The structure was solved by direct methods. Several stages of the method of least squares within the anisotropic approximation in the total-matrix variant by means of the YANX program (A. N. Nesmeyanov Institute of Heteroorganic Compounds of the Academy of Sciences of the USSR, adapted for an ES computer) led to R = 0.089. All of the hydrogen atoms were localized confidently by differential synthesis. Three stages of the method of least squares with refinement of the position of the hydrogen atoms within the isotropic approximation decreased R to 0.057. The final coordinates of the basis atoms of the structure are presented in Table 2.

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SYNTHESIS AND IDENTIFICATION OF ESTERS OF ISOMERIC TETRAHYDROPYRANYL-SUBSTITUTED 1-ARYLTRIAZOLECARBOXYLIC ACIDS

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The reaction of (2,2-dimethyltetrahydropyran-4-yl)propiolic acid esters with pfluorophenyl azide leads to esters of isomeric tetrahydropyranyl-substituted laryltriazolecarboxylic acids, which were identified by means of conversion to disubstituted triazoles; their structures were proved by physicochemical methods.

In order to create previously unknown biheterocyclic systems — tetrahydropyran derivatives — we synthesized  $\beta$ -(2,2-dimethyltetrahydropyran-4-yl)- $\beta$ -oxopropionic acid and (2,2dimethyltetrahydropyran-4-yl)propiolic acid esters [1, 2] as the starting compounds. When we used the latter as dipolarophiles in cyclization with p-fluorophenyl azide, we obtained mixtures of isomeric 1-(p-fluorophenyl)-4-(2,2-dimethyltetrahydropyran-4-yl)-5-carbethoxyand 1-(p-fluorophenyl)-4-carbethoxy-5-(2,2-dimethyltetrahydropyran-4-yl)triazoles, which were separated by fractional crystallization.

In order to ascertain the spectral characteristics that would make it possible to identify the isomers, we hydrolyzed esters Ia, b to the corresponding acids IIa, b, and the latter were then decarboxylated to isomeric disubstituted triazoles VIIIa, b, which can be readily identified on the basis of known criteria [3, 4].

It is known that in triazoles and some other azoles the proton adjacent to the substituted nitrogen atom is more sensitive to the effects of the solvent [5]. It is also known that when both isomers are present, the resonance signals of the 5-H proton are observed at weaker field than the 4-H signals in both solvents in the PMR spectra recorded in deuterochloroform and dimethyl sulfoxide (DMSO). A large  $\Delta \delta = \delta_{\rm DMSO} - \delta_{\rm CDCl_3}$  difference is characteristic for 1,4-

758

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TABLE 1. Mass Spectra of Triazoles I-III\*

| Com-<br>pound | m/z values (relative intensities, $\mathcal{T}_0$ )  |
|---------------|--|
| Ia            | 347 (11), 332 (10), 319 (38), 302 (10), 274 (10), 274 (14), 273 (23), 234 (26), 188 (60), 113 (18), 111 (100), 95 (18)   |
| IЪ            | 347 (3), 332 (22), 319 (12), 304 (27), 274 (16), 246 (94), 253 (40), 191 (54), 188 (100), 111 (50), 95 (22)  |
| Ha            | 319 (7), 304 (58), 286 (71), 234 (43), 206 (11), 190 (30), 188 (48), 162 (33),<br>113 (12), 111 (100), 95 (30)   |
| IIb           | $\begin{cases} 319 & (4), 304 & (42), 263 & (48), 246 & (50), 233 & (76), 191 & (52), 188 & (100), 161 \\ (52), 113 & (12), 111 & (71), 95 & (40) \end{cases}$ |
| IIIa          | 275 (19), 191 (36), 188 (44), 174 (24), 161 (100), 135 (80), 111 (100), 95 (54)  |
| IIIb          | 275 (9), 191 (93), 189 (92), 161 (100), 137 (43), 135 (50), 111 (86), 95 (27)  |

\*Only the peaks of the molecular and characteristic ions are presented.

disubstituted triazoles. Using these data it was not difficult to show the order of substitution in IIIa and IIIb and hence, correspondingly, to assign the entire series of isomers.



There is no unified point of view relative to the regioselectivity of 1,3-dipolar addition reactions. The opinion that the dominant product is that in which the bulkiest substituents are farthest removed from one another seems to be the most acceptable [6]. This point of view is also confirmed in the case presented above. Primarily isomer Ib (45%) is formed as a result of cyclization.

The UV spectra of triazoles Ia-IIIa differ from the spectra of the isomeric Ib-IIIb series with respect to longer-wave absorption.

The mass spectra of the isomers in the investigated I-III series are qualitatively similar. The difference between the isomers is manifested mainly in a decrease in the intensity of the molecular-ion peak and the increase in the peaks of some fragment ions on passing from isomers Ia and IIa to isomers Ib and IIb (Table 1). To evaluate the quantitative differences in the intensities of the molecular-ion peaks we used the stabilities of the molecular ions with respect to electron impact (Table 2).

It is apparent from Table 2 that the stability of the molecular ion decreases by a factor of approximately four on passing from isomer Ia to isomer Ib; a similar decrease by a factor of two is observed for the IIa, b isomer pair, while the stabilities are approximately the same for isomers IIa, b. Thus one can distinguish the isomers by using the  $W_m(a)/W_m(b)$  ratios in the triazole series Ia, b and IIa, b. It is difficult to predict how general this tendency is for trisubstituted triazoles with substituents of another type.

It is interesting to note that when compounds of the Ia-IIIa series are compared with isomeric Ib-IIIb, larger  $R_{\rm f}$  values and lower melting points are observed for the former.

The compounds obtained did not display biologically activity.

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TABLE 2.  $W_{\rm m}$  Values for Triazoles I-III

| Com-<br>pound .                        | Wm   | W <sub>m(a)</sub> /  |
|--|--|----------------------|
| Ia<br>Ib<br>IIa<br>IIb<br>IIIa<br>IIIb | 1,17<br>0,29<br>0,66<br>0,38<br>1,12<br>1,03 | 4,03<br>1,74<br>1,08 |

## EXPER IMENTAL

The IR spectra of mineral oil suspensions of the compounds were recorded with a UR-20 spectrometer. The PMR spectra were recorded with a Varian T-60 spectrometer. The UV spectra of solutions in ethanol were recorded with a Specord UV-vis spectrophotometer. The mass spectra were obtained with an MKh-1303 spectrometer with an ionizing voltage of 70 eV. Thin-layer chromatography was accomplished on KSK silica gel (80-100  $\mu$ m).

 $\frac{1-(p-Fluoropheny1)-4-carbethoxy-5-(2,2-dimethyltetrahydropyran-4-y1)- and 1-(p-Fluoropheny1)-5-carbethoxy-4-(2,2-dimethyltetrahydropyran-4-y1)triazoles (Ia, b). A mixture of 3.5 g (10 mmole) of ethyl 2,2-dimethyltetrahydropyran-4-propiolate and 1.37 g (10 mmole) of p-fluoropheny1 azide in 80 ml of toluene was refluxed for 24 h, after which the solvent was removed by distillation, the residue was dissolved in 150 ml of hot petroleum ether, and the solution was allowed to stand overnight. It was then filtered to give 1.1 g (21%) of triazole Ia with mp 130-131°C and R<sub>f</sub> 0.37 [ether-petroleum ether (3:1)]. IR spectrum: 1720 cm<sup>-1</sup> (C=O). UV spectrum: <math>\lambda_{max}$  232 nm (log  $\varepsilon$  3.73). PMR spectrum (CC14): 1.18 (s, 6H, 2-CH<sub>3</sub>), 1.48 (t, 3H, CH<sub>3</sub>), 1.90 (m, 4H, 3- and 5-CH<sub>2</sub>), 3.65 (s, 3H, 4-CH and O-CH<sub>2</sub>), 4.5 (q, 2H, CH<sub>2</sub>), and 7.35 ppm (m, 4H, aromatic protons). Found: C 62.4; H 6.5; N 12.1%. C<sub>18</sub>H<sub>22</sub>FN<sub>3</sub>O<sub>3</sub>. Calculated: C 62.2; H 6.4; N 12.1%.

The petroleum ether was evaporated, the residue was dissolved in hot cyclohexane, and the solution was allowed to stand overnight. The precipitated crystals were removed by filtration to give 2.4 g (45%) of triazole Ib with mp 120-121°C and R<sub>f</sub> 0.49 [ether-petroleum ether (3:1)]. IR spectrum: 1720 cm<sup>-1</sup> (C=O). UV spectrum:  $\lambda_{max}$  246 nm (log  $\varepsilon$  3.64). PMR spectrum (CCl<sub>4</sub>): 1.32 (s, 6H, 2-CH<sub>3</sub>), 1.20 (t, 3H, CH<sub>3</sub>), 1.90 (m, 4H, 3- and 5-CH<sub>2</sub>), 3.80 (m, 3H, 4-CH and O-CH<sub>2</sub>), 4.30 (q, 2H, CH<sub>2</sub>), and 7.35 ppm (m, 4H, aromatic protons). Found: C 62.3; H 6.4; N 12.2%. C<sub>18</sub>H<sub>22</sub>FN<sub>3</sub>O<sub>3</sub>. Calculated: C 62.2; H 6.4; N 12.1%.

 $\frac{1-(p-Fluoropheny1)-5-(2,2-dimethyltetrahydropyran-4-y1)triazole-4-carboxylic Acid (IIa).}{A solution of 0.112 g (2 mmole) of potassium hydroxide in 0.5 ml of water was added to a solution of 0.35 g (1 mmole) of triazole Ia in 100 ml of ethano1, and the mixture was refluxed on a water bath. The alcohol was removed by distillation, 10 ml of water was added, and the aqueous solution was washed with ether and made slightly acidic with hydrochloric acid. The reaction product was extracted with benzene, and the extract was dried with sodium sulfate. The solvent was removed, and the residue was crystallized to give 0.28 g (88%) of acid IIa with mp 196-197°C (from ether) and R<sub>f</sub> 0.37 [acetic acid-cyclohexane (3:2)]. IR spectrum: 1700 cm<sup>-1</sup> (C=O). UV spectrum: <math>\lambda_{max}$  212 nm (log  $\varepsilon$  4.2). PMR spectrum (CDCl<sub>3</sub>): 1.20 [s, 3H, 2-CH<sub>3</sub> (a)], 1.24 [s, 3H, 2-CH<sub>3</sub> (e)], 1.90 (m, 4H, 3- and 5-CH<sub>2</sub>), 3.74 (m, 3H, 4-H and O-CH<sub>2</sub>), 7.36 (m, 4H, aromatic protons), and 11.00 ppm (broad s, 1H, OH). Found: C 60.8; H 6.0; N 13.5%. C<sub>16</sub>H<sub>18</sub>FN<sub>3</sub>O<sub>3</sub>. Calculated: C 60.2; H 5.7; N 13.2%.

 $\frac{1-(p-Fluoropheny1)-4-(2,2-dimethyltetrahydropyran-4-y1)triazole-5-carboxylic Acid (IIb).}{\text{The similar reaction of 0.35 g of triazole IIb gave 0.17 g (53%) of acid IIb with mp 157-158°C (from hexane) and Rf 0.50 [acetic acid-cyclohexane (3:2)]. IR spectrum: 1700 cm<sup>-1</sup> (C=0). UV spectrum: <math>\lambda_{\text{max}}$  233 nm (log  $\varepsilon$  4.03). PMR spectrum (CDCl<sub>3</sub>): 1.24 [s, 3H, 2-CH<sub>3</sub> (a)], 1.28 [s, 3H, 2-CH<sub>3</sub> (e)], 1.82 (m, 4H, 3- and 5-CH<sub>2</sub>), 3.80 (m, 3H, 4-H and 0-CH<sub>2</sub>), 7.28 (m, 4H, aromatic protons), and 11.00 ppm (broad s, 1H, OH). Found: C 60.1; H 5.8; N 13.1%. C<sub>16</sub>H<sub>18</sub>FN<sub>3</sub>O<sub>3</sub>.

1-(p-Fluoropheny1)-5-(2,2-dimethyltetrahydropyran-4-yl)triazole (IIIa). A 0.15-g (0.5 mmole) sample of acid IIa was heated at 210-220°C until carbon dioxide evolution ceased. The reaction product was extracted with absolute ether, and the solvent was removed by distillation

to give 0.12 g (92%) of triazole IIIa with mp 119-120°C and R<sub>f</sub> 0.41 [cyclohexane-acetone (7:3)]. IR spectrum:  $3120 \text{ cm}^{-1}$  (C-H). UV spectrum:  $\lambda_{\text{max}}$  250 nm (log  $\varepsilon$  4.22). PMR spectrum (CDCl<sub>3</sub>): 1.06 [s, 3H, 2-CH<sub>3</sub> (a)], 1.10 [s, 3H, 2-CH<sub>3</sub> (e)], 1.52 (m, 4H, 3- and 5-CH<sub>2</sub>), 3.00 (m, 1H, 4-H), 3.64 (m, 2H, O-CH<sub>2</sub>), 7.34 (m, 4H, aromatic protons), and 7.58 (s, 1H, triazole ring 5-H). PMR spectrum (d<sub>6</sub>-DMSO): 1.06 [s, 3H, 2-CH<sub>3</sub> (a)], 1.10 [s, 3H, 2-CH<sub>3</sub> (a)], 1.10 [s, 3H, 2-CH<sub>3</sub> (e)], 1.54 (m, 4H, 3- and 5-CH<sub>2</sub>), 2.54 (m, 1H, 4-H), 3.58 (m, 2H, O-CH<sub>2</sub>), 7.60 (m, 4H, aromatic protons), and 7.80 ppm (s, 1H, triazole ring 5-H). Found: C 65.2; H 6.8; N 15.1%. C<sub>15</sub>H<sub>18</sub>FN<sub>3</sub>O. Calculated: C 65.4; H 6.6; N 15.3%.

 $\frac{1-(p-Fluoropheny1)-4-(2,2-dimethyltetrahydropyran-4-y1)triazole (IIIb).$  The similar reaction of 0.1 g (0.3 mmole) of acid IIb gave 0.08 g (93%) of triazole IIIb with mp 108-109°C and Rf 0.54 [cyclohexane-acetone (7:3)]. IR spectrum: 3150 cm<sup>-1</sup> (C-H). UV spectrum:  $\lambda_{max}$  250 nm (log  $\varepsilon$  4.22). PMR spectrum (CDCl<sub>3</sub>): 1.24 [s, 3H, 2-CH<sub>3</sub> (a)], 1.28 [s, 3H, 2-CH<sub>3</sub> (e)], 1.82 (m, 4H, 3- and 5-CH<sub>2</sub>), 3.28 (m, 1H, 4-H), 3.822 (m, 2H, 0-CH<sub>2</sub>), 7.50 (m, 4H, aromatic protons), and 7.70 ppm (s, 1H, triazole ring 4-H). PMR spectrum (d<sub>6</sub>-DMSO): 1.22 [s, 3H, 2-CH<sub>3</sub> (a)], 1.26 [s, 3H, 2-CH<sub>3</sub> (e)], 1.64 (m, 4H, 3- and 5-CH<sub>2</sub>), 3.20 (m, 1H, 4-H), 3.66 (m, 2H, 0-CH<sub>2</sub>), 7.70 (m, 4H, aromatic protons), and 8.60 ppm (s, 1H, triazole ring 4-H). Found: C 65.5; H 6.3; N 15.5%. C<sub>15</sub>H<sub>18</sub>FN<sub>3</sub>O. Calculated: C 65.4; H 6.6; N 15.3%.

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