Structure of the acylation products from 3,6-disubstituted and 3,6,7-trisubstituted 1*H*-pyrazolo[5,1-*c*][1,2,4]triazoles

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Dedicated to Prof. Alexandru T. Balaban on the occasion of his 75th birthday

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Abstract

The monoacyl derivatives from 6-methyl-3-phenyl-1*H*-pyrazolo[5,1-*c*][1,2,4]-triazole **1** may exist in three isomeric forms. Spectroscopic and chemical arguments are presented for the confirmation of the identities of the resulting products.

Keywords: Pyrazolo[5,1-*c*][1,2,4]triazoles, acylation, benzoylation

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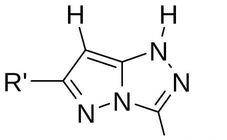
Introduction

Interest in 6-alkyl-3-aryl(alkyl)-1*H*-pyrazolo[5,1-*c*][1,2,4] triazoles **1** is commonly attributed to their use as precursors for color photosensitive materials[1-3], their role in inks and toners, as ingredients in cosmetics and also for their biological activity[4-7]. However, their chemistry is under-represented in the literature[8-12], except perhaps in relation to 3,6,7-trisubstituted-pyrazolo[5,1-*c*][1,2,4]triazoles **2** [13,14]

In these reports, acetylation of 3,6-disubstituted-1*H*-pyrazolo[5,1-*c*][1,2,4]triazole **1d** to form the diacetylated compound **4d**, together with the monoacetylated compound **5d**, has been presented.[15] The formation of monoacetylated compounds **5e,f** in the reactions of 6-methyl-7,8-dihydro-9*H*-1,3,4-triazolo[4,3-*b*][1,2,4]triazepin-8-ones **6e,f** with acetic anhydride also has been described (Scheme 1).[8] There has been no systematic study and that is the purpose of the present report.



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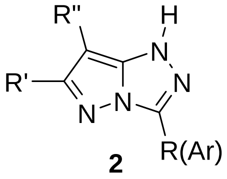

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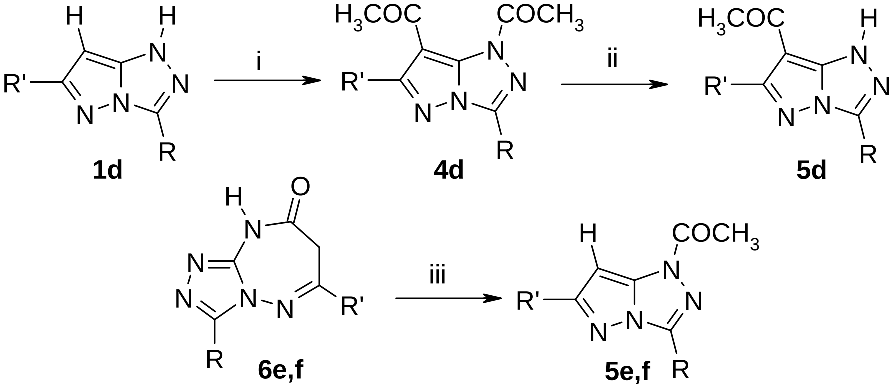


Scheme 1. Acyl derivatives of 3,6-disubstituted pyrazolo[5,1-*c*][1,2,4]triazoles. i: $(CH_3CO)_2O$ / F_3CSO_3H / reflux, ii: HCl / CH_3OH / reflux, iii: $(CH_3CO)_2O$ / reflux **1d**, **4d**, **5d**: R’ = CH_3, R = $(CH_2)_3C_6H_5$; **5e**, **6e**: R’ = CH_3, R = H; **5f**, **6f**: R’ = R= CH_3.

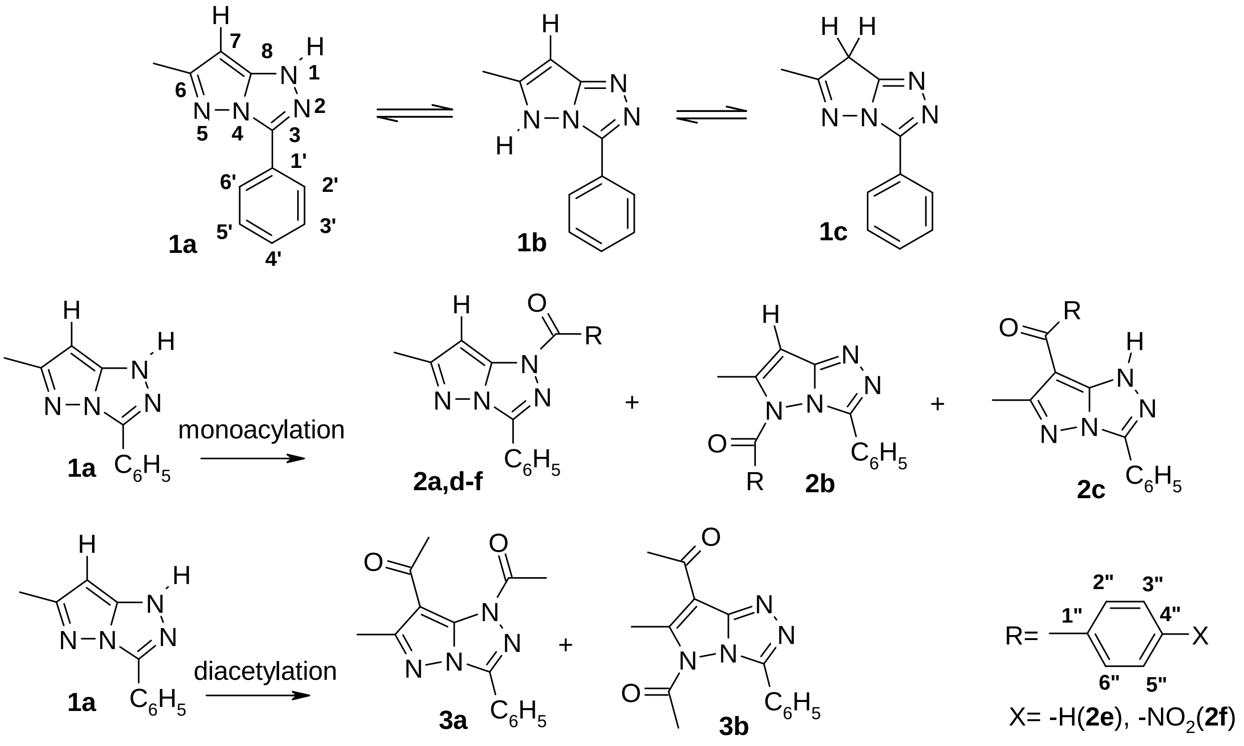
Results and Discussion

Because the pyrazolo[5,1-*c*][1,2,4]triazole system can exist as three tautomeric forms, **1a, 1b, 1c**, monoacylation can produce three isomers: the keto form, 7-acyl-6-methyl-3-phenyl-1*H*-pyrazolo[5,1-*c*][1,2,4]triazole **2c**, and two hydrazides, 1-acyl-6-methyl-3-phenyl-7*H*-pyrazolo[5,1-*c*][1,2,4]triazole **2a** and 5-acyl-6-methyl-3-phenyl-7*H*-pyrazolo[5,1-*c*][1,2,4]triazole **2b**. Diacylation can produce two isomers **3a**, **3b** (Scheme 2). The data in the literature present evidence for the tautomeric 1-*H* form for the 3,6-disubstituted pyrazolo[5,1-*c*][1,2,4]triazoles **1**, while only mentioning the 5-*H* tautomeric form.[17]

The pyrazole and triazole cycles, if considered to be independent, show different reactivity. In electrophilic substitution reactions, pyrazole is more reactive than the other azoles (with the exception of imidazoles). Additionally, its higher level of basicity, suggests pyrazole is more nucleophilic and more reactive in electrophilic substitution reactions than is 1,2,4-triazole.[16]

In order to verify these suppositions, we have carried out the acetylation of 6-methyl-3-phenyl-1*H*-pyrazolo[5,1-*c*][1,2,4]triazole **1** under the following conditions: a) with acetic anhydride, b) with acetic anhydride in the presence of concentrated H_2SO_4, c) with acetyl chloride in pyridine, d) with acetyl chloride in tetrahydrofuran and e) with acetyl chloride in tetrahydrofuran in the presence of tributylamine. The reactions were monitored by TLC and the most appropriate conditions were then used for the synthesis of other acyl derivatives.

All the acetylation reactions of 6-methyl-3-phenyl-*1H*-pyrazolo[5,1-*c*][1,2,4]triazole **1a** led to the same N-monoacetylated compound, as the main product, showing a molecular ion peak at 240 a.m.u., together with unreacted **1a** in experiments (c) and (d) and C-monoacetylated compound **2c** and the diacetylated compound **3a** in experiment (b).



Scheme 2. Acylation of 6-methyl-3-phenyl-1*H*-pyrazolo[5,1-*c*][1,2,4]triazole **1**. **2a-c**: R = CH_3, **2d**: R= CF_3, **2e**: R = C_6H_5, **2f**: R = 4-$O_2NC_6H_4$.

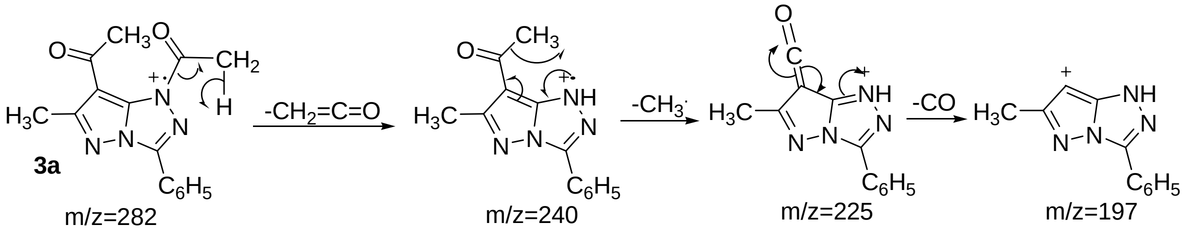
The monoacetylated compound (from e) does not react with 2,4-dinitrophenylhydrazine in alcoholic solution in the presence of concentrated H_2SO_4 (Brady's reagent for ketone) and the IR spectrum shows a valence vibration $\nu_{C=O}$ at 1722 cm^{-1}. The ^{1}H-NMR spectrum shows δ = 6.17 ppm for H7[8] while the δ = 12.5 ppm peak (from 6-methyl-3-phenyl-1*H*-pyrazolo[5,1-*c*][1,2,4]triazole **1**) assigned to H in -NH-, disappears upon acetylation. We conclude that the obtained monoacetylated compound has either structure **2a** or **2b**. The evidence for N-acetylation was supported by the mass spectrum of the obtained compound, which indicated the loss of mass 42 a.m.u. (CH_2=C=O), a typical fragmentation for N-acetyl derivatives. In order to elucidate the position of acetylation, we performed the following 2-D spectra: ^{1}H-^{1}H COSY, ^{1}H-^{13}C COSY: HETCOR (HMQC) and ^{1}H-^{13}C HMBC for the compound formed by the monoacetylation of 6-methyl-3-phenyl-1*H*-pyrazolo[5,1-*c*][1,2,4]triazole **1**.

The ^{1}H-^{1}H COSY spectrum shows the presence of a very low intensity coupling between the protons of the methyl 6-C-CH_3 and the 7-H proton. This observed $^4J_{HH}$ coupling is much more likely to arise in the case of isomer **2b** (R = CH_3), monoacetylated on the 5-N nitrogen atom, in which there is a double bond between the 6-C and 7-C atoms, which can be considered an allylic type coupling. Because the coupling is not as intense as theory would predict for the monoacetylated compound **2a** (R=CH_3), we conclude that the isomer **2b** (R = CH_3) is present to only a small extent.

The ^1H-^{13}C HMBC spectrum shows the following proton-carbon distance-couplings: $^2J_{C=O,\ O=C\text{-}CH3}$, $^2J_{6\text{-}C,\ 6\text{-}C\text{-}CH3}$, $^2J_{6\text{-}C,\ 7\text{-}H}$, $^3J_{8\text{-}C,\ 6\text{-}C\text{-}CH3}$, $^3J_{3\text{-}C,\ 2',6'\text{-}H}$, $^3J_{1'\text{-}C,\ 3',5'\text{-}H}$, $^3J_{3\text{-}C,\ 2',6'\text{-}H}$, $^3J_{2'\text{-}C,\ 6'\text{-}H}$,$^3J_{6'\text{-}C,\ 2'\text{-}H}$, $^3J_{4'\text{-}C,\ 2',6'\text{-}H}$.

The acetylation with acetic anhydride in the presence of concd. H_2SO_4 has led to a mixture (according to ^1H NMR spectra) of 1,7-diacetyl-6-methyl-3-phenylpyrazolo[5,1-*c*] [1,2,4]triazole **3a** (~70%), 7-acetyl-6-methyl-3-phenyl-1*H*-pyrazolo[5,1-*c*][1,2,4]triazole **2c**(~24%) and 1-acetyl-6-methyl-3-phenylpyrazolo[5,1-*c*][1,2,4]triazole **2a**, (~6%) (Scheme1).

The mass spectrum of this mixture indicates the molecular ions for the monoacetylated compounds and for the diacetylated products at 240 a.m.u. and 282 a.m.u., respectively. It also shows the fragmentation of the (CH_3) from the molecular ion, (240 a. m.u.) with the formation of the 225 a.m.u. ion (which is specific to ketones) and which can only take place in the case of compounds acetylated at carbon **2c** or **3a** (Scheme 3).

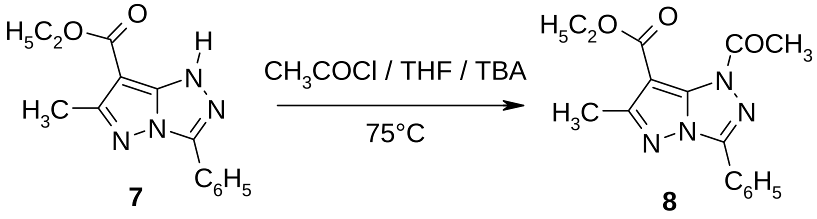


Scheme 3. The fragmentation of the diacetylated compound **3a**.

The reaction of 6-methyl-3-phenyl-1*H*-pyrazolo[5,1-*c*][1,2,4]triazole **1** with trifluoroacetic anhydride leads to the monotrifluoroacetylated compound **2d**, which is unstable over time. The mass spectrum indicated the production of the trifluoroacetylated compound by the presence of the molecular ion at 294 a.m.u. and the peak at 225 a.m.u. produced from the loss of the CF_3 fragment.

Reactions of 6-methyl-3-phenyl-1*H*-pyrazolo[5,1-*c*][1,2,4]triazole **1** with benzoyl chloride and 4-nitrobenzoyl chloride in THF in the presence of tributylamine, lead to compounds **2e** and **2f** (Scheme 2).

Acetylation of 7-ethoxycarbonyl-6-methyl-3-phenyl-1*H*-pyrazolo[5,1-*c*][1,2,4]triazole **7** in THF in the presence of tributylamine, has led to the 1-acetyl-7-ethoxycarbonyl-6-methyl-3-phenyl-pyrazolo[5,1-*c*][1,2,4]triazole **8**, which was characterised by IR, MS and ^1H and ^{13}C NMR spectroscopy (Scheme 4). The mass spectrum identified fragmentation of CH_2=C=O by the presence of the molecular ion at 312 a.m.u., which is a typical fragmentation for N-acetyl derivatives.



Scheme 4. Acetylation of 7-ethoxycarbonyl-6-methyl-3-phenyl-1*H*-pyrazolo[5,1-*c*] [1,2,4]-triazole **7**.

Conclusions

The acetylation of 6-methyl-3-phenyl-1H-pyrazolo[5,1-*c*] [1,2,4]triazole 1 proceeds in different ways according to the reaction conditions.Thus, in the presence or absence of a tertiary amine the acetylation takes place at the 1-N nitrogen atom and in a very small proportion at the 5-N nitrogen atom. In contrast, under acidic conditions, the acetylation takes place at the 1-N nitrogen atom and / or the 7-C carbon atom, with the formation of compounds monoacetylated at atoms 1-N or 7-C and diacetylated at the atoms 1-N and 7-C.

Experimental Section

General Procedures. TLC was performed using aluminium plates precoated with silica gel 60 or 60 F_{254} (Merck) and visualized by iodine or UV light (254 nm). Melting points were determined on a Böetius PHMK (VEB Analytik Dresden) apparatus. The IR-spectra were recorded (KBr) on a Jasco FT/IR-410 instrument. The ^{1}H- and ^{13}C-NMR spectra were recorded on a Bruker 200DPX or Bruker DRX spectrometers. Mass spectrometry was carried out on a Varian FINNIGAN MAT 212 instrument at 54 eV.

The chemical reagents (Fluka, Merck) were used as purchased. 6-Methyl-3-phenyl-1*H*-pyrazolo[5,1-*c*][1,2,4]triazole **1** and 7-ethoxycarbonyl-6-methyl-3-phenyl-1*H*-pyrazolo[5,1-*c*] [1,2,4]triazole **7** were obtained according to the literature from 4-ethoxycarbonyl-5-hydrazino-3-methyl-1*H*-pyrazole[2].

6-Methyl-3-phenyl-1*H*-pyrazolo[5,1-*c*][1,2,4]triazole[2] (1). White powder, m.p. 214-217°C (lit. 216-217°C); IR (KBr): 3147, 2980, 2927, 1668, 1622, 1500, 1486, 1453, 1325, 1233, 1175, 1100, 1068, 1008, 765, 688, 578 cm^{-1}; H^1-NMR [DMSO+TFA, δ (ppm), J (Hz)]: 12,31 (sl, N-H); 8,41-8,35 (m, 2H, 2′-H, 6′-H); 7,58-7,44 (m, 3H, 3′-H, 5′-H, 4′-H); 5,68 (s, 1H, 7-C-H); 2,32 (s, 3H, -CH_3); ^{13}C-NMR [DMSO+TFA, δ (ppm)]:157,48 (6-C); 148,90 (8-C); 137,89 (3-C); 130,11 (4′-C); 129,22 (3′-C, 5′-C); 126,45 (1′-C); 126,10 (2′-C, 6′-C); 77,91 (7-C); 14,79 (-CH_3).

Acylation of 6-methyl-3-phenyl-1*H*-pyrazolo[5,1-*c*][1,2,4]triazole 1

a) Acetylation with acetic anhydride. 6-Methyl-3-phenyl-1*H*-pyrazolo[5,1-*c*][1,2,4]triazole **1** (5 mmol) and acetic anhydride (5 mL) were refluxed for 5 min. After cooling, the resulting solution was precipitated in water (15 mL). After filtering off, washing with water and drying, a white product (0.8 g) was obtained (η=67%).

1-Acetyl-6-methyl-3-phenylpyrazolo[5,1-*c*][1,2,4]triazole (2a). White powder, m.p. 161.5-163°C IR(KBr): 3162, 3063, 2984, 2929, 17IIb, 1596, 1578, 1543, 1489, 1326, 1317, 1154, 1112, 958, 747, 692 (cm^{-1}); ^{1}H-NMR [DMSO, δ (ppm), J (Hz)]: 8,46-8,44(m, 2H, 2′-H, 6′-H); 7,67-7,65(m, 3H, 3′-H, 4′-H, 5′-H); 6,20(s, 1H, 7-C-H); 2,65(s, 3H, CH_3-C=O); 2,40(s, 3H, 6-C-CH_3); ^{13}C-NMR [DMSO, δ (ppm)]: 167,68 (C=O); 159,70 (6-C), 145,05 (8-C), 140,94 (3-C); 132,66 (4′-C), 130,10 (3′-C, 5′-C), 127,95 (2′-C, 6′-C); 124,97(1′-C); 86,81(7-C); 21,65(CH_3-C=O); 15,54(6-C-CH_3), Bruker DRX 400;

MS(54eV): m/e=240(M^+, 21,36%); 198(M^+-CH_2=C=O, 100%). Anal. Calcd. for $C_{13}H_{12}N_4O$: C, 64.99; H, 5.03; N, 23.32. Found: C, 64.69; H, 5.04; N, 22.87.

b) Acetylation with acetic anhydride in the presence of concd. H_2SO_4. 6-Methyl-3-phenyl-1*H*-pyrazolo[5,1-*c*][1,2,4]triazole **1** (2.5 mmol), acetic anhydride (10 mL) and concd. H_2SO_4 (0.03 mL) were refluxed for one hour. After cooling, the resulting solution was precipitated in ice-water (50 mL). After filtering, washing with water and drying, 0.55 g of white product were obtained (η=91%); m.p.=116-120°C; TLC= 2 spots; mixture of monoacetylated and diacetylated products.

The ^{1}H-NMR spectra indicated the presence of a mixture of three compounds in the following percentages: ~70% of diacetylated compound **3a**, ~24% of monoacetylated compound **2c** and ~6% of monoacetylated compound **2a**: ^{1}H-NMR [DMSO, δ(ppm), J (Hz)]: 8,50-8,45 (m, 2H, 2′-H, 6′-H); 7,59-7,26 (m, 3H, 3′-H, 4′-H, 5′-H); 2,77(s, 3H, 7-C-C(=O)-CH_3); 2,56(s, 3H, -N-C(=O)-CH_3); 2,52(s, 3H, 6-C-CH_3).

Monoacetylated products **2a**, **2b**: MS, m/z, I_{rel}: 240 (M^+, 55%); 198 (M^+ - CH_2=C=O, 4%).

Diacetylated product **3a**: MS, m/z, I_{rel}: 282 (M^+, 5%); 240 (M^+ - CH_2=C=O, 55%); 225 ($[240]^+$-CH_3, 100%); 197 ($[240]^+$- CH_3C=O, 9%).

c) Acetylation with acetyl chloride in pyridine. Acetyl chloride (15 mmol) was added dropwise to a solution of 6-methyl-3-phenyl-1*H*-pyrazolo[5,1-*c*][1,2,4]triazole **1** (2.5 mmol) in pyridine (7.5 mL) at room temperature. After 1 hour at 50°C, the resultant solution was cooled and precipitated in ice water (50 mL). The separated product contained unreacted starting material and monoacetylated product (as determined by TLC).

d) Acetylation with acetyl chloride in tetrahydrofuran. Acetyl chloride (3.3 mmol) was added dropwise to a solution of 6-methyl-3-phenyl-1*H*-pyrazolo[5,1-*c*][1,2,4]triazole **1** (2.5 mmol) in tetrahydrofuran (10 mL) at room temperature . After 1 hour at room temperature, the solution was precipitated in ice water (50 mL). TLC indicated that the product contained some unreacted material and monoacetylated product.

e) Acetylation with acetyl chloride in tetrahydrofuran, in the presence of tributylamine. Acetyl chloride (3.3 mmol) was added dropwise to a solution of 6-methyl-3-phenyl-1*H*-pyrazolo[5,1-*c*][1,2,4]triazole **1** (2.5 mmol) and tributylamine (5 mmol) in tetrahydrofuran (10 mL) at room temperature. After 1 hour at room temperature, the solution was washed with water (5 mL), 5% HCl (5 mL), 5% Na_2CO_3 (5mL), water (5mL) and treated with anhydrous Na_2SO_4. After filtration, distillation of the solvent and recrystalisation from ethyl alcohol a white-pink crystalline powder (0.38g) was obtained (η=63%); m.p.=160.5-162.5°C. TLC=1 spot; MS(54eV): m/z= 240($M^{+\cdot}$); IR(KBr) and H^1-NMR ($CDCl_3$) identical with the product from a).

f) Acylation with trifluoroacetic anhydride. Trifluoroacetic anhydride (0.81 mmol) in $CHCl_3$ (4 mL) was added dropwise over 10 minutes to a solution of 6-methyl-3-phenyl-1*H*-pyrazolo[5,1-*c*][1,2,4]triazole **1** (2.52 mmol) in $CHCl_3$ (20 mL) at room temperature. After 30 min of stirring at room temperature and 30 min at 50°C, a clear, pink coloured solution was obtained. (TLC indicated the consumption of starting material). After precipitation in ice-water, filtration and drying, 0.46g (62%) product was obtained. The TLC indicated that the product contains traces of un-reacted material.

6-Methyl-3-phenyl-1-trifluoroacetylpyrazolo[5,1-*c*][1,2,4]triazole (2d). White-brownish powder, m.p. 183-186°C; MS, m/z, I_{rel}: 294(M^+, 10%); 225 (M^+-CF_3, 61%).

g) Acylation with benzoyl chloride. Benzoyl chloride (5.5 mmol) was added dropwise to a solution of 6-methyl-3-phenyl-1*H*-pyrazolo[5,1-*c*][1,2,4]triazole (5 mmol) and tributylamine (5.8 mmol) in THF (20 mL) and the solution maintained at room temperature for 60 min and then heated to 100°C for 3 hours. The solution was diluted with ethyl acetate (25 mL), washed with water, dried with anhydrous Na_2SO_4, filtered then distilled under reduced pressure. The product was recrystalised from ethyl alcool to afford a white-pink powder (0.82 g, 54%).

1-Benzoyl -6-methyl-3-phenyl-7-pyrazolo[5,1-*c*][1,2,4]triazole (2e). White-pink powder; m.p.121-124°C; IR(KBr): 3151, 3061, 3033, 3007, 2912, 1692, 1593, 1579,1543, 1494, 1462, 1336, 1164, 1109, 792, 765, 698, 687 cm^{-1} ; ^{1}H-NMR [$CDCl_3$, δ (ppm)]: 8,51-8,46(m, 2H, 2″-H, 6″-H); 8,32-8,27 (m, 2H, 2′-H, 6′-H); 7,69-7,50 (m, 6H, 3″-H, 5″-H, 3′-H, 5′-H, 4″-H, 4′-H); 6,29(s, 1H, 7-C-H); 2,51(s, 3H, -CH_3); ^{13}C-NMR[$CDCl_3$, δ (ppm)]: 163,12(C=O); 159,59(6-C); 145,96(8-C); 141,87(3-C); 132,91(1″-C), 131,51(4″-C); 131,17(2″-C, 6″-C); 130,88(4′-C); 128,88(3″-C, 5″-C); 128,18(3′-C, 5′-C), 127,7(2′-C, 5′-C), 124,61(1′-C); 87,53(7-C); 15,09(-CH_3). MS, m/z, I_{rel}: 302 (M^+, 25%); 197 (M^+ - C_6H_5C=O, 3%), 105 ($C_6H_5C{=}O^+$, 100%). Anal. Calcd. for $C_{18}H_{14}N_4O$: C, 71.51; H, 4.67; N, 18.53. Found: C, 71.02; H, 4.56; N, 17.95.

h) Acylation with 4-nitrobenzoyl chloride. A solution of 4-nitrobenzoyl chloride (5,5 mmol) in THF (6 mL) was added dropwise to a solution of 6-methyl-3-phenyl-1*H*-pyrazolo[5,1-*c*][1,2,4]triazole **1** (5 mmol) and tributylamine (5.8 mmol) in THF (20 mL) and the solution was maintained for 60 min at room temperature then 60 min at 100°C. After precipitation in ice-water and filtration, the product was suspended for 30 min in 50 mL 5% Na_2CO_3 solution, filtered again and dried. 1.58 g (83%) of a pale yellow powder was obtained.

6-Methyl-1-(4-nitrobenzoyl)-3-phenyl-7-pyrazolo[5,1-*c*][1,2,4]triazole (2f). Pale yellow powder (83%), m.p. 195-200°C; IR(KBr):3147, 3109, 1697, 1594, 1524, 1495, 1465, 1425, 1350, 1337, 1108, 792, 765, 698, 687 cm^{-1}; ^{1}H-NMR [$CDCl_3$, δ (ppm)]: 8,50-8,37 (m, 6H, 2"-H, 6″-H, 3″-H, 5″-H, 2′-H, 6′-H); 7,59-7,53 (m, 3H, 3′-H, 5′-H, 4′-H); 6,35 (s, 1H, 7-C-H); 2,53 (s, 3H, $-CH_3$); ^{13}C-NMR [$CDCl_3$, δ (ppm)]: 166,25 (C=O); 160,00 (6-C); 154,06 (4″-C); 145,62 (8-C); 140,87 (3-C); 136,56 (1″-C); 132,15 (2″-C, 6″-C); 131,97 (4′-C); 129,01 (3′-C, 5′-C); 127,80 (2′-C, 6′-C); 124,37 (1′-C); 123,24 (3″-C, 5″-C); 88,08 (7-C); 15,11 (CH_3). Anal. Calcd. for $C_{18}H_{13}N_5O_3$: C, 62.25; H, 3.77; N, 20.16. Found: C, 62.34; H, 3.85; N, 20.29.

Acetylation of 7-ethoxycarbonyl-6-methyl-3-phenyl-1H-pyrazolo[5,1-*c*][1,2,4]triazole (7). Acetyl chloride (3 mmol) was added dropwise to a solution of 7-ethoxycarbonyl-6-methyl-3-phenyl-1*H*-pyrazolo[5,1-*c*] [1,2,4]triazole **7** (2.5 mmol) and tributylamine (4.03 mmol) in tetrahydrofuran (10 mL) at room temperature. After 90 min at 75°C, the solution was diluted with ethyl acetate (25mL), washed with water (5 mL), 5% HCl (5 mL), water (5mL) and dried with anhydrous Na_2SO_4. After filtration and distillation of the solvent the product was recrystalised from methyl alcohol to afford a white crystalline powder (0.75g, 80%)

1-Acetyl-7-ethoxycarbonyl-6-methyl-3-phenylpyrazolo[5,1-*c*][1,2,4]triazole (8). White powder (80%), m.p. 94-97°C; IR(KBr): 3059, 2974, 2900, 1746, 1701, 1595, 1578, 1549, 1495, 1327, 1247, 1158, 763, 689, 640 cm^{-1}; ^{1}H-NMR [DMSO, δ (ppm), J (Hz)]: 8,37-8,34 (m, 2H, 2′-H, 6′-H); 7,64-7,61 (m, 3H, 3′-H, 4′-H, 5′-H); 4,22 (q, 2H, *J*=7,1, $-O-CH_2CH_3$); 2,65 (CH_3-C=O); 2,44 (6-C-CH_3); 1,28 (t, 3H, *J*=7,1, $-O-CH_2CH_3$); ^{13}C-NMR [DMSO, δ (ppm)]: 165,75 (CH_3-C=O); 162,03 (O=C-O-C_2H_5); 158,88 (6-C); 142,57 (8-C); 139,86 (3-C); 131,83 (4′-C); 129,08 (3′-C, 5′-C); 127,05 (2′-C, 6′-C); 123,51 (1′-C); 94,35(7-C); 60,03 ($-O-CH_2CH_3$), 21,49 (CH_3-C=O); 14,20 (6-C-CH_3); 14,13 ($-O-CH_2CH_3$). MS, m/z, I_{rel}: 312 (M^+, 6 %); 270 (M^+ $-CH_2$=C=O, 80%). Anal. Calcd. for $C_{16}H_{16}N_4O_3$: C, 61.53; H, 5.16; N, 17.94. Found: C, 61.08; H, 4.88; N, 17.55.

Aknowledgements

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References

1. Bailey, J. *J.Chem.Soc., Perkin Trans.I* **1977**, *18*, 2047.
2. Bailey, J.; Bowes E.; Marr P. A. Brit. 1247493 1967.
3. Diehl, D. R.; Mbiya, K.; Wray, C. S. Eur. Pat. Appl. 2000; EP 20000628.
4. Tawara, K.; Akira, O. Eur.Pat. Appl. 1997, EP 0763569.
5. Plos, G.; Lagrange, A. Eur. Pat. Appl. 2000, EP 1062937.

6. Audousset, M. *Eur. Pat. Appl.* 2000, EP 1040818.
7. Katsunori, K.; Takayuki, S.; Hiromi I. JP 2002167305.
8. Claramunt, R-M.; Fabregà, J-M.; Elguero, J. *J. Het. Chem.* **1974**, *11,* 751.
9. Elfahham, H. E.; Sadek, K. U.; Elgemeie, G. E.; Elnagdi, M. H. *J.Chem.Soc., Perkin Trans.I* **1982**, 2663.
10. Kirshke, K.; Wolff, E.; Ramm, M.; Schulz, B. *Liebigs Ann. Chem*. **1994**, 1037.
11. Ghozlan, S. A. S.; Hafez, A.; El-Bannany, A. *Arch. Pharm.(Weinheim*) **1987**, *320*, 850.
12. Csunderlik, C.; Bercean, V.; Peter, F.; Badea. V. *ARKIVOC* **2002**, (ii), 133.
13. Nishijima, T.; Onodera, K. U.S.Pat. Appl. 1988 US 4,752,561.
14. Katoh, K.; Kawakatsu, S.; Masuda, K.; Miyagi, K.; Nakayama, N.; Kimura,T. U.S.Pat. Appl.1986 US 4,581,326.
15. Arnold, R. W.; Maggiulli, A. C. U.S.Pat. Appl. 1990 U.S. 4914209.
16. Benjes, P. A.; Grimmett, M. R. *N-Alkylation of nitrogen azoles, Advances in detailed reaction mechanisms*, JAI Press-Inc. 1994, vol. 3, 199.
17. Stanovnik, B.; Tišler, M.; Kirn, B.; Kovač, I. *J.Het.Chem.* **1979**, *16*, 195.