Mass Spectra of Some 5-Substituted 1-Phenyl and 1-Phenyl-4-methyltetrazolines (1)

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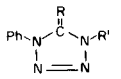
We wish to report the first evidence for specific mass spectral fragmentations of the tetrazoline ring system. Several compounds were prepared by previously documented procedures and all compounds were identified structurally by standard methods.



I	R = O		R' = H
II	R = O		R' = CH_3
III	R = S		R' = H
IV	R = NH		R' = CH_3
V	R = NCH_3		R' = CH_3

The mass spectral data for compounds I-V are shown in the Table. Molecular ions were observed in all instances and were > 6% of the base peak. Only minimal fragment peaks were observed between the molecular ion and the base peak and these peaks had m/e ratios which could not be explained by loss of Ph, R, or R'.

Major fragments were observed for phenylisocyanate from I and II, phenylisothiocyanate from the thione, III, and phenylcarbodiimides from the 5-iminotetrazolines, IV and V. These fragments represented the base peaks in all of the compounds studied. Evidence to support these

fragmentations results from the observation of an F and F + 2 fragment cluster in the mass spectrum of III. The F + 2 fragment (m/e 137) was 5% of F (m/e 135) which established the presence of one sulfur atom. Comparison of the intensities of the m/e 119 and 91 peaks of I and II with those of phenyl isocyanate (2) and phenyl azide (3) indicates that fragmentation of I and II to phenyl isocyanate is predominant. The mass of the neutral portion left no alternative in the structural assignment and fragmentation pathway. This type of fragmentation may be useful in the structure elucidation of compounds containing the tetrazoline ring in a similar environment.

In addition to being useful in structure elucidation, these fragmentations are significant since they represent retro-1,3-dipolar cycloadditions induced by electron impact. Only a few examples of such electron impact induced reactions have been reported (4,5,6). The thermal retro-1,3-dipolar cycloaddition of 1-alkyl-4-sulfonyltetrazolin-5-ones has been reported (7).

Earlier work on substituted tetrazoles (8) indicated the loss of $HN_2^{\cdot}$ as verified by deuterium labeling. Loss of N_2 has been observed in the mass spectra of tetrazoles (9) and of metal organic complexes containing a tetrazoline ring (10). Such fragmentations were not observed in the tetrazolines we investigated.

EXPERIMENTAL

Melting points were taken on a Thomas Hoover capillary melting point apparatus and are uncorrected. The ir spectra were obtained with a Perkin-Elmer 700 infrared spectrophotometer. The nmr spectra were obtained with a 60 MHz Varian A-60A spectrophotometer. Tetramethylsilane was used as an external standard. All mass spectra were run on a Finnigan 3000 quadrupole mass spectrometer at 70 eV. The ion source temperature was 175°. The variable temperature solid probe which was used to introduce samples was not heated. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tennessee.

1-Phenyltetrazolin-5-one (I).

The procedure used was a modification of that reported by Horwitz, Fisher, and Tomasewski (11). Sodium azide (58.5 g., 0.90 mole) was placed in a 1000 ml. round bottomed flask. Three solutions, each containing 14.7 g. (0.11 mole) of anhydrous aluminum chloride in 100 ml. of tetrahydrofuran, were added. An additional 100 ml. of tetrahydrofuran was added and the mixture was brought to reflux. After 1 hour the mixture was cooled to room temperature and a solution of 35.6 g. (0.30 mole) of phenyl isocyanate in 200 ml. of tetrahydrofuran was added. The mixture was maintained at reflux for 24 hours. After the mixture had cooled to room temperature, 60 ml. of 6*N* hydrochloric acid was added. The solvent was then removed under vacuum. To the residue was added 600 ml. of 5% sodium hydroxide and the mixture was stirred for 1 hour. A small amount of insoluble material was removed by filtration. Acidification of the filtrate with 6*N* hydrochloric acid produced a colorless solid which was isolated by filtration washed with water, and air dried. The yield was 30.0 g. (62%), m.p. 189-190° dec., lit. m.p. (11), 189-190° dec.; ir (nujol mull) 1705, 1595, 1350, 1170, 1150, 1060, 750, 730, and 680 cm^{-1}.

Table

Major Fragmentations for Substituted Tetrazolines I-V

Compound	Molecular Ion m/e (% Base Peak)	Base Peak m/e	Other Important Fragments m/e (% of Base Peak)
I	162 (6)	119	91 (72), 65 (12), 64 (71), 63 (33), 52 (12), 51 (28), 50 (19), 43 (14), 41 (14), 39 (31), 38 (33), 37 (18), 27 (13), 15 (10),
II	176 (9)	119	91 (50), 77 (12), 64 (33), 63 (13), 51 (21), 39 (16), 38 (12), 15 (22),
III	178 (86)	135	118 (34), 91 (34), 77 (70), 64 (16), 51 (30), 36 (13),
IV	175 (13)	118	119 (11), 91 (37), 77 (35), 65 (12), 64 (28), 63 (13), 56 (12), 51 (31), 50 (10), 43 (13), 41 (12), 39 (21), 38 (11), 29 (11),
V	189 (15)	132	160 (13), 133 (15), 131 (28), 91 (87), 77 (81), 70 (19), 69 (27), 65 (23), 64 (38), 63 (20), 52 (11), 51 (60), 50 (20), 44 (12), 43 (72), 42 (55), 41 (20), 39 (32), 38 (15), 15 (96)

1-Phenyl-4-methyltetrazolin-5-one (II).

A mixture of 12.5 g. (0.077 mole) of I and 9.7 g. (0.077 mole) of dimethyl sulfate was heated on a hot plate until an enothermic reaction occurred and for 30 minutes thereafter. After the mixture had cooled to room temperature, 50 ml. of 6*N* sodium hydroxide was added. The product solidified when the mixture was cooled in an ice bath. The product was isolated by suction filtration and recrystallized from 95% ethanol. The yield of II was 7.0 g. (51%), m.p. 71-72°, lit. m.p. (12) 72°; ir (nujol mull): 1720, 1590, 1495, 1425, 1385, 1270, 1135, 1045, 800, 760, 725, and 685 cm^{-1}; nmr (carbon tetrachloride): 3.49 δ (s, 3H, CH_3), 7.0-7.9 δ (m, 5 H, aromatic H's).

Anal. Calcd. for $C_8H_8N_4O$: C, 54.54; H, 4.58; N, 31.80. Found: C, 54.34; H, 4.61; N, 31.55.

1-Phenyltetrazoline-5-thione (III).

The procedure reported by Lieber and Ramachandran (13) was used, yield 16.0 g. (90%), m.p. 149-150° dec., lit. m.p. (13) 150°; ir (nujol mull): 1590, 1490, 1360, 1320, 1300, 1270, 1210, 1160, 1105, 1095, 1075, 1050, 990, 910, 800, 750, 690, 680, and 660 cm^{-1}.

1-Phenyl-4-methyl-5-iminotetrazoline (IV).

A mixture of 1.61 g. (0.01 mole) of 1-phenyl-5-aminotetrazole (14) and 1.26 g. (0.01 mole) of dimethyl sulfate in 25 ml. of benzene was maintained at reflux for 3 hours. After cooling, the solid which had formed was isolated by filtration and treated with 25 ml. of concentrated ammonium hydroxide. The mixture was extracted with three 25 ml. portions of diethyl ether. The combined ether extracts were dried over calcium chloride and the solvent was removed under vacuum, yield, 0.50 g. (29%), m.p. 56-57°, ir (nujol mull): 3340, 1650, 1600, 1510, 1230, 1140, 1080, 1030, 800, 770, 720, and 700 cm^{-1}; nmr (carbon tetrachloride): 3.44 δ (s, 3H, CH_3), 4.60 δ (s, 1H, NH), 7.0-7.8 δ (m, 5H, aromatic H's).

Anal. Calcd. for $C_8H_9N_5$: C, 54.85; H, 5.18; N, 39.97. Found: C, 54.81; H, 5.20; N, 39.97.

A sample of IV was heated under reflux with 5 ml. of acetic anhydride for 30 minutes. After cooling, 10 ml. of 2-propanol was added and the solvent was removed under vacuum until only a small volume remained. Water was added until permanent turbidity developed. The product which crystallized upon chilling was isolated by filtration and recrystallized from 95% ethanol, m.p. 71-72°, mixed m.p. with II 71-72°. The ir spectrum was identical to that of II.

1-Phenyl-4-methyl-5-methyliminotetrazoline (V).

A mixture of 16.1 g. (0.10 mole) of 1-phenyl-5-aminotetrazole (14) and 12.6 g. (0.10 mole) of dimethyl sulfate was warmed on a hot plate until an exothermic reaction took place. The mixture was heated for an additional 30 minutes. The cooled solid was dissolved in concentrated sodium hydroxide solution. The basic solution was extracted with three 50 ml. portions of benzene. The combined benzene layers were dried over calcium chloride and the solvent was removed under vacuum. The viscous residue weighed 16.9 g.

This residue was treated with 12.6 g. (0.10 mole) of dimethyl sulfate. An exothermic reaction took place. After the reaction ceased, the viscous residue was dissolved in water and the chilled solution was treated with concentrated sodium hydroxide. The resulting mixture was extracted with three 50 ml. portions of benzene. The benzene extracts were dried over calcium chloride and the solvent was removed under vacuum. The liquid residue was distilled giving 12.9 g. of straw-yellow liquid, b.p. 120-125° at 0.4 mm.

A solution of 10.0 g. of the straw-yellow liquid in 100 ml. of diethyl ether was prepared. Dry hydrogen chloride gas was passed through the solution until precipitation ceased. The mixture was filtered with suction and the precipitate was recrystallized from acetonitrile to give 9.6 g. (55% based on 1-phenyl-5-aminotetrazole) of 1-phenyl-4-methyl-5-methyliminotetrazoline hydrochloride, m.p. 215-217°; ir (nujol mull): 1680, 1600, 1500, 1200, 1130, 1070, 1040, 820, 775, 720, 700, and 680 cm^{-1}; nmr (DMSO-d_6): 2.42 δ (s, 3H, 4-CH_3), 4.07 δ (s, 3H, CH_3), 7.4-7.8 δ (m, 5H, aromatic H's).

The free base was obtained by dissolving 0.5 g. of the hydrochloride salt in water and making the solution basic by the addition of anhydrous potassium carbonate. The oil which formed was solidified by freezing the entire mixture and then allowing it to thaw. The yield of V was 0.3 g. (39% based on 1-phenyl-5-aminotetrazole), m.p. 33.5-35.3°; ir (nujol mull): 1680, 1600, 1500, 1410, 1285, 1165, 1140, 1090, 1040, 1025, 800, 780, 750, 720 and 690 cm^{-1}; nmr (carbon tetrachloride): 2.65 δ (s, 3H, NCH_3), 3.46 δ (s, 3H, 4-CH_3), 6.95-7.6 δ (m, 5H, aromatic H's).

A sample of V was heated with 6*N* sodium hydroxide. A product solidified when the mixture was cooled in an ice bath. The product was isolated by filtration and recrystallized from 95% ethanol. Its melting point (71-72°) and ir spectrum identified it as II.

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