Synthesis and Spectroscopic Characterization of 1-[1,2,3-Triazol-1-yl]-4-aroylazetidin-2-ones

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1-(*N*-Phenacylidene)amino-1,2,3-triazoles **3** react with propionylchloride and phenoxyacetylchloride in the presence of triethylamine to give *trans*- (**5**) and *cis*- (**6**) 1-(1,2,3-triazol-1-yl)-4-aroylaztidin-2-ones in a 1:1 ratio, on the contrary to the 1-(*N*-arylidene)amino-1,2,3-triazoles, which do not give any reaction product with the same acid chlorides. The spectroscopic characteristics of these new *N*-triazolyl-β-lactams are also discussed.

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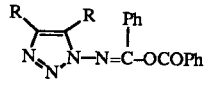
The importance of the azetidin-2-one ring as part of β-lactam antibiotics has forced many scientific groups to synthesize new azetidinone derivatives with various functional groups with potential therapeutic properties or to use them as intermediates for the preparation of other pharmacologically active compounds [1,2].

Although there is a very large number of azetidin-2-ones that have been prepared, there are only few examples in the literature [1b,3,4], where the azetidin-2-one ring is linked to a nitrogen atom from the 1-position and, to our knowledge, only in one case this nitrogen atom constitutes part of a heteroaromatic ring [3b].

In the course of our work on the chemistry of the 1-amino-1,2,3-triazole derivatives [5,6,7] some 1-[1,2,3-triazol-1-yl]azetidin-2-one derivatives **5** and **6** were synthesized, using the acid chloride-imine reaction, and their spectroscopic characteristics were studied. In these compounds the azetidinone ring is 1-(*N*-triazolyl)-substituted and bears in the 4-position the aroyl group, which provides the possibility to be used as starting compounds for further reactions [8,9].

Results and Discussion.

It is well known [1,2,10] that the substituted acetyl chlorides react with imines in the presence of a base and give azetidin-2-ones in moderate to very good yields. However the reaction of acetyl chlorides with 1-(α-aroyloxyarylidene)amino- and 1-(arylidene)amino-1,2,3-triazoles **1** and **2** respectively, in the presence of triethylamine and under different experimental conditions did not give the expected azetidinones but tars and the starting material along with their decomposition products, in the case of compounds **1**.



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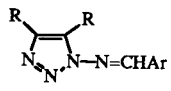
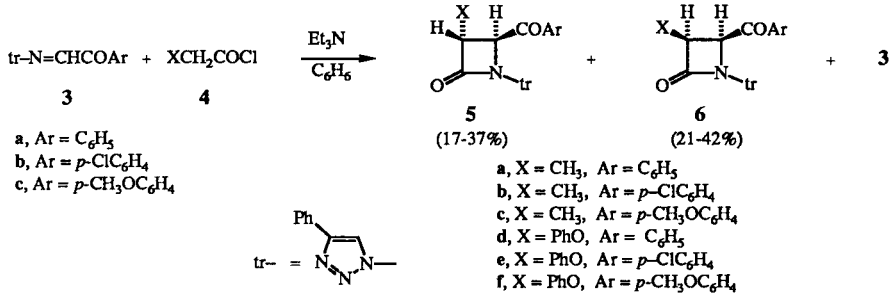


2

When the same reaction was performed with 1-(phenacylidene)-amino-1,2,3-triazoles **3** both *trans*-, (**5**) and *cis*-, (**6**), azetidinones have been isolated in a ratio of about 1:1 except for compounds **6f** and **5f** where the *cis*:*trans* ratio were 2.2:1 and in 44-79% overal yields. From the reaction mixture the unreacted compounds **3** were also isolated in 20-53% yields.

The reaction was carried out under nitrogen in benzene solution and the triethylamine was added dropwise to a mixture of acid chloride **4** and 1-(phenacylidene)amino-triazoles **3**. When the reaction was performed by adding the acid chloride to a mixture of **3** and triethylamine the yield of azetidinones was very small. Compounds **5** and **6** were separated from the reaction mixture by column chromatography and were differentiated by their ^{1}H nmr spectra, where 3-H and 4-H of the azetidinone ring showed a small coupling constant, $^3J = 2.4$-3.0 Hz, for the *trans*-



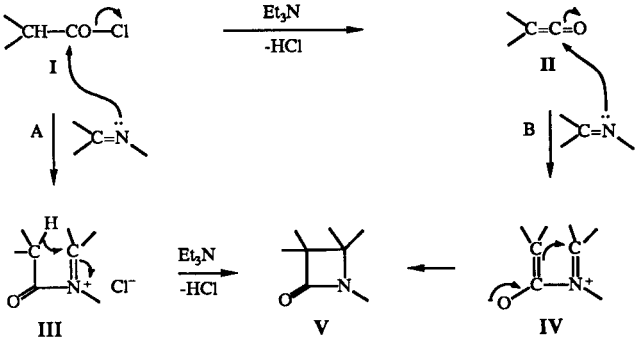
isomers **5** and a large one, $^3J = 5.7$-6.4 Hz, for the *cis*-isomers **6**.

In order to remove the triazole ring and to obtain *N*-unsubstituted azetidinones, compound **5d** was treated with cerium ammonium nitrate [11] but these attempts proved unsuccessful.

It seems rather difficult to explain the difference in the behaviour of compounds **1**, **2** and **3** towards the reaction with acid chloride in the presence of triethylamine. Two mechanisms have been mainly proposed [12,13] for this reaction, according to which there is a nucleophilic attack of the nitrogen non bonding electrons of the C=N group either to the acid chloride itself, path **A**, or to the carbonyl-carbon of the ketene **II**, which is generated by the action of triethylamine on the acid chloride, path **B**, Scheme 1. In both cases the intermediates **III** or **IV** give, with ring closure, the corresponding azetidinone ring **V**.

Whatever the assumed reaction mechanism, it is apparent that the reaction will proceed more easily and faster with increasing nucleophilicity of the nitrogen atom of the C=N bond assuming there are no other hindrance factors and the acid chloride being the same. As expected, the electron-withdrawing groups, such as C=O, will reduce the electron density of the C=N bond and consequently the nucleophilic character of the nitrogen. This is

Scheme 1



indeed the case for the compounds **2** and **3**, and is supported by CNDO/2 calculations reported [6,7,13] for these compounds. According to the above discussion, compounds **2** are expected to be more reactive than **3** with acid chloride in the presence of triethylamine or with ketenes generated in this reaction, which however contradicts the observed experimental results. On the other hand, in a previous study [6,7] we have shown that compounds **3** were more reactive than compounds **2** with diphenylnitrilimine in 1,3-dipolar cycloaddition reactions and this was explained by molecular orbital calculations. It has been shown by CNDO/2 calculations that the introduction of an electron-withdrawing group lowers the LUMO energy level of the C=N group thus facilitating the cycloaddition, which is HOMO-dipole controlled. In particular compound **3** reacted more easily with diphenylnitrilimine almost at room temperature and within a few hours, compared with compounds **2**, which reacted under more strong conditions [6].

The similar behaviour and reactivity of compounds **3** in these two reactions might suggest that the reaction of these compounds with acid chlorides in the presence of triethylamine could also have some characteristics of a concerted reaction.

Spectroscopic and analytical data of compounds **5** and **6** are in agreement with their structures. Thus their ir spectra show bands at 1775-1810 cm^{-1} and 1670-1690 cm^{-1} for the C=O bond of the azetidinone ring and the aroyl-group respectively. It should be noted that the absorptions of the azetidinone C=O group, which appear at higher frequences, are comparable to those of the fused β-lactams, whereas the monocyclic azetidinones generally show maxima [2] at 1730-1760 cm^{-1}. This indicates that the triazole ring acts inductively as an electron-attracting group in these compounds.

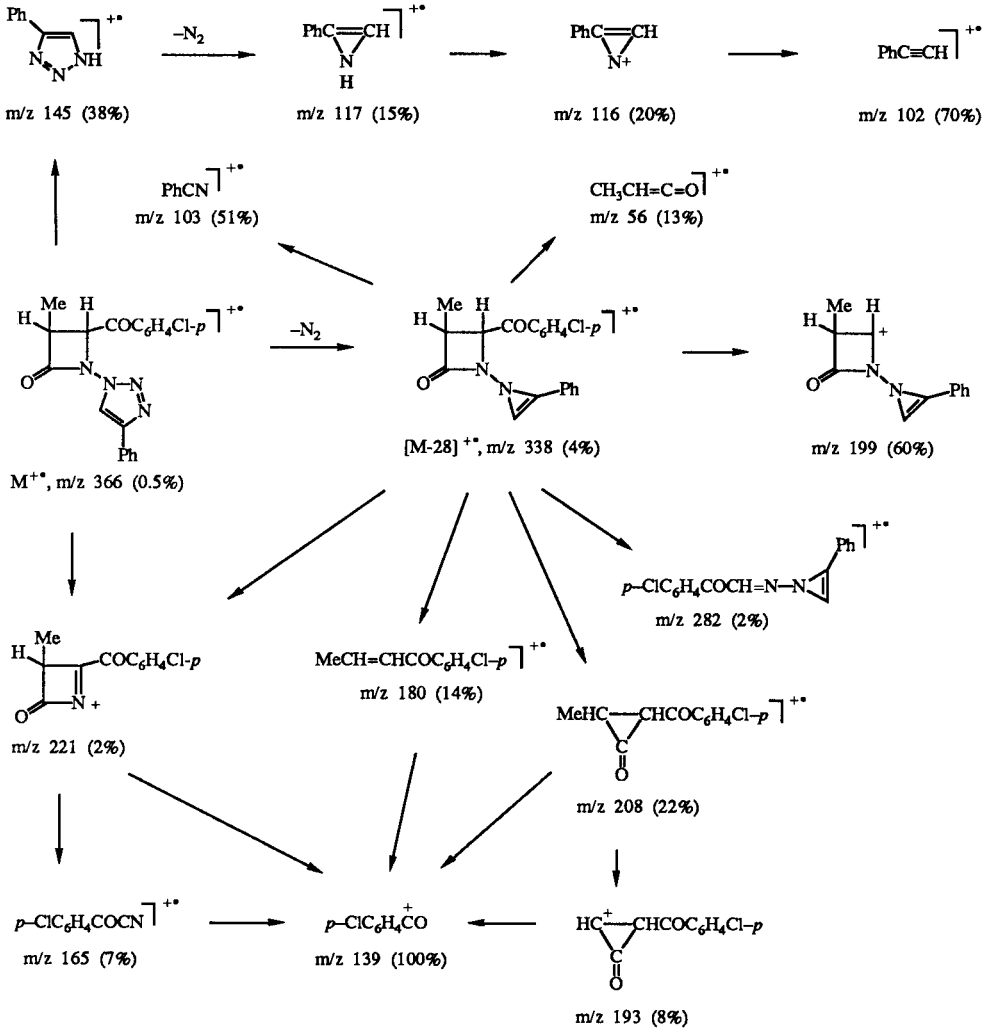
In the ^1H nmr spectra there is a differentiation in the coupling constants and in the shifts of 3-H and 4-H of the azetidinone ring between the *trans*- **5** and the *cis*- **6** isomers. Thus coupling constants of 3-H and 4-H are small, 2.4-3.0 Hz, in the *trans*- and large, 5.7-6.2 Hz, in the *cis*-derivatives. Also the shifts of 3-H and 4-H atoms appear at lower field in the *trans*- and at higher field in the *cis*-isomers. Thus 3-H appears at $\delta = 3.35$ in compounds **5a-c** and at $\delta = 3.9$-4.0 in compounds **6a-c** whereas 4-H appears at $\delta = 5.5$ and at $\delta = 5.9$ in **5a-c** and **6a-c** respectively. In the 3-phenoxy-derivatives, 3-H and 4-H appear at $\delta = 5.3$-5.9 in compounds **5d-f** and at $\delta = 5.9$-6.2 in compounds **6d-f**. The 5-H of the triazole ring in all compounds **5** and **6** resonates at $\delta = 8.2$-8.5 and the aromatic protons show the expected pattern in the aromatic region of the spectrum.

The ^{13}C nmr spectra of compounds **5e-f** and **6d-f** exhibit the expected absorption peaks for all carbon atoms in agreement with their structures. The C-3 and C-4 atoms of the azetidinone ring resonate at $\delta = 81.1$-82.5 ppm and at $\delta = 68.5$-69.1 ppm, respectively in both **5e-f** and **6d-f**. The C=O atoms of the azetidinone and of the aroyl-group appear at $\delta = 156.5$ and 190 ppm, respectively, whereas the C-4 and C-5 atoms of the triazole ring resonate at $\delta = 146.5$ and 121.4-122.8 ppm, respectively, as expected for the 1-substituted-1,2,3-triazole derivatives [14,15].

The EI mass spectra of compounds **5** and **6** are characteristic and represent a fragmentation pattern of the two main components of the molecule, *i.e.* the azetidinone and the triazole ring. The molecular ion $M^{+\cdot}$ appears with a very low intensity and the base peak corresponds to the $ArCO^+$ ion in the 3-methyl-derivatives and

Scheme 2

Main Fragmentation Pattern in the Mass Spectrum of Compound **5b**



to the $PhOH^{1+\cdot}$ ion in the 3-phenoxyderivatives.

All compounds give the $[M-28]^{+\cdot}$ ion peak, which corresponds to the N_2 elimination of the molecular ion and is characteristic of the 1-substituted-1,2,3-triazoles [16,17]. There is also cleavage of the N-N bond, giving rise to the corresponding ions of the triazole and the azetidinone part of the molecule. The $[M-28]^{+\cdot}$ ion is splitted according to the azetidinone ring retrocycloaddition fragmentation pattern, giving fragments [18,19] corresponding to the $ArCOCH=N\text{-}(tr\text{-}28)^{1+\cdot}$, $XCH=CHCOAr^{1+\cdot}$ and $XCH=C=O^{1+\cdot}$ ions, whereas the triazole ring ion is splitted to the $PhCN^{1+\cdot}$ and $PhC\equiv CH^{1+\cdot}$ ions at m/z 103 and m/z 102 respectively. It should be noted that except for some differences in the intensities of the peaks, there is no any other differentiation between *cis*- and *trans*-isomers in the mass spectra of compounds **5** and **6**. A fragmentation pattern in the mass spectrum of compound **5b** is given in Scheme 2.

EXPERIMENTAL

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. The ir spectra were recorded on a Perkin-Elmer 297 spectrometer as nujol muls or potassium bromide disks. The ^1H nmr spectra were obtained on a Bruker AW 80 and on a Bruker WN 250 spectrometers and the ^{13}C nmr spectra were obtained on a Bruker WN 250 spectrometer, in deuteriochloroform with tetramethylsilane (TMS) as internal standard. The mass spectra were obtained on a Hitachi-Perkin-Elmer RMU-6L spectrometer. Elemental microanalyses were performed with a Perkin-Elmer 240 B CHN analyser. Column chromatography was performed over Merk Kieselgel 60.

Compounds **3**.

These were prepared from the 4-phenyl-1-amino-1,2,3-triazole by condensation with the appropriate arylglyoxals as described previously [7].

Reaction of 1-(*N*-Phenacylidene)amino-1,2,3-triazoles **3** with Acid Chlorides **4**.

General Procedure.

To a stirred solution of **3** (1 mmole) in sodium dried benzene (10 ml) under cooling (ice bath) the corresponding acid chloride **4** (2 mmoles) was added dropwise for about 30 minutes. The system then was put under nitrogen and a solution of triethylamine (2 mmoles) in dried benzene (10 ml) was added slowly over a period of 1 hour. Stirring was continued for 6-7 hours and then the reaction mixture was kept at room temperature for 48 hours, where the solution becomes yellow to dark. To this mixture methylenechloride (30 ml) and water (20 ml) were added and the organic layer was separated and washed with water (3 x 20 ml). The organic solvent after drying was evaporated and the residue was chromatographed on a silica gel column with ethyl acetate-hexane (bp 67-69°) slowly increasing the polarity of the eluant.

Reaction of Compound **3a** with Propionyl Chloride.

To a solution of compound **3a** (0.43 g, 1.5 mmoles) and propionyl chloride (0.278 g, 3.0 mmoles) in benzene (10 ml) a solution of triethylamine (3 mmoles, 0.4 ml) was added dropwise. After the mixture had been kept at room temperature for 48 hours it was treated as above and the residue chromatographed on a silica gel column to give the following.

a: Unreacted compound **3a** was obtained in 53% yield (0.23 g).

b: *trans*-1-(4-Phenyl-1,2,3-triazol-1-yl)-3-methyl-4-benzoylazetidin-2-one (**5a**).

This compound was obtained in 22% yield (0.11 g), mp 154-156° (from ethanol); ir: 3120, 1805 and 1680 (C=O) cm^{-1}; ^1H nmr: (80 MHz) δ 1.76 (3H, d, J = 7.4 Hz, CH_3), 3.35 (1H, dq, J = 7.4, 3.0 Hz, 3-H), 5.48 (1H, d, J = 3.0 Hz, 4-H), 7.36-7.65 (6H, m), 7.76-8.08 (4H, m), 8.28 (1H, s, 5-Htr [20]); ms: m/z (%), 332 (M^+, 0.2), 304 (M^+-28, 2), 276 (1), 248 (1.5), 199 (38), 187 (1), 174 (16), 159 (5), 146 (24), 145 (20), 131 (14), 117 (12), 116 (13), 105 (100), 103 (37), 102 (46), 77 (53), 56 (12).

Anal. Calcd. for $C_{19}H_{16}N_4O_2$: C, 68.66; H, 4.85; N, 16.86. Found: C, 68.73; H, 5.08; N, 16.84.

c: *cis*-1-(4-Phenyl-1,2,3-triazol-1-yl)-3-methyl-4-benzoylazetidin-2-one (**6a**).

This compound was obtained in 22% yield (0.11 g), mp 134-136° (from ether-hexane); ir: 3140, 1800, 1775 and 1690 (C=O) cm^{-1}; ^1H nmr: (80 MHz) δ 1.19 (3H, d, J = 7.6 Hz, CH_3), 3.88 (1H, dq as qnt, J = 7.6, 6.4 Hz, 3-H), 5.93 (1H, d, J = 6.4 Hz, 4-H), 7.36-7.65 (6H, m), 7.78-7.98 (4H, m), 8.36 (1H, s, 5-Htr); ms: m/z (%), 332 (M^+, 0.2), 304 (M^+-28, 1), 276 (0.2), 248 (0.6), 199 (28), 187 (0.5), 174 (31), 159 (10), 146 (8), 145 (13), 131 (13), 117 (8), 116 (10), 105 (100), 103 (11), 102 (45), 77 (42), 56 (3).

Anal. Calcd. for $C_{19}H_{16}N_4O_2$: C, 68.66; H, 4.85; N, 16.86. Found: C, 68.40; H, 4.80; N, 16.76.

Reaction of **3b** with Propionyl Chloride.

To a solution of compound **3b** (0.31 g, 1 mmole) and propionyl chloride (0.278 g, 3 mmoles) in benzene (10 ml) a solution of triethylamine (3 mmoles, 0.4 ml) in the same solvent (10 ml) was added dropwise. After the mixture had been kept at room temperature for 48 hours it was treated as above and the residue was chromatographed on a silica gel column to give the following.

a: Unreacted compound **3b** was obtained in 52% yield (0.16 g).

b: *trans*-1-(4-Phenyl-1,2,3-triazol-1-yl)-3-methyl-4-(*p*-chlorobenzoyl)azetidin-2-one (**5b**).

This compound was obtained in 27% yield (0.1 g), mp 168-169° (from ethanol); ir: 3120, 1803 and 1680 (C=O) cm^{-1}; ^1H nmr: (80 MHz) δ 1.75 (3H, d, J = 7.2 Hz, CH_3), 3.33 (1H, dq, J = 7.2, 3.0 Hz, 3-H), 5.45 (1H, d, J = 3.0 Hz, 4-H), 7.34-7.50 (3H, m), 7.50 (2H, d, J = 8.0 Hz), 7.75-7.94 (2H, m), 7.84 (2H, d, J = 8.0 Hz), 8.25 (1H, s, 5-Htr); ms: m/z (%), 368/366 (M^+, 0.6), 340/338 (M^+-28, 4), 312/310 (1), 284/282 (2), 235/233 (5), 223/221 (2), 210/208 (22), 199 (60), 195/193 (8), 182/180 (14), 167/165 (7), 145 (38), 141/139 (100), 117 (16), 116 (19), 103 (51), 102 (70), 77 (19), 76 (35), 56 (13).

Anal. Calcd. for $C_{19}H_{15}ClN_4O_2$: C, 62.22; H, 4.12; N, 15.27. Found: C, 62.22; H, 4.28; N, 15.17.

c: *cis*-1-(4-Phenyl-1,2,3-triazol-1-yl)-3-methyl-4-(*p*-chlorobenzoyl)-azetidin-2-one (**6b**).

This compound was obtained in 25% yield (0.09 g), mp 173-175° (from ethanol); ir: 3140, 1800, 1775 and 1683 (C=O) cm^{-1}; ^1H nmr: (80 MHz) δ 1.24 (3H, d, J = 7.6 Hz, CH_3), 4.00 (1H, dq as qnt, J = 7.6, 6.2 Hz, 3-H), 5.89 (1H, d, J = 6.2 Hz, 4-H), 7.35-7.52 (3H, m), 7.50 (2H, d, J = 8.5 Hz), 7.77-7.94 (2H, m), 7.85 (2H, d, J = 8.5 Hz), 8.32 (1H, s, 5-Htr); ms: m/z (%), 368/366 (M^+, 0.01), 340/338 (M^+-28, 4), 312/310 (10), 284/282 (3), 257/255 (2), 235/233 (3), 223/221 (3), 210/208 (14), 199 (20), 195/193 (5), 182/180 (17), 167/165 (8), 145 (59), 141/139 (100), 117 (27), 116 (28), 103 (78), 102 (83), 77 (38) 76 (45) 56 (28).

Anal. Calcd. for $C_{19}H_{15}ClN_4O_2$: C, 62.22; H, 4.12; N, 15.27. Found: C, 62.23; H, 4.25; N, 15.30.

Reaction of **3c** with Propionyl Chloride.

To a solution of compound **3c** (0.306 g, 1 mmole) and propionyl chloride (0.278 g, 3 mmoles) in benzene (10 ml) a solution of triethylamine (3 mmoles, 0.4 ml) in the same solvent (10 ml) was added dropwise. After the mixture had been kept at room temperature for 48 hours it was treated as above and the residue chromatographed on a silica gel column to give the following.

a: Unreacted compound **3c** was obtained in 50% yield (0.15 g).

b: *trans*-1-(4-Phenyl-1,2,3-triazol-1-yl)-3-methyl-4-(*p*-methoxybenzoyl)azetidin-2-one (**5c**).

This compound was obtained in 24% yield (0.085 g) mp 49-51° (from ether-hexane); ir: 3140, 3800, 1675 (C=O) cm^{-1}; ^1H nmr: (80 MHz) δ 1.72 (3H, d, J = 7.2 Hz, CH_3), 3.32 (1H, dq, J = 7.2 and 3.0 Hz, 3-H), 3.80 (3H, s, CH_3O), 5.44 (1H, d, J = 3.0 Hz, 4-H), 6.95 (2H, d, J = 8.0 Hz), 7.30-7.50 (3H, m), 7.73-7.96 (2H, m), 7.86 (2H, d, J = 8.0 Hz), 8.26 (1H, s, 5-Htr); ms: m/z (%), 362 (M^+, 0.02), 334 (M^+-28, 0.7), 306 (0.4), 278 (0.5), 251 (0.1), 229 (1), 217 (0.5), 204 (15), 199 (7), 189 (8), 176 (8), 161 (11), 145 (6), 135 (100), 117 (6), 116 (16), 103 (19), 102 (86), 77 (79), 76 (48), 56 (7).

Anal. Calcd. for $C_{20}H_{18}N_4O_3$: C, 66.29; H, 5.01; N, 15.46. Found: C, 66.30; H, 5.09; N, 15.46.

c: *cis*-1-(4-Phenyl-1,2,3-triazol-1-yl)-3-methyl-4-(*p*-methoxybenzoyl)azetidin-2-one (**6c**).

This compound was obtained in 21% yield (0.075 g) mp 148-149° (from ethanol); ir: 3140, 1795, 1775 and 1675 (C=O) cm^{-1}; ^1H nmr: (80 MHz) δ 1.23 (3H, d, 7.6 Hz, CH_3), 3.88 (3H, s, CH_3O), 3.94 (1H, dq as qnt, J = 7.6, 6.2 Hz, 3-H), 5.87 (1H, d, J = 6.2 Hz, 4-H), 6.96 (2H, d, J = 9.0 Hz), 7.30-7.50 (3H, m), 7.75-7.96

(2H, m), 7.86 (2H, d, J = 9.0 Hz), 8.36 (1H, s, 5-Htr); ms: m/z (%), 362 (M^+, 0.2), 334 (M^+-28, 7), 306 (2), 278 (6), 263 (4), 251 (2), 247 (5), 229 (53), 217 (1.5), 204 (16), 199 (12), 189 (15), 177 (25), 176 (24), 161 (16), 145 (37), 135 (100), 117 (18), 116 (17), 103 (38), 102 (67), 77 (38), 76 (26), 56 (12).

Anal. Calcd. for $C_{20}H_{18}N_4O_3$: C, 66.29; H, 5.01; N, 15.46. Found: C, 66.22; H, 5.21; N, 15.26.

Reaction of **3a** with Phenoxyacetyl Chloride.

To a solution of **3a** (0.31 g, 1.1 mmoles) and phenoxyacetyl chloride (0.375 g, 2.2 mmoles) in benzene (10 ml) a solution of triethylamine (2.2 mmoles, 0.3 ml) in the same solvent (10 ml) was added dropwise. After the mixture had been kept at room temperature for 48 hours it was treated as above and the residue chromatographed on a silica gel column to give the following.

a: Unreacted compound **3a** was obtained in 32% yield (0.1 g).

b: *trans*-1-(4-Phenyl-1,2,3-triazol-1-yl)-3-phenoxy-4-benzoylazetidin-2-one (**5d**).

This compound was obtained in 33% yield (0.15 g) mp 205-208° (from ethanol); ir: 3120, 1815, 1800, 1690 (C=O) cm^{-1}; ^1H nmr: (80 MHz) δ 5.35 (1H, d, J = 2.4 Hz, 3-H), 5.97 (1H, d, J = 2.4 Hz, 4-H), 7.0-7.6 (11H, m), 7.7-7.8 (4H, m), 8.28 (1H, s, 5-Htr).

Anal. Calcd. for $C_{24}H_{18}N_4O_3$: C, 70.23; H, 4.42; N, 13.65. Found: C, 69.80; H, 4.40; N, 13.49.

c: *cis*-1-(4-Phenyl-1,2,3-triazol-1-yl)-3-penoxy-4-benzoylazetidin-2-one (**6d**).

This compound was obtained in 33% yield (0.15 g) mp 183-186° (from ethanol); ir: 3170, 1805, 1670 (C=O) cm^{-1}; ^1H nmr: (250 MHz) δ 6.04 (1H, d, J = 5.9 Hz), 6.19 (1H, d, J = 5.9 Hz), 6.86 (2H, m as d), 7.0 (1H, m as t), 7.17-7.25 (2H, m), 7.34-7.50 (5H, m), 7.63 (1H, m as t), 7.84-7.90 (2H, m), 7.94-7.96 (2H, m), 8.52 (1H, s, 5-Htr); ^{13}C nmr: (62.5 MHz) δ 68.69 (C-4), 81.92 (C-3), 122.11 (C-5tr), 146.60 (C-4tr), 156.77 (N-C=O), 191.35 (C=O); 4-phenyl: 125.82 (C-2, C-6), 128.91 (C-3, C-5), 128.75 (C-4); PhCO: 128.27 (C-2, C-6), 128.96 (C-3, C-5), 134.35 (C-1), 134.49 (C-4); PhO: 116.18 (C-2, C-6), 123.34 (C-4), 129.61 (C-3, C-5), 162.23 (C-1); ms: m/z (%), 410 (M^+, 0.1), 382 (M^+-28, 2), 354 (0.6), 309 (1), 289 (5), 277 (4), 265 (3), 248 (11), 224 (16), 207 (6), 184 (3), 161 (19), 159 (13), 147 (22), 145 (13), 134 (2), 131 (7), 117 (16), 116 (25), 105 (100), 103 (77), 102 (59), 94 (89), 77 (99).

Anal. Calcd. for $C_{24}H_{18}N_4O_3$: C, 70.23; H, 4.42; N, 13.65. Found: C, 70.19; H, 4.55; N, 13.80.

Reaction of **3b** with Phenoxyacetyl Chloride.

To a solution of **3b** (0.25 g, 0.79 mmole) and phenoxyacetyl chloride (0.27 g, 1.58 mmoles) in benzene (10 ml) a solution of triethylamine (1.58 mmoles, 0.22 ml) in the same solvent was added dropwise. After the mixture had been kept at room temperature for 48 hours it was treated as above and the residue was chromatographed on a silica gel column to give the following.

a: Unreacted compound **3b** was obtained in 20% yield (0.05 g).

b: *trans*-1-(4-Phenyl-1,2,3-triazol-1-yl)-3-phenoxy-4-(*p*-chlorobenzoyl)azetidin-2-one (**5e**).

This compound was obtained in 37% yield (0.13 g) mp 158-160° (from ethanol); ir (nujol): 3140, 1805, 1785 (C=O) cm^{-1}; ^1H nmr: (250 MHz) δ 5.36 (1H, d, J = 2.6 Hz, H-3), 5.95 (1H, d, J = 2.6 Hz, H-4), 7.08-7.17 (3H, m), 7.30-7.49 (7H, m), 7.82 (2H, m as d), 7.93 (2H, d, J = 8.6 Hz), 8.23 (1H, s, 5-Htr); ^{13}C nmr: (62.5 MHz) δ 68.68 (C-4), 82.49 (C-3), 121.39 (C-5tr), 146.49 (C-4tr), 156.53 (N-C=O), 190.68 (C=O); 4-Phenyl: 125.83 (C-2, C-6), 128.87 (C-3, C-5 and C-4), 129.43 (C-1); *p*-ClC_6H_4CO: 129.69 (C-2, C-6), 129.79 (C-3, C-5), 131.43 (C-1), 141.93 (C-4); PhO: 116.29 (C-2, C-6), 123.85 (C-4), 129.96 (C-3, C-5), 162.05 (C-1); ms: m/z (%), 446/444 (M^+, 0.01), 418/416 (M^+-28, 0.3), 325/323 (0.7), 301/299 (0.3), 284/282 (0.5), 277 (0.5), 260/258 (1), 243/241 (1), 195/193 (2), 181/179 (3), 167/165 (5), 161 (38), 145 (11), 141/139 (19), 134 (2), 117 (25), 116 (12), 103 (19), 102 (19), 94 (100), 77 (45), 76 (17).

Anal. Calcd. for $C_{24}H_{17}ClN_4O_3$: C, 64.80; H, 3.85; N, 12.59. Found: C, 64.45; H, 3.79; N, 12.25.

c: *cis*-1-(4-Phenyl-1,2,3-triazol-1-yl)-3-phenoxy-4-(*p*-chlorobenzoyl)azetidin-2-one (**6e**).

This compound was obtained in 42% yield (0.15 g) mp 211-214° (from ethanol); ir: 3130, 3100, 1810, 1680 (C=O) cm^{-1}; ^1H nmr (dimethyl sulfoxide-d_6): (250 MHz) δ 6.50 (1H, d, J = 5.7 Hz), 6.58 (1H, d, J = 5.7 Hz), 6.87 (2H, m as d), 7.01 (1H, m as t), 7.26 (2H, m as t), 7.38-7.54 (3H, m), 7.61 (2H, d, J = 8.5 Hz), 7.99 (2H, m as d), 8.05 (2H, d, J = 8.5 Hz), 9.13 (1H, s, 5-Htr); ^{13}C nmr (dimethyl sulfoxide-d_6): (62.5 MHz) δ 69.11 (C-4), 81.06 (C-3), 122.85 (H-5tr), 145.33 (C-4tr), 156.31 (N-C=O), 191.11 (C=O); 4-Phenyl: 125.40 (C-2, C-6), 128.59 (C-4), 128.99 (C-3, C-5); *p*-ClC_6H_4CO: 128.99 (C-3, C-5), 129.64 (C-2, C-6), 133.13 (C-1), 139.11 (C-4); PhO: 115.56 (C-2, C-6), 122.85 (C-4), 130.09 (C-3, C-5), 162.91 (C-1); ms: m/z (%), 446/444 (M^+, 0.2), 418/416 (M^+-28, 1), 390/388 (0.5), 325/323 (3), 324/322 (3), 301/299 (3), 284/282 (6), 277 (3), 260/258 (12), 243/241 (8), 195/193 (7), 182/180 (8), 167/165 (9), 161 (19), 145 (35), 141/139 (75), 117 (17), 116 (24), 103 (60), 102 (41), 94 (100), 77 (73), 76 (36).

Anal. Calcd. for $C_{24}H_{17}ClN_4O_3$: C, 64.80; H, 3.85; N, 12.59. Found: C, 64.89; H, 3.95; N, 12.30.

Reaction of **3c** with Phenoxyacetyl Chloride.

To a solution of compound **3c** (0.24 g, 0.78 mmole) and phenoxyacetyl chloride (0.26 g, 1.56 mmoles) in benzene (10 ml) a solution of triethylamine (1.56 mmoles, 0.22 ml) in the same solvent was added dropwise. After the mixture had been kept at room temperature for 48 hours it was treated as above and the residue was chromatographed on a silica gel column to give the following.

a: Unreacted compound **3c** was obtained in 42% yield (0.1 g).

b: *trans*-1-(4-Phenyl-1,2,3-triazol-1-yl)-3-phenoxy-4-(*p*-methoxybenzoyl)azetidin-2-one (**5f**).

This compound was obtained in 17% yield (0.06 g) mp 139-141° (from ether-hexane); ir (nujol): 3150, 1825 w, 1800, 1685 (C=O) cm^{-1}; ^1H nmr: (250 MHz) δ 3.85 (3H, s, CH_3), 5.36 (1H, d, J = 2.3 Hz, H-4), 5.94 (1H, d, J = 2.3 Hz, H-3), 6.94 (2H, d, J = 8.5 Hz), 7.06-7.17 (3H, m), 7.29-7.46 (5H, m), 7.84 (2H, m as d), 7.97 (2H, d, J = 8.5 Hz), 8.31 (1H, s, 5-Htr); ^{13}C nmr: (62.5 MHz) δ 68.60 (C-4), 82.59 (C-3), 121.56 (C-5tr), 146.40 (C-4tr), 156.68 (N-C=O), 190.02 (C=O); 4-Phenyl: 125.83 (C-2, C-6), 128.67 (C-4), 128.85 (C-3, C-5), 129.56 (C-1); *p*-$CH_3OC_6H_4CO$: 55.64 (CH_3O), 114.55 (C-3, C-5), 126.19 (C-1), 130.96 (C-2, C-6), 165.11 (C-4); PhO: 116.25 (C-2, C-6), 123.61 (C-4), 129.90 (C-3, C-5), 162.33 (C-1); ms: m/z (%), 412 (M^+-28, 0.1), 319 (0.5), 318 (0.4), 295 (0.6), 278 (0.4), 277 (0.7), 254 (0.6), 251 (0.5), 189 (3), 161 (4), 145 (18), 135 (18), 134 (1), 117 (5), 116 (4), 103 (11), 102 (8), 94 (100) 77 (24).

Anal. Calcd. for $C_{25}H_{20}N_4O_4$: C, 68.17; H, 4.58; N, 12.72. Found: C, 67.66; H, 4.68; N, 12.30.

c: *cis*-1-(4-Phenyl-1,2,3-triazol-1-yl)-3-phenoxy-4-(*p*-methoxybenzoyl)azetidin-2-one (**6f**).

This compound was obtained in 38% yield (0.13 g) mp 181-182° (from ethyl acetate-hexane); ir (nujol): 3140, 1805, 1678 (C=O) cm^{-1}; ^1H nmr: (250 MHz) δ 3.83 (3H, s, CH_3O), 6.03 (1H, d, J = 5.8 Hz), 6.15 (1H, d, J = 5.8 Hz), 6.90 (2H, d, J = 8.8 Hz), 6.87 (2H, m as d), 6.99 (1H, m as t), 7.20 (2H, m as t), 7.33-7.46 (3H, m), 7.84 (2H, m as d), 7.91 (2H, d, J = 8.8 Hz), 8.52 (1H, s, 5-Htr); ^{13}C nmr: (62.5 MHz) δ 68.51 (C-4), 81.75 (C-3), 122.17 (C-5tr), 146.49 (C-4tr), 156.82 (N-C=O), 189.50 (C=O); 4-Phenyl: 125.53 (C-2, C-6), 128.85 (C-3, C-5), 128.87 (C-4); *p*-$CH_3OC_6H_4CO$; 55.50 (CH_3O), 114.17 (C-3, C-5), 127.37 (C-1), 130.68 (C-2, C-6), 164.49 (C-4); PhO: C, 116.19 (C-2, C-6), 123.20 (C-4), 129.56 (C-3, C-5), 162.40 (C-1); ms: m/z (%), 412 (M^+-28, 0.2), 319 (0.3), 318 (1), 295 (2), 278 (2), 277 (0.4), 254 (1), 251 (1), 237 (1), 189 (1), 161 (10), 145 (11), 135 (26), 134 (2), 117 (11), 116 (7), 103 (43), 102 (44), 94 (100) 77 (34).

Anal. Calcd. for $C_{25}H_{20}N_4O_4$: C, 68.17; H, 4.58; N, 12.72. Found: C, 68.49; H, 4.63; N, 12.63.

Reaction of **6d** with Cerium (IV) Ammonium Nitrate (CAN).

A solution of **6d** (0.4 g, 1 mmole) in acetonitrile (15 ml) was treated with a solution of CAN (1.65 g, 3 mmoles) as described in the literature [11]. After working up, the reaction mixture was extracted with ethyl acetate and the residue was chromatographed on a silica gel column to give the starting compound **6d** (0.2 g, 50%), the *trans*-isomer **5d** (0.1 g, 25%), along with unidentified products.

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[20] tr refers to the triazole ring.