

## Gas chromatography of carbamates

### X. N-(*p*-Toluenesulfonyl) derivatives

This investigation was undertaken in order to examine the gas chromatographic behavior of a new class of carbamate compounds, namely the N-*p*-toluenesulfonyl (tosyl) derivatives. Related structures such as ethyl benzenesulfonyl carbamates<sup>1</sup> and N-(*p*-tosyl)-urethans<sup>2</sup> have been studied as potential oral hypoglycemic agents. Likewise, *para*-substituted benzenesulfonyl carbamates have stimulated interest for herbicidal applications<sup>3</sup>.

The thin-layer chromatography of N-(*p*-tosyl)-carbamates has recently been reported<sup>4</sup>; gas chromatographic analysis of these derivatives however, has as yet been unreported.

#### *Experimental*

The N-(*p*-tosyl) derivatives were synthesized via reaction of *p*-toluenesulfonyl isocyanate with a selection of alcohols and substituted phenols according to the method of MCFARLAND AND HOWARD<sup>5</sup>. The compounds were recrystallized from benzene-petroleum ether, and their melting points measured on a Fisher-Johns melting point apparatus. The melting points are reported in a previous paper<sup>4</sup>. Gas chromatography was carried out on a 5.5 ft. × 0.25 in. O.D. copper coil column packed with 12% SE-30 on 60-80 mesh HMDS-pretreated Chromosorb W, which was housed in an F & M Model 720 dual column oven containing a hot-wire detector, coupled to an F & M Model 500 gas chromatograph. Specific operating conditions are given in the footnotes to Table I.

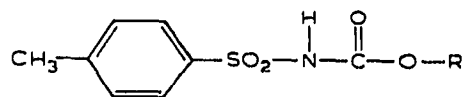
#### *Results and discussion*

The gas chromatographic retention data for the alkyl, cyclic and substituted aryl N-(*p*-tosyl)-carbamates are given in Table I. With the exception of the methyl, ethyl, allyl and propyl derivatives, all carbamates were observed to cleave thermally with the release of the parent alcohol or phenol and *p*-toluenesulfonamide. The *tert*.-butyl derivative revealed only the latter component with the *tert*.-butyl alcohol fragment eluting in the solvent front. All other carbamates produced both alcohol (or phenol) and sulfonamide components on the chromatogram with the exception of the tetra- and pentachlorophenyl carbamates for which no phenol peak was observed. The above comments apply to Conditions I (175°) of Table I. Under Conditions II (225°), all carbamates chromatographed revealed only the *p*-toluenesulfonamide peak.

For comparative purposes, a group of substituted aryl N-(*p*-tolyl)-carbamates were analyzed. The results are reported relative to *p*-toluenesulfonamide in Table II. These derivatives were also found to be unstable to gas chromatographic analysis as observed by the production of the respective phenols and *p*-toluidine on the chromatogram.

In an attempt to stabilize such derivatives (tosyl and tolyl) against thermal lysis, several derivatives were N-trimethylsilylated via reaction of the carbamates with HMDS in pyridine, catalyzed by trimethylchlorosilane; or alternately by N-(trimethylsilyl)-acetamide, as per the following reactions:

TABLE I

GAS CHROMATOGRAPHY OF N-(*p*-TOSYL)-CARBAMATES

| <i>R</i>                       | Relative retention <sup>a</sup> |                   |                            |
|--------------------------------|---------------------------------|-------------------|----------------------------|
|                                | Conditions I <sup>b</sup>       |                   | Conditions II <sup>c</sup> |
|                                | Carbamate                       | Alcohol or phenol | Carbamate                  |
| <i>Alkyl</i>                   |                                 |                   |                            |
| Methyl                         | 0.40                            | d                 | f                          |
| Ethyl                          | 0.40                            | d                 | f                          |
| Allyl                          | 0.39                            | d                 | f                          |
| Propyl                         | 0.41                            | d                 | f                          |
| <i>tert.</i> -Butyl            | 1.00                            | d                 | f                          |
| Amyl                           | 0.030 <sup>e</sup>              | 0.030             | f                          |
| Octyl                          | 0.090 <sup>e</sup>              | 0.090             | f                          |
| <i>Cyclic</i>                  |                                 |                   |                            |
| Cyclopentyl                    | 0.031 <sup>e</sup>              | 0.031             | f                          |
| Cyclohexyl                     | 0.049 <sup>e</sup>              | 0.049             | f                          |
| <i>Aryl</i>                    |                                 |                   |                            |
| Phenyl                         | 0.051 <sup>e</sup>              | 0.051             | f                          |
| <i>o</i> -Cl $\phi$            | 0.074 <sup>e</sup>              | 0.074             | f                          |
| <i>m</i> -Cl $\phi$            | 0.15 <sup>e</sup>               | 0.15              | f                          |
| <i>p</i> -Cl $\phi$            | 0.15 <sup>e</sup>               | 0.15              | f                          |
| 2,3-Cl <sub>2</sub> $\phi$     | 0.16 <sup>e</sup>               | 0.16              | f                          |
| 2,4-Cl <sub>2</sub> $\phi$     | 0.15 <sup>e</sup>               | 0.15              | f                          |
| 2,5-Cl <sub>2</sub> $\phi$     | 0.15 <sup>e</sup>               | 0.15              | f                          |
| 2,6-Cl <sub>2</sub> $\phi$     | 0.16 <sup>e</sup>               | 0.16              | f                          |
| 3,4-Cl <sub>2</sub> $\phi$     | 0.41 <sup>e</sup>               | 0.41              | f                          |
| 3,5-Cl <sub>2</sub> $\phi$     | 0.30 <sup>e</sup>               | 0.30              | f                          |
| 2,4,5-Cl <sub>3</sub> $\phi$   | 0.32 <sup>e</sup>               | 0.32              | f                          |
| 2,4,6-Cl <sub>3</sub> $\phi$   | 0.29 <sup>e</sup>               | 0.29              | f                          |
| 2,3,4,6-Cl <sub>4</sub> $\phi$ | — <sup>e</sup>                  | —                 | f                          |
| Cl <sub>5</sub> $\phi$         | — <sup>e</sup>                  | —                 | f                          |
| Benzyl                         | 0.080 <sup>e</sup>              | 0.080             | f                          |
| Phenethyl                      | 0.12 <sup>e</sup>               | 0.12              | f                          |
| <i>p</i> -Anisyl               | 0.28 <sup>e</sup>               | 0.28              | f                          |
| 3,4-MDO-Phenyl                 | 0.23 <sup>e</sup>               | 0.23              | f                          |
| 3,4-MDO-Benzyl                 | 0.37 <sup>e</sup>               | 0.37              | f                          |

<sup>a</sup> Relative to *p*-toluenesulfonamide as 1.00, which eluted at 16.20 min under Conditions I and at 4.25 min under Conditions II.

<sup>b</sup> Column temperature 175°; injector temperature 200°; bridge 175 mA; helium carrier 33 ml/min. Column: 12% SE-30 on 60–80 mesh HMDS-pretreated Chromosorb W, 5.5 ft. × 0.25 in. O.D. copper coil column.

<sup>c</sup> Same as Conditions I, except: column temperature 225°.

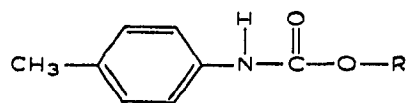
<sup>d</sup> Eluted in solvent front.

<sup>e</sup> Also a peak at 1.00 (*p*-toluenesulfonamide).

<sup>f</sup> Only peak for *p*-toluenesulfonamide at 4.125 min was observed. Alcohol/phenol carbamate components eluted in the solvent front.

— = not detected.

TABLE II  
N-(*p*-TOLYL)-CARBAMATES



| <i>R</i>                       | Relative retention <sup>a</sup> |
|--------------------------------|---------------------------------|
| Phenyl                         | 0.051 <sup>b</sup>              |
| <i>o</i> -Cl $\phi$            | 0.074 <sup>b</sup>              |
| <i>m</i> -Cl $\phi$            | 0.15 <sup>b</sup>               |
| <i>p</i> -Cl $\phi$            | 0.15 <sup>b</sup>               |
| 2,3-Cl <sub>2</sub> $\phi$     | 0.16 <sup>b</sup>               |
| 2,4-Cl <sub>2</sub> $\phi$     | 0.15 <sup>b</sup>               |
| 2,5-Cl <sub>2</sub> $\phi$     | 0.15 <sup>b</sup>               |
| 2,6-Cl <sub>2</sub> $\phi$     | 0.16 <sup>b</sup>               |
| 3,4-Cl <sub>2</sub> $\phi$     | 0.41 <sup>b</sup>               |
| 3,5-Cl <sub>2</sub> $\phi$     | 0.30 <sup>b</sup>               |
| 2,4,6-Cl <sub>3</sub> $\phi$   | 0.29 <sup>b</sup>               |
| 2,3,4,6-Cl <sub>4</sub> $\phi$ | <sup>c</sup>                    |
| Cl <sub>5</sub> $\phi$         | <sup>c</sup>                    |
| Benzyl                         | 0.080 <sup>b</sup>              |

<sup>a</sup> Relative to *p*-toluenesulfonamide. Column and conditions: same as for Conditions I of Table I.

<sup>b</sup> Second peak at 0.097 corresponding to the retention of *p*-toluidine.

<sup>c</sup> Only peak at 0.097 corresponding to *p*-toluidine was detected.

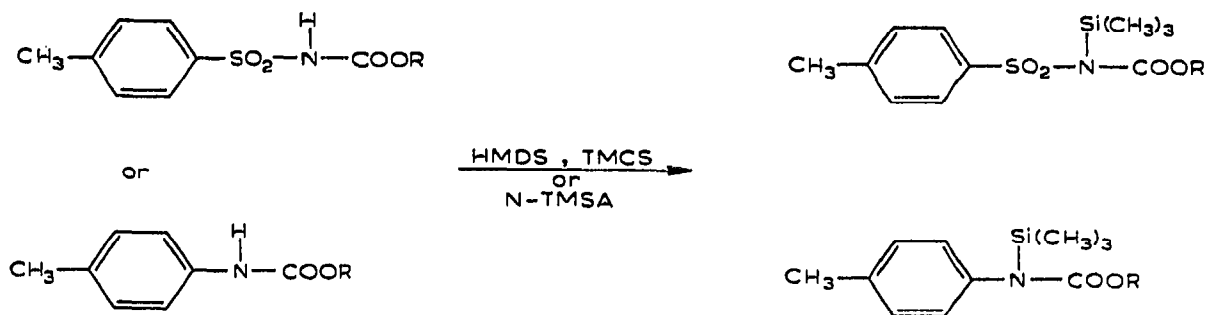
TABLE III

INFLUENCE OF SUBSTITUENT POSITION ON DEGREE OF SILYLATION OF MONOCHLOROPHENYL N-(*p*-TOLYL)-CARBAMATES

| Silylated compound             | Relative peak areas (%)                                 |  |
|--------------------------------|---|--|
|                                | Peak No. 1<br>( <i>p</i> -toluidine)                    | Peak No. 2<br>( <i>N</i> -trimethylsilyl- <i>p</i> -toluidine) |
|                                |   |  |
| <i>R</i> = <i>o</i> -Cl $\phi$ | Rep 1 83.8<br>Rep 2 81.7<br>Rep 3 82.9<br>(Mean) (82.9) | 16.2<br>18.3<br>17.1<br>(17.1)                                 |
| <i>R</i> = <i>m</i> -Cl $\phi$ | Rep 1 60.4<br>Rep 2 59.5<br>(Mean) (60.0)               | 39.6<br>40.5<br>(40.0)   |
| <i>R</i> = <i>p</i> -Cl $\phi$ | Rep 1 49.5<br>Rep 2 50.9<br>(Mean) 50.2                 | 50.5<br>49.1<br>(49.8)   |

Relative degree of silylation, *o*:*m*:*p* = 1.00:2.34:2.91

Relative degree of steric hindrance: *o*/*m* 1.38; *o*/*p* 1.65; *m*/*p* 1.19



This endeavor was in vain, however, and the silyl derivatives were observed to cleave also. An interesting piece of information was obtained, nonetheless.

It was found upon silylation of the isomeric monochlorophenyl N-(*p*-tolyl)-carbamates that the substituent position influenced the degree of silyl attack, as observed by measuring the relative peak areas produced on the chromatogram for the *p*-toluidine and N-trimethylsilyl-*p*-toluidine components released upon analysis of these silylated carbamates. These data are given in Table III. The relative percentage of N-trimethylsilyl-*p*-toluidine (peak No. 2) observed, was taken as a quantitative indication of the degree of the silylation reaction given above. The degree of steric hindrance by the position of the chloro atom towards the reaction was observed to be *ortho* > *meta* > *para* as per the figures given in Table III. This observation presents an interesting application of gas chromatography in measuring steric influences in organic reactions.

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