Electrophilic 1,5-Addition of Acyl Chlorides to Conjugated Azocyclopropanes

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Addition reactions of acetyl and benzoyl chlorides to 1-pyrazolines containing a spiro cyclopropane fragment at the adjacent azo group lead selectively and in high yields to the corresponding 1-acyl-3-(chloroethyl)-2-pyrazolines, resulting in opening of the three-membered ring.

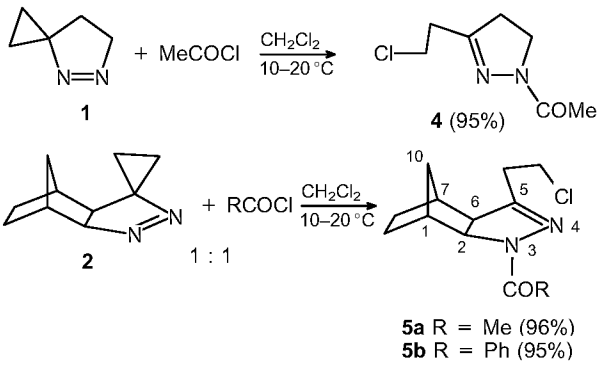
Cyclopropyl-substituted azo compounds can be regarded as analogues of vinylcyclopropanes, cyclopropylketones and other similar compounds with various heteroatoms, forming a double bond in the adjacent three-membered rings. In chemical reactions (*e.g.*, with radical or electrophilic reagents) such systems, owing to conjugation of the double bond and the cyclopropane ring, give the products of electrophilic attack on the terminal atom of the double bond with opening of the three-membered ring and nucleophilic addition to the CH_2-group.[1,2]

Cyclopropanes with a connected N=N group have not been studied sufficiently. In the main, the known chemical transformations of azocyclopropanes are confined to their thermal or photochemical isomerization and radical reduction in which opening of the three-membered ring also takes place.[3,4]

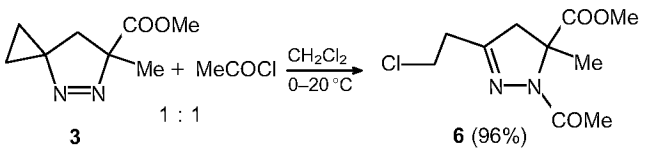
This communication describes a novel reaction of acyl chlorides with 1-pyrazolines containing an unsubstituted spiro cyclopropane fragment, compounds **1**–**3**. Pyrazolines **1** and **2** were obtained by previously described methods,[5,6] and compound **3** was synthesized in ~75% yield by addition of diazocyclopropane generated *in situ* to methyl methacrylate at −30 °C in a methanol–methylene dichloride solution (molar ratio *N*-cyclopropyl-*N*-nitrosourea:olefin = 1:1.2).

We determined that the interaction of pyrazolines **1** and **2** with an equimolar quantity of acetyl chloride in halogenoalkane solution at 10–20 °C proceeds exothermically, giving rise to the corresponding 1-acetyl-3-(2-chloroethyl)-2-pyrazolines (**4** and **5a**) in very high yields. Benzoyl chloride also reacts actively with pyrazoline **2** and leads to the product of conjugated addition **5b** in 95% yield.

The prepared compounds are sufficiently stable under the usual conditions and can be purified and analysed by TLC (silica gel, hexane–ether 1:1). At high temperatures (above 150 °C), 3-(2-chloroethyl)-2-pyrazolines have been shown in the case of **5a,b** to undergo partial dehydrochlorination to 3-acetyl(benzoyl)-5-vinyl-3,4-diazatricyclo[5.2.1.$0^{2,6}$]dec-4-ene (15–20%) with formation of resin.



The addition reaction of acetyl chloride with pyrazoline **3**, containing an electron-withdrawing group in the heterocycle, proceeds analogously to pyrazolines **1** and **2** as a 1,5-addition and leads to 1-acetyl-3-(2-chloroethyl)-5-methoxycarbonyl-5-methyl-2-pyrazoline **6** in 96% yield (^{1}H NMR) after removal of solvent.



The structures of the synthesized 2-pyrazolines **4**–**6** were established by satisfactory elemental analyses, mass- and ^{1}H and ^{13}C NMR spectroscopy.† The existence of a 2-chloroethyl fragment is typical of all the compounds. In the ^{1}H NMR spectra of pyrazolines **4** and **6** the two CH_2-groups are shown as two triplets at δ 3.7 and 2.8 ppm. In the case of compounds **5a,b** the CH_2-group signal, connected with the double bond, is a complicated multiplet which is caused by geminal non-equivalence of protons owing to the asymmetric structure of this polycyclic molecule.

Under the same conditions the addition of acetic anhydride to pyrazoline **2** in $CDCl_3$ does not give rise to any transformations (^{1}H NMR) and a reaction readily takes place only when an equimolar amount of $AlCl_3$ is added. However, in this case the anion which attacks the CH_2-group of the cyclopropane ring is chloride but not acetate. After washing with water compound **5a** was obtained in about 90% yield.

The results obtained show that, regardless of the nature of the substituents in the initial pyrazolines **1**–**3**, reactions with acyl chlorides easily proceed with high selectivity by electrophilic attack on the *N*-atom distant from the cyclopropane framework, with ring opening and nucleophile addition. Thus, the orthogonal fixed orientation of the azo group and cyclopropane ring in spirocyclopropane pyrazolines, as for **1**–**3**, is more favourable for overlap of their electronic orbitals. In our opinion, this conjugation probably leads to a high thermal stability of these pyrazolines[7] and, on the other hand, to a greater reactivity with electrophilic agents giving the products of 1,5-addition to the azocyclopropane system.

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References

† Compound **4**: ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.86 (NCH_2, t, *J* 9.2 Hz), 2.90 (CH_2 in ring, t, *J* 9.2 Hz), 3.69 (CH_2Cl, t, *J* 6.5 Hz), 2.80 (CH_2, t, *J* 6.5 Hz), 2.30 (Me, s). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 170.0 (CO), 161.9 (N=C), 43.9 (NCH_2), 39.9, 34.9 and 33.2 (all CH_2), 19.9 (Me).

5a: ^{1}H NMR (250 MHz, $CDCl_3$) δ 4.10 (H^2, br. d, *J* 8.0 Hz), 3.72 (CH_2Cl, t, *J* 6.8 Hz), 2.91 (H^6, d, *J* 8.0 Hz), 2.58–2.82 (3H, m, H^1 and $=CCH_2$), 2.33 (H^7, m), 2.19 (Me, s), 1.40–1.68 (2H, m, *exo*-$H^{8,9}$), 1.05–1.30 (4H, m, *endo*-$H^{8,9}$ and $2H^{10}$). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 168.7 (CO), 157.2 (N=C), 63.8 (C^2), 57.1 (C^6), 40.8 (C^1), 40.3 (CH_2Cl), 39.2 (C^7), 32.4 (C^{10}), 32.2 ($=CCH_2$), 27.4 and 24.4 (C^8 and C^9), 21.8 (Me).

6: ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.74 (CH_2Cl, t, *J* 6.6 Hz), 3.70 (OMe, s), 3.15 and 2.75 (CH_2 in ring, d, ^2J 17 Hz), 2.78 (CH_2, br.t, *J* 6.6 Hz), 2.21 (MeCO, s), 1.59 (Me, s). ^{13}C NMR (50.3 MHz, C_6D_6) δ 172.0 (CO), 168.0 (COO), 152.9 (N=C), 65.5 (C^5), 52.4 (OMe), 48.7 (C^4), 40.5 (CH_2Cl), 32.9 (CH_2), 21.9 and 21.7 (MeCO and Me).

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