THE CHEMISTRY OF PYRAZOLIDINE.

XIII. Thin Layer Chromatography of 3,5-Dioxopyrazolidines on Alumina*

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The conditions for the thin-layer chromatographic separation of some groups of 3,5-dioxopyrazolidines on alumina have been established. It is shown that the chromatographic behavior of these compounds depends mainly on their ability to undergo keto-enol and lactim-lactam tautomerism.

While carrying out investigations into the chemistry of 3,5-dioxopyrazolidines (DOP), we have investigated the thin-layer chromatographic behavior on alumina of various derivatives of this type. In choosing the chromatographic conditions, the presence in the molecule of the CO and NH groups, and their ability to undergo keto-enol and lactim-lactam tautomerism, were taken into account. The DOP derivatives were divided into the following groups: 1, 2, 4, 4-tetrasubstituted, with the "fixed" diketo-form (compounds I–IX, first group); 1, 2, 4, 4-trisubstituted, capable of keto-enol tautomerism (compounds X–XVI, second group); 4, 4-disubstituted, capable of lactim-lactam tautomerism (compounds XVII–XIX, third group); 1-mono- and 1, 4-disubstituted, with the "fixed" diketo-form (compounds XXI–XXXI, fourth group); and 4-ylidene derivatives of 1, 2-diphenyl-DOP, which exist in the fixed diketo form (compounds XXXII–XXXVI, fifth group) (Tables 1 and 2).

The adsorbability of compounds of the first group is comparatively low, since they exist in the fixed diketo form. The $R_f$ values of these compounds, therefore, lie between 0.6 and 0.7 even using active alumina and solvent systems of low polarity (benzene–chloroform, 1:3). Use of methanol increases the $R_f$ values to 0.8–0.9, and the spots become less compact. The nature of the substituents (alkyl, aryl, aralkyl, halogen) has little effect on the $R_f$ values. The most strongly adsorbed compound is 4, 4-dichloro-1, 2-diphenyl-DOP (IX), possibly as a result of the less shielded carbonyl group.

Compounds of the second group are of similar acidity to the aliphatic carboxylic acids [1], and they are somewhat more strongly adsorbed than those of the first group. Therefore, they hardly move on alumina of grade III activity, even in methanol. Only on changing to adsorbent of grade V activity, and using methanol, do the $R_f$ values fall within the optimal region (0.5–0.7). The $R_f$ values of compounds X–XVI under these conditions are very similar, and it is found more convenient for the separation of the compounds of this group to use acid adsorbents. On alumina with 2% acetic acid, using benzene–chloroform (1:3), we have successfully separated 4-phenyl- (XIII), 4-dimethylaminomethyl- (XVI), and 4-unsubstituted (X) compounds from the 4-alkyl substituted compounds (XI, XII, XIV, and XV). Compounds X, XIII, and XVI are well-separated on this adsorbent when methanol is used. On more acid adsorbents, the $R_f$ values of all the compounds were close to 1. Only the 4-dialkylaminoalkyl-com- pounds XV and XVI moved more slowly than the other compounds under these conditions, and could be separated from them.

In comparing the $R_f$ values of compounds of the second group with their $pK$ values, a direct relationship is observed in some cases between reduction in acidity and increase in $R_f$ (compounds XII–XIV). At the same time, compounds X–XII, which have very similar $pK$ values, differ markedly in their adsorbability. This may be explained by the shielding of the enol hydroxy group by the alkyl groups in XI and XII, in a similar way to that shown for o-alkylphenols [2]. The increased adsorbability of XIII may be explained as being due to the presence of a phenyl ring in the 4-position, which is apparently in the same plane as the 3,5-dioxopyrazolidine ring, thus creating favorable conditions for the interaction with the adsorbent.

Compound XIX, which contains an NH group and is capable of forming a hydoxy-imine, behaves similarly to compounds of the second group. The adsorbability of XVII and XVIII is greatly increased by the presence in their molecules of two NH groups. These compounds do not move on grade V alumina even in methanol, but they are well-separated on alumina containing 2% acetic acid using methanol, or on alumina containing 10% acetic acid, using benzene–chloroform (1:3).

Compounds of the fourth group are adsorbed as strongly as XVII and XVIII, and they move only on acid adsorbents. The introduction of phenyl or alkyl substituents in the 4-position of 1-phenyl-DOP leads to increased mobility in these compounds, with 1, 4-diphenyl-DOP (XXII) being characteristically less mobile than 1-phenyl–4-butyl-DOP (XXI).

1, 2-Diphenyl-DOP (X), the isomer of XXII in which both phenyl radicals are noncoplanar with the heterocyclic ring, possesses greater $R_f$ values under all the chromatographic conditions examined.

Compounds of the fifth group occur in the fixed diketo form, but in contrast to the first group, they have a semi-cyclic double bond in the 4-position of the heterocyclic ring. The latter apparently favors interaction of the molecule with the adsorbent. Compounds XXXIII–XXXVI, which are closest in size to the group I compounds, are therefore adsorbed much more strongly than the latter (Tables 1 and 2). Thus, XXXIII–XXXVI on grade III alumina move only in the polar solvent methanol,
**Table 1**

\( R_f \times 100 \) of Substituted DOP’s

<table>
<thead>
<tr>
<th>Compound</th>
<th>( R' )</th>
<th>( R'' )</th>
<th>Chromatographic conditions a</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
<th>G</th>
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<td>( \text{C}_6\text{H}_5 )</td>
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- Chromatographic systems: A) grade III activity, methanol; B) grade III activity, benzene-chloroform (1:3); C) grade V activity, methanol; D) grade II activity + 2% glacial acetic acid, benzene-chloroform (1:3); E) grade II activity + 2% glacial acetic acid, methanol; F) grade V activity + 5% glacial acetic acid, benzene; G) grade V activity + 10% glacial acetic acid, benzene-chloroform (1:3).

- \( pK_a \) values [1]: X 5.3; XI 5.4; XI1 5.2; XttI 2.9; IV 5.1.

**Table 2**

\( R_f \times 100 \) for 4-Ethylidene- and 4-Benzylidene-derivatives of 1,2-Diphenyl-DOP

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