

## New Examples of the Ritter Reaction

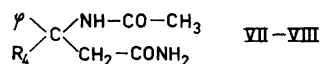
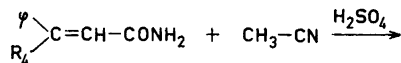
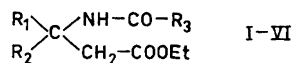
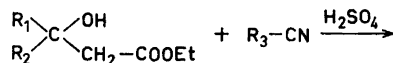
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N-Alkylation of nitriles with carbonium ions in sulfuric acid is known as the Ritter reaction.<sup>1</sup> The reaction has been used to prepare six new esters (I–VI) and two new amides (VII, VIII) of  $\beta,\beta$ -disubstituted- $\beta$ -acylamino propionic acids. The reaction sequences are shown below. The structures of the individual compounds are given in the experimental part.

One of the esters (IV) and one of the amides (VII) have been reduced with lithium aluminum hydride to the expected reaction products (IX, respectively, X).

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IX and X were prepared as potential intermediates in the syntheses of pharmacologically valuable ring compounds.

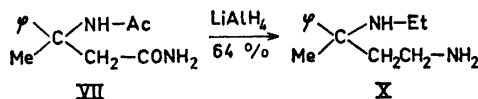
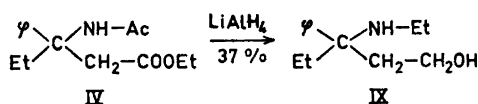
*Experimental.*  $\beta,\beta$ -Disubstituted- $\beta$ -acylamino propionic esters (I–VI). Concentrated sulfuric acid (10 ml) was added dropwise with stirring to a mixture of hydroxyester (0.05 mole) and nitrile (0.06 mole) at 0° during 30 min. The

Table 1.

Compound	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>	Yield %	M.P. °C	Formula		C	H	N
I	Ph	Me	Me	64	80	C <sub>14</sub> H <sub>19</sub> NO <sub>3</sub> (249.3)	found calc.	67.4 67.4	7.7 7.7	5.6 5.6
II	Ph	Me	Et	73	83	C <sub>15</sub> H <sub>21</sub> NO <sub>3</sub> (263.3)	found calc.	68.2 68.4	8.2 8.0	5.2 5.3
III	Ph	Me	Vinyl	62	93	C <sub>15</sub> H <sub>19</sub> NO <sub>3</sub> (261.3)	found calc.	68.9 68.9	7.3 7.3	5.3 5.4
IV	Ph	Et	Me	70	56	C <sub>15</sub> H <sub>21</sub> NO <sub>3</sub> (263.3)	found calc.	68.5 68.4	8.0 8.0	5.4 5.3
V	Ph	Ph	Me	42	114	C <sub>16</sub> H <sub>21</sub> NO <sub>3</sub> (311.4)	found calc.	73.3 73.3	6.8 6.8	4.6 4.5
VI	<i>p</i> -Cl-Ph	Me	Me	72	68	C <sub>14</sub> H <sub>13</sub> ClNO <sub>3</sub> (283.8)	found calc.	59.4 59.3	6.2 6.4	5.0 4.9
								found: Cl 12.6		
								calc. 12.5		

Table 2.

Compound	R <sub>4</sub>	Yield %	M.P. °C	Formula		C	H	N
VII	Me	67	172	C <sub>13</sub> H <sub>16</sub> N <sub>2</sub> O <sub>2</sub> (220.3)	found calc.	65.5 65.4	7.3 7.3	12.5 12.7
VIII	Et	22	198	C <sub>15</sub> H <sub>18</sub> N <sub>2</sub> O <sub>2</sub> (234.3)	found calc.	66.6 66.6	7.9 7.7	11.8 12.0



mixture became viscous after about half of the sulfuric acid had been added. The mixture was left standing overnight at room temperature and then poured into ice water (100 ml). The amido ester formed was isolated in the usual way and crystallized to constant melting point from methylcyclohexane. Data for the new esters are given in Table 1.

*β,β*-Disubstituted-*β*-acylamino propionamides (VII, VIII). Concentrated sulfuric acid (10 ml) was added dropwise with stirring to a mixture of unsaturated amide (0.05 mole) and acetonitrile (0.06 mole) at such a rate that the reaction mixture was kept at 50° (addition time about 1 h). The mixture was left standing overnight at room temperature and then poured into ice water (200 ml) with stirring. The aqueous solution was neutralized by dropwise addition of a 50 % potassium hydroxide solution at room temperature. The amide was isolated by continuous extraction with ethyl acetate (6 h), evaporation of the solvent, and washing of the remaining white cake of crystals with ether. Data for the new amides are given in Table 2.

*3-Ethylamino-3-phenyl-1-pentanol* (IX). IV (0.097 mole) was dissolved in ether (100 ml) and the solution added dropwise with stirring to lithium aluminum hydride (0.132 mole) in ether (200 ml) during 3 h, and the mixture was heated under reflux for 2 h. Ethyl acetate (10 ml) was added, and the precipitate formed removed by filtration and washed with ether (200 ml). The combined ethereal filtrates were distilled. 7.5 g of IX (37 %) was isolated hereby, b.p.<sub>0.35</sub> 105°, *n*<sub>D</sub><sup>24</sup> 1.5244. [Found: C 75.2; H 10.4; N 6.5. Calc. for C<sub>13</sub>H<sub>21</sub>NO (207.3): C 75.3; H 10.2; N 6.8].

*N*<sup>2</sup>-Ethyl-3-phenyl-1,3-butanediimine (X). VII (0.050 mole) was suspended in ether (200 ml), and the suspension added dropwise with stirring to lithium aluminum hydride (0.30 mole) in ether (600 ml) during 15 min, and the mixture heated under reflux for 24 h. Water (11 ml), 15 % sodium hydroxide solution (11 ml) and water (35 ml) were added successively (*cf.* Ref. 2). The precipitate formed was removed by filtration and washed with ether (100 ml). The combined ethereal filtrates were extracted with 3 N hydrochloric acid (100 ml) and the amine regenerated from the acidic solution in the usual way and distilled. 6.2 g of X (64 %) was isolated hereby, b.p.<sub>0.1</sub> 78–80°, *n*<sub>D</sub><sup>20</sup> 1.5301. [Found: C 75.1; H 10.4; N 14.3. Calc. for C<sub>12</sub>H<sub>20</sub>N<sub>2</sub> (192.3): C 75.0; H 10.5; N 14.6].

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