ cm}^{-1}$  strongly interferes. The amide-I band was determined on comparison with spectra of deuterated substances and the solid phase spectra. With unsubstituted and 4-monosubstituted semicarbazones, this band lies at about  $1722\text{ cm}^{-1}$  in the chloroform solution; this value decreases by about  $15-20\text{ cm}^{-1}$  on deuteration and by about  $20-30\text{ cm}^{-1}$  by conversion into the solid phase. With 2,4-disubstituted compounds, the amide-I band probably lies between  $1710$  and  $1715\text{ cm}^{-1}$ . When compared with values of analogously substituted ureas<sup>6</sup>, the amide-I band value is shifted to higher wavenumbers in both the above cases. With the (*E*)-isomers of the

TABLE VII  
IR Spectra of  $R^2NHCONH-N=CHCOOCH_3$  ( $cm^{-1}$ ; in chloroform)

| Band  | <i>VIa</i> <sup>a</sup> | <i>VIIa</i> <sup>a</sup> | <i>VIIa-d</i> <sub>2</sub> <sup>b</sup> |
|---|-------------------------|--------------------------|---|
| $\nu(N^4H), \nu(N^4D)$                          | 3 406m <sup>c</sup>     | 3 422m <sup>c</sup>      | 2 539w <sup>d</sup>                     |
| $\nu(N^2H), \nu(N^2D)$                          | 3 343m <sup>c</sup>     | 3 342m <sup>c</sup>      | 2 492vw, sh                             |
| $\nu(N^2H), \nu(N^2D)$ of dimer                 | 3 030w, vbr             | 3 030w, vbr              | 2 320vw, vbr                            |
| $\nu(CO)$ ( $C_6H_5COO$ )<br>amide I of monomer | 1 726s                  | 1 725vs                  | 1 724s                                  |
| $\nu(CO)$ ( $COOCH_3$ )<br>amide-I of dimer     |                         |                          |   |
|   | 1 704m, sh              | 1 710s, sh               | 1 712m, sh                              |
|   | 1 690m, sh              | 1 693m, sh               | 1 692m, sh <sup>e</sup>                 |
| $8a^f$  | 1 602m                  | 1 602m                   | 1 601w                                  |
| $\nu(C=N)$                                      |                         |                          |   |
| $8b^f$  | 1 589w, sh              | 1 589w, sh               | 1 589w, sh                              |
| amide-II  | 1 533m                  | 1 539w, sh               | —                                       |
|   | 1 515w, sh              | 1 513m                   | —                                       |
|   | —                       | 1 504m, sh               | —                                       |
| 1 500—1 350 $cm^{-1}$                           | 1 495w                  | 1 496m, sh               | 1 494vw                                 |
| $19a^f$   | —                       | —                        | 1 471w, sh                              |
| $19b^f$   | 1 453m                  | 1 452m                   | 1 453m                                  |
| $\delta(CH_3)$                                  | 1 438w                  | 1 436w                   | 1 427m                                  |
|   | —                       | —                        | 1 375m                                  |
| amide-III <sup>g</sup>                          | 1 149m                  | 1 138s                   | 1 139m                                  |
|   | 1 125s                  |                          |   |
| $\gamma(CH)$ ( $N=CH$ )                         | 915w, br                | 907w, br                 | 911w, br                                |

<sup>a</sup> 0.0505M, 0.1 mm; <sup>b</sup>  $\sim$ 0.05M, 0.1mm; <sup>c</sup> 0.003M, 1 cm; <sup>d</sup>  $\sim$ 0.002M, 1 cm; <sup>e</sup> increase of intensity after deuteration (along with amide-I' band of the dimer) and a simultaneous intensity decrease of both the  $\nu(CO)$  upper bands; <sup>f</sup> vibrational modes of the phenyl group; <sup>g</sup> along with the internal vibration of the 2',3',5'-tri-O-benzoylribofuranosyl group.

4-monosubstituted derivatives in chloroform solution, an additional amide-I band may be observed which is shifted by about 20  $cm^{-1}$  to lower wavenumbers, and which probably corresponds to the dimeric form of these semicarbazones.

With (*E*)-isomers of semicarbazones unsubstituted by the tri-O-benzoylribofuranosyl residue, the principal band of the ester carbonyl group and the amide-I band overlap. Furthermore, a relatively intensive inflex near 1737  $cm^{-1}$  may be observed

TABLE VIII  
IR Spectra of  $R^2NHCONR^1-N=CHCOOCH_3$  ( $cm^{-1}$ )

| Compound   | <i>VIb</i>  | <i>VIIb</i>  | <i>VIc</i>  | <i>VIIc</i>  |
|--|---|--|---|--|
| $R^2$<br>$R^1$   | $\beta$ -Bz <sub>3</sub> Rf <sup>a</sup><br>CH <sub>3</sub> | $\alpha$ -Bz <sub>3</sub> Rf <sup>a</sup><br>CH <sub>3</sub> | $\beta$ -Bz <sub>3</sub> Rf <sup>a</sup><br>CH <sub>3</sub> | $\alpha$ -Bz <sub>3</sub> Rf <sup>a</sup><br>CH <sub>2</sub> C <sub>6</sub> H <sub>5</sub> |
| Medium   | CHCl <sub>3</sub> <sup>b</sup>                              | CHCl <sub>3</sub> <sup>b</sup>                               | CHCl <sub>3</sub> <sup>c</sup>                              | CHCl <sub>3</sub> <sup>c</sup>   |
| $\nu(NH)$ , $\nu(ND)$                                      | 3 410m <sup>i</sup>   | 3 421m <sup>i</sup>  | 3 404m <sup>i</sup>   | 3 417m <sup>i</sup>  |
| $\nu(CO)$ (COOCH <sub>3</sub> )                            | <i>j</i>  | <i>j</i>   | <i>j</i>  | <i>j</i>   |
| $\nu(CO)$ (C <sub>6</sub> H <sub>5</sub> COO)              | 1 727vs   | 1 725s   | 1 727s  | 1 724s   |
| amide-I, amide-I' }<br>$\nu(CO)$ (. COOCH <sub>3</sub> ) } | 1 712s, sh  | 1 712s, sh   | 1 711s, sh  | 1 712s, sh   |
|  | 1 693m, sh  | 1 692w, sh   | 1 692m, sh  | 1 691w, sh   |
| $\nu(C=N)$   | 1 590m  | 1 590m   | 1 595m  | 1 594m   |
| amide-II, amide-II'  | 1 515s  | 1 495s   | 1 514m  | 1 491s   |
| amide-III <sup>m</sup>                                     | 1 123s  | 1 137m   | 1 153m, sh<br>1 125s  | 1 136s   |
| $\nu(CH)$ (N=CH)   | 886w, br<br>871w  | 887w, br<br>872w   | 893w, br<br>874w  | 893w<br>874w   |

with all compounds of this type. Since similarly to esters of  $\alpha,\beta$ -unsaturated carboxylic acids<sup>21,22</sup> a coexistence of the more stable *s-trans* conformer and the less stable *s-cis* conformer could be assumed in solutions of the present (*E*)-isomers, the two bands could be assigned to  $\nu(C=O)$  of these two conformers. The  $\Delta\nu$  value of the two bands ( $\sim 15\text{ cm}^{-1}$ ) would be in this case higher than with esters of  $\alpha,\beta$ -unsaturated carboxylic acids<sup>21</sup> which resisted all attempts to resolve the carbonyl bands of the two conformers. This assignment could be corroborated by the intensity dependence of both components of the  $\nu(C=O)$  band on the polarity of the solvent or on temperature. With the relatively more soluble (*E*)-isomer *Ib* however, the situation is considerably complicated by the simultaneous presence of a monomer-dimer equilibrium in non polar solvents. In an acetonitrile solution where the existence of dimers is poorly probable, the (*E*)-isomer *Ib* exhibits a  $\nu(C=O)$  doublet only, 1715  $cm^{-1}$ , s, and 1745  $cm^{-1}$ , m. In the principal maximum, the amide-I band of monomer and the ester  $\nu(C=O)$  band overlap.

TABLE VIII  
(Continued)

|                                      |  | <i>IIIc</i>                                   |   | <i>IIIc-d<sub>1</sub></i>                 |  | <i>IIIId</i>  | <i>V</i>   |
|--------------------------------------|--|---|---|---|--|---|--|
|                                      |  | $\text{C}_6\text{H}_5$<br>$\text{CH}_3$       |   | $\text{C}_6\text{H}_5$<br>$\text{CH}_3$   |  | $\text{C}_6\text{H}_5$<br>$\text{CH}_2\text{C}_6\text{H}_5$ | $\text{C}_6\text{H}_5$<br>$\beta\text{-Bz}_3\text{Rf}^a$ |
| $\text{C}_2\text{Cl}_4^d$            | $\text{CHCl}_3^e$                              | $\text{CH}_3\text{CN}^f$                      | KBr   | $\text{CHCl}_3^e$                         | $\text{CHCl}_3^g$                              | $\text{CHCl}_3^h$   |  |
| <i>z</i>                             | 3 390 <sup>m</sup> <sup>i</sup>                | <i>z</i>                                      | 3 391 <sup>w</sup>  | 2 516 <sup>m</sup> <sup>i</sup>           | 3 389 <sup>m</sup> <sup>i</sup>                | 3 389 <sup>m</sup> <sup>i</sup>                             |  |
| 1 745 <sup>m</sup>                   | 1 737 <sup>s</sup> , sh                        | 1 743 <sup>s</sup>                            | 1 737 <sup>m</sup> , sh                                       | 1 737 <sup>m</sup> , sh                   | 1 737 <sup>m</sup> , sh                        | 1 737 <sup>s</sup> , sh                                     | 1 727 <sup>vs</sup>                                      |
| 1 718 <sup>vs</sup>                  | 1 711 <sup>vs</sup>                            | 1 711 <sup>vs</sup>                           | { 1 718 <sup>m</sup> , sh<br>1 706 <sup>s</sup>               | 1 709 <sup>s</sup>                        | 1 710 <sup>s</sup>                             | 1 712 <sup>s</sup> , sh                                     |  |
| 1 685 <sup>w</sup> , sh              | 1 693 <sup>m</sup> , sh                        | 1 691 <sup>m</sup> , sh                       | 1 692 <sup>m</sup> , sh                                       | 1 693 <sup>m</sup> , sh                   | 1 693 <sup>m</sup> , sh                        | 1 691 <sup>w</sup> , sh                                     |  |
| 1 594 <sup>s</sup>                   | 1 594 <sup>s</sup>                             | 1 594 <sup>s</sup>                            | 1 595 <sup>m</sup>  | 1 591 <sup>m</sup>                        | 1 595 <sup>s</sup>                             | 1 603 <sup>m</sup> <sup>k</sup>                             |  |
| 1 528 <sup>vs</sup>                  | 1 531 <sup>vs</sup><br>1 518 <sup>s</sup> , sh | 1 533 <sup>s</sup><br>1 521 <sup>m</sup> , sh | 1 531 <sup>s</sup>  | 1 164 <sup>s</sup>                        | 1 531 <sup>vs</sup><br>1 520 <sup>s</sup> , sh | 1 531 <sup>s</sup><br>1 515 <sup>m</sup> , sh               |  |
| 1 130 <sup>s</sup>                   | 1 129 <sup>vs</sup>                            | 1 127 <sup>vs</sup>                           | 1 130 <sup>m</sup> , br                                       | —   | 1 137 <sup>vs</sup>                            | 1 156 <sup>s</sup><br>1 121 <sup>s</sup>                    |  |
| 880 <sup>w</sup><br>874 <sup>w</sup> | 883 <sup>w</sup> , sh<br>873 <sup>w</sup>      | 890 <sup>w</sup> , br<br>871 <sup>w</sup>     | 910 <sup>w</sup><br>875 <sup>w</sup> , sh<br>869 <sup>m</sup> | 885 <sup>w</sup> , br<br>873 <sup>w</sup> | 890 <sup>w</sup> , br<br>874 <sup>w</sup> , sh | 901 <sup>m</sup> , br<br>874 <sup>w</sup> , br              |  |

<sup>a</sup> 2',3',5'-Tri-O-benzoylribofuranosyl; <sup>b</sup> 0.049M, 0.1 mm; <sup>c</sup> 0.044M, 0.1 mm; <sup>d</sup> 0.124M, 0.1 mm; <sup>e</sup> 0.126M, 0.1 mm; <sup>f</sup> 0.115M, 0.1 mm; <sup>g</sup> 0.096M, 0.1 mm; <sup>h</sup> 0.067M, 0.1 mm; <sup>i</sup> 0.003M, 1 cm; <sup>j</sup> asymmetrical  $\nu(\text{CO})$  benzoate band, increased absorption at about  $1\,737\text{ cm}^{-1}$ ; <sup>k</sup> along with the vibration 8a of the phenyl group; <sup>m</sup> along with the internal vibration of the tribenzoylribofuranosyl group; *z* the region was not measured.

In the crystalline state, the presence of a single conformation may be expected. Compound *Ib* when measured in solid state, exhibits a symmetrical band of the ester  $\nu(\text{C}=\text{O})$  value at  $1\,730\text{ cm}^{-1}$  without any indication of an inflex at about  $1\,740\text{ cm}^{-1}$ . On the other hand, the  $\sim 910\text{ cm}^{-1}$  band is in chloroform considerably extended in contrast to the solid state measurements; in the acetonitrile solution, it is replaced by an unresolved doublet, 909 and 919 (sh)  $\text{cm}^{-1}$ . No other bands which would confirm the presence of any equilibrium have not been found by measurements in solutions.



With the (*Z*)-isomers of methyl glyoxylate semicarbazones, the ester carbonyl band is shifted to about  $1703\text{ cm}^{-1}$ . The lower  $\nu(\text{C}=\text{O})$  value of the (*Z*)-isomers than in the case of the (*E*)-isomers is due to the presence of an intramolecular hydrogen bond on the ester carbonyl group. Because of the absence of any additional  $\nu(\text{C}=\text{O})$  band in solutions of (*Z*)-isomers, the presence of an intramolecular hydrogen bond on the ethereal oxygen atom under the simultaneous existence of the *s-trans* conformation may be excluded. Consequently, the *s-cis* conformation of the  $\text{N}=\text{C}-\text{C}=\text{O}$  bond system must be involved in the case of the (*Z*)-isomers. The spectral shape of the 4-phenyl derivative *IIB* solutions is almost independent of the solvent (tetrachloromethane, chloroform, acetonitrile); the difference between the spectra in solution and in the solid state is also very small.

The 2-substituted semicarbazones cannot form the chelate ring, the (*Z*)- and (*E*)-isomers cannot be isolated. Compounds lacking the tri-*O*-benzoylribofuranosyl substituent exhibit an inflex near  $1737\text{ cm}^{-1}$  in addition to the main maximum at about  $1711\text{ cm}^{-1}$ . The latter one could be attributable to the more abundant *s-trans* conformers of both the (*Z*)- and (*E*)-isomer while the inflex would belong to the less stable planar or nonplanar *s-cis* conformers of both the isomers. The amide-I band of most 2-substituted derivatives is probably shifted to lower wavenumbers and overlaps with the ester  $\nu(\text{C}=\text{O})$  at about  $1711\text{ cm}^{-1}$ .

With the 2-methylsemicarbazone *IIIa*, an equilibrium of at least two forms has been found. In contrast to the crystalline state, solutions exhibit bands at about  $710$  and  $880\text{ cm}^{-1}$  split into doublets and a doublet in the  $1000$  to  $1050\text{ cm}^{-1}$  region split into a quadruplet. Moreover, the intensity of the  $1240\text{ cm}^{-1}$  band strongly increases in solutions and a new band may be observed at  $1300\text{ cm}^{-1}$ . The form occurring in solutions only, is less polar. In the chloroform solution, this form is present to a greater extent than in acetonitrile. It is not clear whether a (*Z*)/(*E*) or a *s-cis*/*s-trans* equilibrium is involved or if both the equilibria exist simultaneously.

Some preliminary measurements have also been performed on the temperature dependence of the spectrum in the tetrachloroethylene solution of the 4-phenyl-2-methylsemicarbazone *IIIc* in the range of about  $50^\circ\text{C}$ . We have not found any perceptible change in the relative intensity of the two components of the  $\nu(\text{C}=\text{O})$  band. Similarly, no change has been observed in dependence on the solvent polarity. Explanation of the  $\nu(\text{C}=\text{O})$  band splitting by the Fermi resonance would be therefore improbable. The origin of the inflex on the  $\nu(\text{C}=\text{O})$  band at  $1692\text{ cm}^{-1}$  also remains unclear. This inflex shown by all compounds in Tables V, VII, and VIII does not disappear by dilution; it cannot be consequently explained by intermolecular association.

In measurements of the temperature dependence in the IR spectrum of compound *IIIc*, some changes have been observed in the  $1200\text{ cm}^{-1}$  region indicating an equilibrium of two components. When the solution is cooled down, the intensity of the  $1200\text{ cm}^{-1}$  band increases more fastly than that of the  $1182$  and  $1224\text{ cm}^{-1}$  bands.

TABLE IX

Probable Structures of Methyl Glyoxylate Semicarbazone Derivatives

| Compound                 | R <sup>2</sup>   | HN—C=O       | O=C—NR <sup>1</sup> | R <sup>1</sup>   | (O=)CN—N=C                  | N=C  | N=C—C=O                     | O=C—OCH <sub>3</sub> |
|--------------------------|--|--------------|---------------------|--|-----------------------------|--|-----------------------------|----------------------|
| <i>Ia</i>                | H  | —            | <i>cis</i>          | H  | <i>s-trans</i> <sup>d</sup> | ( <i>E</i> )                               | <i>s-trans</i> <sup>e</sup> | ( <i>Z</i> )         |
| <i>IIa</i>               | H  | —            | <i>cis</i>          | H  | <i>s-trans</i>              | ( <i>Z</i> )                               | <i>s-cis</i>                | ( <i>Z</i> )         |
| <i>IIIa</i>              | H  | —            | (E) <sup>a,d</sup>  | $\left\{ \begin{array}{l} \text{CH}_3 \\ \text{C}_6\text{H}_5\text{CH}_2 \\ \beta\text{-Bz}_3\text{Rf}^b \end{array} \right\}$                   | c                           | (( <i>E</i> ) + ( <i>Z</i> )) <sup>d</sup> | c                           | (Z)                  |
| <i>IIIb</i>              |  |              |                     |  |                             |  |                             |                      |
| <i>IV</i>                |  |              |                     |  |                             |  |                             |                      |
| <i>Ib</i>                | C <sub>6</sub> H <sub>5</sub>  | <i>trans</i> | <i>cis</i>          | H  | <i>s-trans</i> <sup>d</sup> | ( <i>E</i> )                               | <i>s-trans</i> <sup>e</sup> | (Z)                  |
| <i>IIb</i>               | C <sub>6</sub> H <sub>5</sub>  | <i>trans</i> | <i>cis</i>          | H  | <i>s-trans</i>              | (Z)  | <i>s-cis</i>                | (Z)                  |
| <i>V Ia, (E)-isomer</i>  | β-Bz <sub>3</sub> Rf <sup>b</sup><br>α-Bz <sub>3</sub> Rf <sup>b</sup>   | <i>trans</i> | <i>cis</i>          | H  | <i>s-trans</i> <sup>d</sup> | (E)  | <i>s-trans</i> <sup>e</sup> | (Z)                  |
| <i>V IIa, (E)-isomer</i> |  |              |                     |  |                             |  |                             |                      |
| <i>IIIc</i>              | C <sub>6</sub> H <sub>5</sub>  | <i>trans</i> | (E) <sup>a,d</sup>  | $\left\{ \begin{array}{l} \text{CH}_3 \\ \text{C}_6\text{H}_5\text{CH}_2 \\ \beta\text{-Bz}_3\text{Rf}^b \end{array} \right\}$                   | c                           | (( <i>E</i> ) + ( <i>Z</i> )) <sup>d</sup> | c                           | (Z)                  |
| <i>IIId</i>              |  |              |                     |  |                             |  |                             |                      |
| <i>V</i>                 |  |              |                     |  |                             |  |                             |                      |
| <i>VIb</i>               | β-Bz <sub>3</sub> Rf <sup>b</sup><br>α-Bz <sub>3</sub> Rf <sup>b</sup><br>β-Bz <sub>3</sub> Rf <sup>b</sup><br>α-Bz <sub>3</sub> Rf <sup>b</sup> | <i>trans</i> | (E) <sup>a,d</sup>  | $\left\{ \begin{array}{l} \text{CH}_3 \\ \text{CH}_3 \\ \text{C}_6\text{H}_5\text{CH}_2 \\ \text{C}_6\text{H}_5\text{CH}_2 \end{array} \right\}$ | c                           | (( <i>E</i> ) + ( <i>Z</i> )) <sup>d</sup> | c                           | (Z)                  |
| <i>VIIb</i>              |  |              |                     |  |                             |  |                             |                      |
| <i>VIIc</i>              |  |              |                     |  |                             |  |                             |                      |
| <i>VIIc</i>              |  |              |                     |  |                             |  |                             |                      |

<sup>a</sup> C=O and NR<sup>1</sup> *cis*; <sup>b</sup> 2',3',5'-tri-O-benzoylribofuranosyl; <sup>c</sup> see the text on page 2397; <sup>d</sup> these data are probable only; <sup>e</sup> probably with the *s-cis* conformer more or less planar.

The  $1200\text{ cm}^{-1}$  band must therefore belong to the more stable equilibrium component. The intensity of this band increases with the increasing solvent polarity. The energetically more stable form of compound *IIIc* is thus simultaneously more polar. It is of interest in this connection that with methyl acrylate, the *s-trans* and the „non-*s-trans*” equilibrium has been examined *inter alia* on the  $1180$  and  $1202\text{ cm}^{-1}$  doublet which has been ascribed to the  $\nu_a(\text{C}=\text{CO}=\text{O})$  vibrations of the less stable and the more stable component<sup>21</sup>. With compound *IIIc*, a *Z-E* isomerism might also be involved.

The stretching vibration of the  $\text{C}=\text{N}$  bond in chloroform solution has been found between  $1573$  and  $1604\text{ cm}^{-1}$ . In the case of derivatives with aromatic rings, the  $\nu(\text{C}=\text{N})$  band either overlaps with bands of  $\nu(\text{ring})$  vibrations 8a or 8b, or is located between them. As indicated by the observed  $\nu(\text{C}=\text{N})$  values, the correct assignment of this band in IR spectra of phenylhydrazones has been made by Tanner<sup>16</sup> and Yao<sup>18</sup> but not by Elguero and coworkers<sup>19</sup>.

In the amide-II region, the 2-monosubstituted and unsubstituted semicarbazones of methyl glyoxylate exhibit a single band of the practically pure scissoring vibration of the  $\text{NH}_2$  group similarly to *N,N*-dimethylurea<sup>3</sup>. The absence of another amide-II band in the case of unsubstituted semicarbazones may be regarded as an additional confirmation of their *cis* conformation on the  $\text{N}_{(2)}\text{-C}_{(3)}$  bond.

The 4-monosubstituted semicarbazones exhibit in the  $1120$  to  $1160\text{ cm}^{-1}$  region a very strong band (with some compounds, this band is the most intensive from the whole spectrum) which disappears by deuteration; its intensity decreases in the case of derivatives substituted by the tribenzoylribofuranosyl group. A simultaneous formation of less intensive bands may be observed in the  $900\text{--}1000\text{ cm}^{-1}$  region. With the (*E*)-isomers, the intensive band is situated higher than with the (*Z*)-isomers. Its position depends on the character of the 4-substituent; thus, with the  $\alpha$ -anomers of the tribenzoylribofuranosyl derivatives, the band is situated at higher wavenumbers than in the case of the  $\beta$ -anomers. On the basis of resemblance to *N,N'*-dialkylureas<sup>3</sup>, an amide-III band might be involved. When compared with symmetrically disubstituted ureas however, this band is shifted by more than  $150\text{ cm}^{-1}$  towards lower wavenumbers.

The (*Z*)-isomers of the 2-unsubstituted semicarbazones exhibit an intensive band in the  $1200$  to  $1230\text{ cm}^{-1}$  region probably attributable to the  $\nu_a(\text{C}=\text{C}=\text{O})$  (ref.<sup>21</sup>) or  $\nu(\text{C}=\text{OR})$  (ref.<sup>41</sup>) *s-cis* conformation of the unsaturated ester stabilised by a chelation. This intensive band is absent in the same spectral region of the (*E*)-isomers.

The isolated (*Z*)- and (*E*)-isomers also differ from each other in the region at about  $900\text{ cm}^{-1}$ . In chloroform solutions, the (*Z*)-isomers exhibit a  $860\text{ cm}^{-1}$  band while a band at  $910\text{ cm}^{-1}$  is shown by the (*E*)-isomers both in solution and in the solid state. A similar band corresponding to the azomethine group has been observed at  $885 \pm 10\text{ cm}^{-1}$  in the IR spectra of benzalanilines<sup>42</sup> and ascribed to  $\gamma(\text{CH})$ . This band has also been recorded (at  $880\text{ cm}^{-1}$ ) by Šagidullin and coworkers<sup>32</sup> in the solid

state spectra of aldehyde semicarbazones. The two isolated isomers exhibit also in the solid state characteristic differences on the  $\gamma(\text{NH})$  bands at about  $600\text{ cm}^{-1}$ .

The probable spatial structures of the present derivatives of methyl glyoxylate semicarbazone are summarised in Table IX. The (*Z*)- and (*E*)-isomers of the 2-unsubstituted semicarbazones obviously occur in the planar forms IX and X.

The derivatives substituted at position 2 probably occur as mixtures of (*E*)- and (*Z*)-isomers in *s-trans* and „non-*s-trans*” conformations on the  $\text{N}=\text{C}-\text{C}=\text{O}$  bond system. The (*Z*)-isomers of these derivatives cannot possess the planar structure, only the gauche conformation can be involved on the  $\text{N}-\text{N}$  bond or on the  $\text{N}=\text{C}-\text{C}=\text{O}$  bond system or simultaneously on these two bond systems. In the case of nonplanar (*Z*)- $\text{N},\text{N}$ -gauche- $\text{NC},\text{CO}$ -*s-trans* or gauche conformers of 2-substituted methyl glyoxylate semicarbazones, an easier cyclisation may be assumed than with planar (*Z*)-isomers of the 2-unsubstituted analogues possessing the  $\text{N},\text{N}$ -*s-trans*- $\text{NC},\text{CO}$ -*s-cis* conformation and the cyclisation of which would require rotation by  $180^\circ$  about these bonds.

## EXPERIMENTAL

Melting points were taken on a heated microscope stage (Kofler block). UV spectra were measured on an Optica Milano CF 4 spectrophotometer. IR spectra were recorded on a Zeiss UR 20 and UR 10 apparatus. The wavenumber scale was adjusted to the  $1601.5$  and  $2850.5\text{ cm}^{-1}$  poly(styrene) bands. Solutions of deuterated substances were prepared by refluxing repeatedly the solution with a drop of  $\text{D}_2\text{O}$  and evaporating subsequently the azeotropic mixture into a condenser. CD spectra were taken on a Roussel-Jouan Dichrograph II Model CD 185 apparatus. Optical rotations were recorded on a Perkin-Elmer Model 141 MC polarimeter. NMR spectra were measured on a Varian HA 100 apparatus at  $100\text{ MHz}$ .

### Mercuric Salts of Methyl Glyoxylate Semicarbazone (*Ia*) and of the 2-Alkyl and 4-Phenyl Derivatives *IIIa*, *IIIb*, *Ib*

A mixture of the appropriate semicarbazone ( $50\text{ mmol}$ ) and  $1\text{M}$  methanolic sodium methoxide ( $50\text{ ml}$ ) was stirred at room temperature for  $30\text{ min}$  and then treated dropwise with a solution of mercuric chloride ( $13.6\text{ g}$ ;  $50\text{ mmol}$ ) in methanol ( $40\text{ ml}$ ) over  $30\text{ min}$ . The stirring was continued for additional  $30\text{ min}$  and the precipitate collected with suction, washed with two  $10\text{ ml}$  portions of methanol, three  $10\text{ ml}$  portions of water, and finally with ethanol ( $10\text{ ml}$ ). The mercuric salt was then dried at  $80^\circ\text{C}/0.1\text{ Torr}$  for  $6\text{ h}$ .

### Methyl Glyoxylate Semicarbazone (*Ia*) Lithium Salt

A mixture of the semicarbazone *Ia* ( $725\text{ mg}$ ;  $5\text{ mmol}$ ),  $1\text{M}$  methanolic lithium methoxide ( $5\text{ ml}$ ), and absolute ether ( $7\text{ ml}$ ) was stirred at room temperature until the semicarbazone dissolved (for  $30\text{ min}$ ) and evaporated under diminished pressure. The residual lithium salt ( $770\text{ mg}$ ) was dried at  $40^\circ\text{C}/0.1\text{ Torr}$  for  $6\text{ h}$ .

Methyl Glyoxylate Semicarbazone (*Ia*) Silver Salt

The semicarbazone *Ia* (725 mg; 5 mmol) was dissolved with stirring in 0.5M methanolic sodium methoxide (10 ml). After 30 min, powdered silver nitrate (850 mg) was added and the stirring continued at room temperature for 2 h. The precipitate was collected with suction, washed with two 5 ml portions of methanol, three 5 ml portions of water, and finally with ethanol (5 ml), and dried at 50°C/0.1 Torr for 6 h. Yield, 1.25 g of the silver salt.

Ribosylation of Methyl Glyoxylate Semicarbazone (*Ia*)

*A.* A solution of 2,3,5-tri-O-benzoyl-D-ribofuranosyl bromide (2 mmol) in acetonitrile (15 ml) was treated with the mercuric salt of the semicarbazone *Ia* (950 mg), the whole mixture stirred at room temperature for 20 h, and evaporated under diminished pressure. The residue was dissolved in chloroform (50 ml), the solution washed with three 20 ml portions of 10% aqueous potassium iodide and two 20 ml portions of water, dried over anhydrous magnesium sulfate, and evaporated under diminished pressure. The residue was chromatographed on a column of silica gel (particle size, 30–60  $\mu$ ; 160 g) in the solvent system benzene–acetone (4 : 1), 8 ml fractions being taken. Evaporation of fractions 64–67 yielded a gel which was dried by coevaporation with three 2 ml portions of methanol. Yield, 30 mg (2.5%) of compound *Vla* in the form of a powder. UV spectrum (ethanol):  $\lambda_{\max}$  233 and 268 nm ( $\log \epsilon$  4.28 and 4.07),  $\lambda_{\min}$  252 nm ( $\log \epsilon$  3.95). For the IR spectrum see Table VII. CD spectrum (ethanol): 231.5 nm (+49800), sh 255.5 (–27200), 262.5 nm (–29200). For the NMR spectrum see Table II. For  $C_{30}H_{27}N_3O_{10}$  (589.5) calculated: 61.12% C, 4.62% H, 7.13% N; found: 60.91% C, 4.69% H, 7.05% N. Evaporation of fractions 69–78 yielded 130 mg (11%) of the chromatographically homogeneous substance *VIIa* in the form of a foam. UV spectrum (ethanol):  $\lambda_{\max}$  232 and 268 nm ( $\log \epsilon$  4.36 and 4.23),  $\lambda_{\min}$  250 nm ( $\log \epsilon$  4.08). For the IR spectrum see Table VII. CD spectrum (ethanol): 211 nm (–3100), 235 nm (+47100), sh 256.5 nm (+2050). For the NMR spectrum see Tables II and III. For  $C_{30}H_{27}N_3O_{10}$  (589.5) calculated: 61.12% C, 4.62% H, 7.13% N; found: 61.07% C, 4.70% H, 7.07% N. Evaporation of fractions 84–94 yielded 172 mg (14.5%) of the chromatographically homogeneous compound *IV* in the form of a foam. For the IR spectrum see Table V and for the NMR spectrum Table II. Optical rotation:  $[\alpha]_D^{25}$  –25.7° (*c* 0.58, ethyl acetate). For  $C_{30}H_{27}N_3O_{10}$  (589.5) calculated: 61.12% C, 4.62% H, 7.13% N; found: 61.30% C, 4.90% H, 7.01% N. Compound *IV* is identical with the specimen obtained by the silylation process<sup>2</sup>.

*B.* To a solution of 2,3,5-tri-O-benzoyl-D-ribofuranosyl bromide (2 mmol) in acetonitrile (15 ml) there was added the silver salt of the semicarbazone *Ia* (630 mg) and the whole mixture stirred at room temperature for 20 h. The insoluble portion was filtered off and washed with two 10 ml portions of acetonitrile. The filtrate and washings were combined and evaporated under diminished pressure. The residue (1.5 g) was chromatographed on a column of silica gel analogously to paragraph *A*. Evaporation of fractions 62–78 and the subsequent coevaporation of the residue with methanol yielded 248 mg (21%) of compound *Vla*. Fractions 84–90 yielded 30 mg (2.5%) of compound *VIIa*, fractions 98–106 afforded 40 mg (3.5%) of the 2-isomer *IV*.

*C.* To a solution of 2,3,5-tri-O-benzoyl-D-ribofuranosyl bromide (2 mmol) and the lithium salt of the semicarbazone *Ia* (385 mg) in acetonitrile (10 ml) there were added the molecular sieves Potassit 3 (1 g) and the whole mixture was stirred at room temperature for 3 h. The sieves were then filtered off and washed with three 5 ml portions of acetonitrile. The filtrate and washings were combined and evaporated under diminished pressure. The residue was dissolved in chloroform (50 ml), the solution washed with three 15 ml portions of water, dried over anhydrous magnesium sulfate, and evaporated under diminished pressure. The residue (1.3 g) was chromatographed on a column of silica gel (particle size, 30–60  $\mu$ ; 160 g) in the solvent system benzene–

-acetone (4 : 1) to afford 30 mg (2.5%) of compound *VIa*, 380 mg (32%) of compound *VIIa*, and 48 mg (4%) of the 2-isomer *IV*.

#### Methyl Glyoxylate 2-(2,3,5-Tri-O-benzoyl- $\beta$ -D-ribofuranosyl)-4-phenylsemicarbazone (*V*)

Condensation of the mercuric salt of the 4-phenylsemicarbazone *Ib* (920 mg) with 2,3,5-tri-O-benzoyl-D-ribofuranosyl bromide (2 mmol) was performed analogously to that of the semicarbazone *Ia* mercuric salt. Chromatography on a column of silica gel (30–60  $\mu$ ; 150 g) in the solvent system benzene-ethyl acetate (4 : 1) and the subsequent crystallisation from ethanol yielded 276 mg of compound *V*, m.p. 144–146°. Rechromatography of mother liquors and recrystallisation from ethanol yielded additional 72 mg of the same substance. Total yield of compound *V*, 26%. UV spectrum (ethanol):  $\lambda_{\max}$  237 and 274 nm ( $\log \epsilon$  4.23 and 3.99),  $\lambda_{\min}$  263 nm ( $\log \epsilon$  3.97). For the IR spectrum see Table VIII. CD spectrum (ethanol): 223.5 nm (+25900), 239.5 nm (–40600), sh 257 nm (–19900). For the NMR spectrum see Table II. For  $C_{36}H_{31}N_3O_{10}$  (665.6) calculated: 64.96% C, 4.69% H, 6.31% N; found: 64.81% C, 4.77% H, 6.24% N. The compound-*V*-containing eluate was followed by fractions which were evaporated and the residue crystallised from benzene-acetone (5 : 1) to afford 35 mg of compound *IIB*, m.p. 147–149°C, undepressed on admixture with authentic methyl glyoxylate (*Z*)-4-phenylsemicarbazone<sup>1</sup>.

#### Methyl Glyoxylate 4-(2,3,5-Tri-O-benzoyl- $\alpha$ - and $\beta$ -D-ribofuranosyl)-2-methylsemicarbazone (*VIIb* and *VIIb*)

A solution of 2,3,5-tri-O-benzoyl-D-ribofuranosyl bromide (2 mmol) in acetonitrile (15 ml) was stirred with the mercuric salt of the 2-methylsemicarbazone *IIIa* (986 mg) for 12 h at room temperature. The mixture was then evaporated under diminished pressure and the residue dissolved in chloroform (50 ml). The insoluble portion was filtered off and washed with three 5 ml portions of chloroform. The filtrate and washings were combined, shaken with three 20 ml portions of 10% aqueous potassium iodide and two 20 ml portions of water, dried over anhydrous magnesium sulfate, and evaporated under diminished pressure. The residue (1.4 g) was chromatographed on a column of silica gel (particle size, 30–60  $\mu$ ; 200 g) in the solvent system benzene-ethyl acetate (4 : 1) to afford 380 mg (31.5%) of a chromatographically faster pure compound *VIIb* in the form of a foam. UV spectrum (ethanol):  $\lambda_{\max}$  231.5 nm and 273 nm ( $\log \epsilon$  4.33 and 4.23),  $\lambda_{\min}$  250 nm ( $\log \epsilon$  3.94). For the IR spectrum see Table VIII. CD spectrum (ethanol): 213 nm (–6350), 236.5 nm (+46600), sh 261.5 nm (+9500). NMR spectrum, see Table II and III. Optical rotation:  $[\alpha]_D^{25} +120.3^\circ$  ( $c$  0.069, ethyl acetate). For  $C_{31}H_{29}N_3O_{10}$  (603.6) calculated: 61.69% C, 4.84% H, 6.96% N; found: 61.62% C, 4.85% H, 6.92% N. The subsequent fractions yielded 220 mg of a mixture of the two isomers and 270 mg of the chromatographically homogeneous isomer *VIIb*. UV spectrum (ethanol):  $\lambda_{\max}$  231 and 274 nm ( $\log \epsilon$  4.44 and 4.25),  $\lambda_{\min}$  252 nm ( $\log \epsilon$  3.99). For the IR spectrum see Table VIII. CD spectrum (ethanol): 234 nm (+49300), sh 259 nm (–24650), 267 nm (–28000). For the NMR spectrum see Table II. Optical rotation:  $[\alpha]_D^{25} -61.7^\circ$  ( $c$  0.21, ethyl acetate). For  $C_{31}H_{29}N_3O_{10}$  (603.6) calculated: 61.69% C, 4.84% H, 6.96% N; found: 61.46% C, 4.98% H, 6.92% N. Repeated chromatography of the above isomeric mixture on silica gel (particle size, 30–60  $\mu$ ; 50 g) in the above mentioned solvent system afforded additional crops of the isomers *VIIb* (41 mg) and *VIIb* (180 mg). Total yields: 35% of the isomer *VIIb* and 37% of the isomer *VIIb*.

Methyl Glyoxylate 4-(2,3,5-Tri-O-benzoyl- $\alpha$ - and  $\beta$ -D-ribofuranosyl)-2-benzylsemicarbazone (*Vlc* and *Vllc*)

Condensation of the mercuric salt of the 2-benzylsemicarbazone *Illb* (1.18 g) with 2,3,5-tri-O-benzoyl-D-ribofuranosyl bromide (2 mmol) was performed analogously to that of the semicarbazone *Ia* mercuric salt. Chromatography on a column of silica gel (particle size, 30–60  $\mu$ ; 200 g) in the solvent system benzene–acetone (20 : 1) yielded 945 mg (69.5%) of the chromatographically homogeneous compound *Vllc*. UV spectrum (ethanol):  $\lambda_{\max}$  231 and 273 nm (log  $\epsilon$  4.41 and 4.24),  $\lambda_{\min}$  251 nm (log  $\epsilon$  4.04). For the IR spectrum see Table VIII. CD spectrum (ethanol): 220 nm (–6600), 238 nm (+32200), sh 264 nm (+10700). For the NMR spectrum see Tables II and III. Optical rotation:  $[\alpha]_D^{25} +114.0^\circ$  (c 0.52, ethyl acetate). For  $C_{37}H_{33}N_3O_{10}$  (679.65) calculated: 65.38% C, 4.89% H, 6.18% N; found: 65.54% C, 4.94% H, 6.09% N. The subsequent chromatographic fractions yielded 84 mg (6%) of compound *Vlc*. UV spectrum (ethanol):  $\lambda_{\max}$  232 and 273 nm (log  $\epsilon$  4.42 and 4.17),  $\lambda_{\min}$  252 nm (log  $\epsilon$  3.99). For the IR spectrum see Table VIII. CD spectrum (ethanol): 209 nm (+4600), 219 nm (–5100), 235 nm (+53000), sh 256 nm (–29800), 266 nm (–31900). For the NMR spectrum see Table II. Optical rotation:  $[\alpha]_D^{25} -81.2^\circ$  (c 0.26, ethyl acetate). For  $C_{37}H_{33}N_3O_{10}$  (679.65) calculated: 65.38% C, 4.89% H, 6.18% N; found: 65.33% C, 5.08% H, 6.25% N.

*The authors wish to thank Mrs J. Hlaváčková for the excellent assistance and Mr V. Štěrba for elemental analyses. Thanks are also due to Mr P. Formánek for measurement of IR spectra, Dr M. Masojdková for measurement and interpretation of NMR spectra, and Dr I. Frič for measurement of CD spectra.*

## REFERENCES

- Hřebabeký H., Beránek J.: This Journal 40, 2364 (1975).
- Hřebabeký H., Beránek J.: This Journal 40, 2402 (1975).
- Mido Y., Murata H.: Bull. Chem. Soc. Jap. 42, 3372 (1969).
- Mido Y.: Spectrochim. Acta 28A, 1503 (1972).
- Mido Y.: Spectrochim. Acta 29A, 1 (1973).
- Mido Y.: Spectrochim. Acta 29A, 431 (1973).
- Hadži D., Jan J.: Spectrochim. Acta 23A, 571 (1967).
- Hadži D., Jan J.: Rev. Roum. Chim. 10, 1183 (1965).
- Durig J. R., Harris W. C.: J. Chem. Phys. 55, 1735 (1971).
- Kitaev Ju. P., Nivorozhkin I. E., Flegontov S. A., Raevskij O. A., Titova Z. S.: Dokl. Akad. Nauk SSSR 178, 1328 (1968).
- Tabei K., Saitou E.: Bull. Chem. Soc. Jap. 42, 1440 (1969).
- Raevskij O. A., Shagidullin R. R., Kitaev Ju. P.: Dokl. Akad. Nauk SSSR 170, 114 (1966).
- Gabe E. J., Taylor M. R., Glusker J. P., Minkin J. A., Patterson A. L.: Acta Crystallogr. (B) 25, 1620 (1969).
- Mathew M., Palenik G. J.: J. Chem. Soc. (D) 1969, 1086.
- Abramovitch R. A., Spenser I. D.: J. Chem. Soc. 1957, 3767.
- Tanner E. M.: Spectrochim. Acta 15, 20 (1959).
- De Mayo P., Stoessl A.: Can. J. Chem. 38, 950 (1960).
- Yao H. C.: J. Org. Chem. 29, 2959 (1964).
- Elguero J., Jacquier R., Tarrago G.: Bull. Soc. Chim. Fr. 1966, 2981.
- Vénien F., Mandrier C.: Bull. Soc. Sci. Bretagne 46, 161 (1971).
- Bowles A. J., George W. O., Cunliffe-Jones D. B.: J. Chem. Soc. (B) 1970, 1070.

22. George W. O., Hassid D. V., Maddams W. F.: *J. Chem. Soc. Perkin 2*, 400 (1972).
23. Arriau J., Campillo J. - P., Deschamps J., Tarrago G., Jacquier R.: *Bull. Soc. Chim. Fr.* 1973, 1398.
24. Jones G. I. L., Owen N. L.: *J. Mol. Struct.* 18, 1 (1973).
25. Dirlikov S., Štokr J., Schneider B.: *This Journal* 36, 3028 (1971).
26. Katon J. E., Griffin M. G.: *J. Chem. Phys.* 59, 5868 (1973).
27. Jones G. I. L., Summers T. D., Owen N. L.: *J. Chem. Soc. Faraday Trans. 2*, 100 (1974).
28. George W. O., Houston T. E., Harris W. C.: *Spectrochim. Acta* 30A, 1035 (1974).
29. Naves Y. - R., Jacob - Guillarmod A., Zanesco C. R.: *Helv. Chim. Acta* 50, 1461 (1967).
30. Le Goaller R., Arnaud P.: *C. R. Acad. Sci. Ser. B* 264, 800 (1967).
31. Raevskij O. A., Šagidullin R. R., Kitaev Ju. P.: *Zh. Org. Khim.* 1968, 1520.
32. Shagidullin R. R., Sattatova F. K., Raevskij O. A., Budnikov G. K., Kitaev Ju. P.: *Izv. Akad. Nauk SSSR Ser. Khim* 1964, 960.
33. Davison W. H. T., Christie R. E.: *J. Chem. Soc.* 1955, 3389.
34. Karabatsos G. J., Graham J. D., Vane F. M.: *J. Amer. Chem. Soc.* 84, 753 (1962).
35. Karabatsos G. J., Vane F. M., Taller R. A., Hsi N.: *J. Amer. Chem. Soc.* 86, 3351 (1964).
36. Coburn R. A., Dudek G. O.: *J. Phys. Chem.* 72, 1177 (1968).
37. Dyall L. K.: *Aust. J. Chem.* 20, 93 (1967).
38. Stevens J. D., Fletcher H. G.: *J. Org. Chem.* 33, 1799 (1968).
39. Prystaš M.: Unpublished results.
40. Piskala A.: Unpublished results.
41. Wilmhurst J. K., Horwood J. F.: *Aust. J. Chem.* 24, 1183 (1971).
42. Tabei K., Saitou E.: *Bull. Chem. Soc. Jap.* 42, 2693 (1969).

Translated by J. Plíml.