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Studies on Azole-to-Azole Interconversions. Substituent Effects on the Ring-degenerate Equilibration between 3-Aroylamino-5-methyl-1,2,4-oxadiazoles and 3-Acetylamino-5-aryl-1,2,4-oxadiazoles

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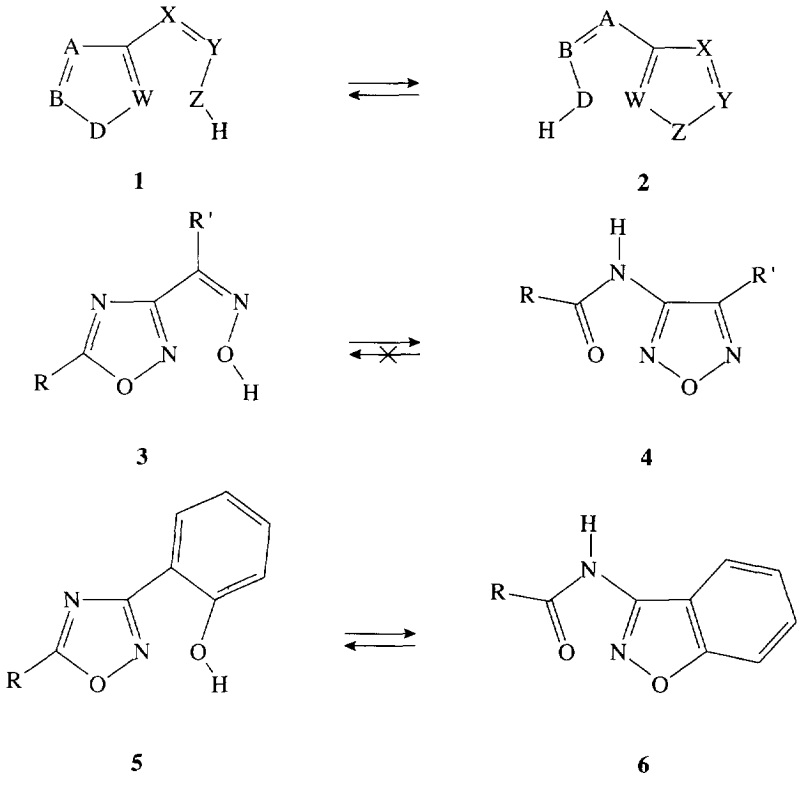
Abstract: The title reaction has been studied both in CD_3OD and $^tBuOK/CD_3OD$ by means of ^1H NMR measurements. The equilibrium composition and the effect exerted thereon by X-substituents in the aryl moiety have been found to be quite different whether neutral or anionic forms are involved. In the first case the effect of X is meagre and 3-acetylamino-5-aryl-1,2,4-oxadiazoles are more stable than the 3-aroylamino-5-methyl isomers. *Vice-versa,* when anions are involved the substituent effect is remarcable and the equilibrium can be, for strongly electron-withdrawing X-groups, even largely shifted towards the anions of the 3-aroylamino-5-methyl-1,2,4-oxadiazoles.

INTRODUCTION

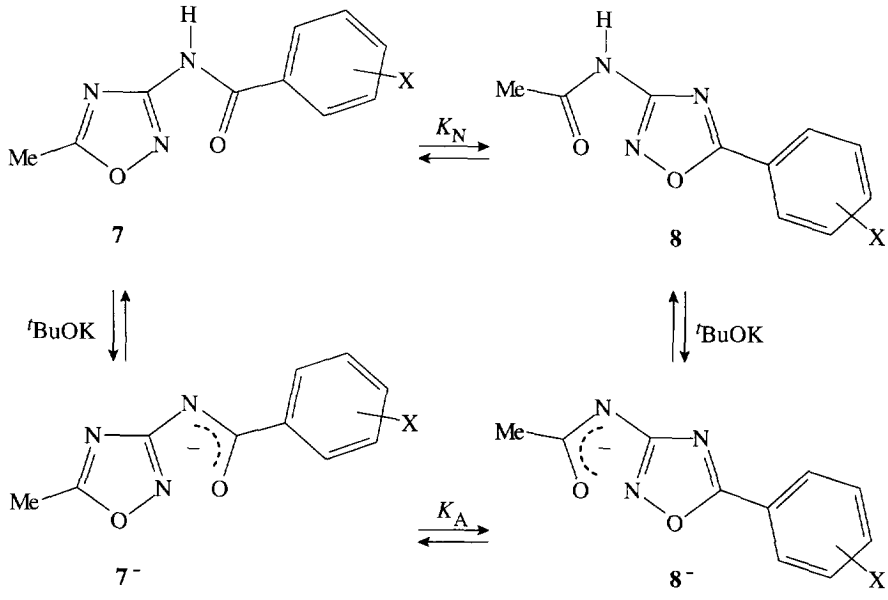
Molecular rearrangements of five-membered heterocycles involving a three-atom side-chain (**1** → **2**) are well documented[1] and largely used for the synthesis of many heterocyclic systems.[1,2]



Scheme 1

Peculiar rearrangements are those where an O-N bond is both cleaved and formed (e.g. **1** ⇌ **2** with W = N and D = Z = O): these reactions are potentially reversible, although the large stability of one component with respect to the other sometimes does not allow to prove the occurrence of an equilibrium. Thus, considering 1,2,4-oxadiazole derivatives, it is well known[3] that (*Z*)-oximes of 3-acyl-1,2,4-oxadiazoles (**3**) easily rearrange into the corresponding 3-acylamino-1,2,5-oxadiazoles (**4**), whereas the reverse does not occur. On the other hand the position of the equilibrium between 3-(*o*-hydroxyphenyl)-1,2,4-oxadiazoles (**5**) and 3-acylaminobenzisoxazoles (**6**) depends on the nature of R and of the base employed: strong bases favouring **5** with respect to **6**, probably because of the large resonance stabilization provided by the phenoxide function in the anion of **5**.[4] If in the **1** ⇌ **2** reaction ABD ≡ XYZ, *i.e.* the starting and the final heterorings are equal, an iso-heterocyclic (or ring-degenerate) rearrangement occurs and it can be reversible.[1] When substituents on ABD and XYZ, if any, are equal, then the rearrangement is fully-degenerate.[1e,f]

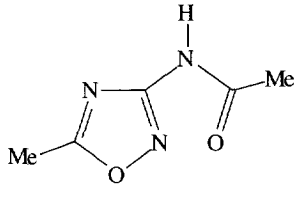
Some years ago we reported[5-7] examples of ring-degenerate rearrangement in the 1,2,4-oxadiazole series.[8] Thus, for instance, the equilibrium between the 3-aroylamino-5-methyl-1,2,4-oxadiazoles **7a-c** and the corresponding 3-acetylamino-5-aryl-1,2,4-oxadiazoles **8a-c** has been found to be always shifted towards **8** both in the melt and in solution.[5,7] The behaviour of the same 1,2,4-oxadiazoles **7a-c** and **8a-c** in methanol under irradiation at λ 254 nm has been related to both the nature of the partecipating chromophore and the multiplicity of the excited states involved.[7,12] Moreover, the fully-degenerate rearrangement of the



a: X = *p*-OMe
b: X = *p*-Me
c: X = H
d: X = *p*-Cl
e: X = *p*-CF_3
f: X = *p*-CN
g: X = *p*-NO_2
h: X = *m*-OMe
i: X = *m*-Me
j: X = *m*-Cl
k: X = *m*-CF_3
l: X = *m*-NO_2

Scheme 2

anion of 3-acetylamino-5-methyl-1,2,4-oxadiazole **9** in DMSO has been detected by dynamic ^{1}H NMR,[6] while the *quasi*-fully-degenerate rearrangement of the derivative of **9** with a trideuteriated acetyl group in the same solvent has been studied at different temperatures.[13] A semiempirical approach to these reactions has been also reported.[13,14]



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In connection with the just cited[5-7,12] studies on the chemical and photochemical reactivity of

3-acylamino-1,2,4-oxadiazoles and continuing our researches on both synthetic[1d,f,15] and mechanistic[16] implications of azole-to-azole interconversions we report herein on the substituent effects in the ring-degenerate equilibration between some 3-aroylamino-5-methyl-1,2,4-oxadiazoles **7a-l** and the corresponding 3-acetylamino-5-aryl-1,2,4-oxadiazoles **8a-l** both in CD_3OD and $^tBuOK/CD_3OD$: the X substituent should affect the nucleophilicity of the oxygen atom of the side-chain in **7** and, in the reverse reaction, both the polarization of the O(1)-N(2) bond and the leaving group ability of O(1). An influence of X on the thermodynamic stability of the aroylamino moiety in **7** and of the diaryloid system in **8** is also expected.

RESULTS AND DISCUSSION

Equilibration Reactions in CD_3OD

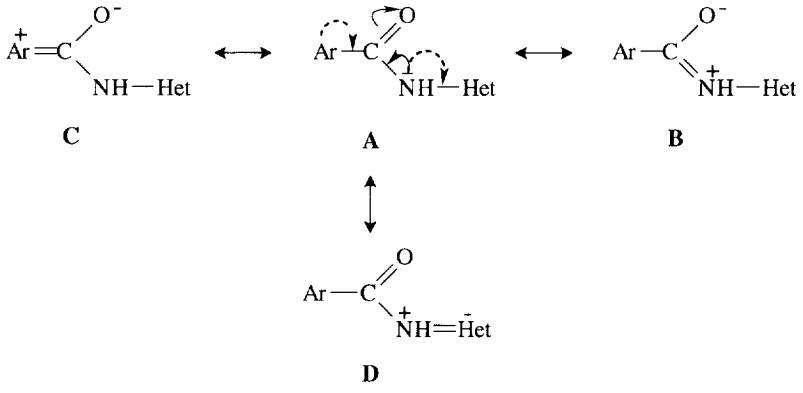
Methanolic solutions of **7** or **8** were kept at 313.15 K until analytical (^1H NMR) determinations gave constant mixture composition. It is noteworthy that, wathever the substituent X, the equilibrium was found to lie well on the side of **8**, with K_N ranging from 3.55 to 13.3 (Table 1).

As far as the substituent effect on K_N is concerned, electron withdrawal significantly shifts the equilibrium towards **7**, while electron release displays an overall, although less marked, favourable effect on **8**. Interestingly, the effects of *para* and *meta* X-groups are better correlated by two separate free-energy relationships, with K_N showing an appreciably higher susceptibility to the *meta*-substituent effect (ρ_{para} -0.37 ± 0.01, *i* 0.00 ± 0.01, *n* 7, *r* 0.996; ρ_{meta} -0.62 ± 0.03, *i* -0.03 ± 0.01, *n* 6, *r* 0.995). It seems first of

Table 1. Equilibrium constants and relevant compositions (%) for the rearrangement 7a-l ⇌ 8a-l at 313.15 K

X	in CD_3OD		in $CD_3OD/^tBuOK$	
	[7]/[8]	K_N	$[7^-]/[8^-]$	K_A
a : *p*-MeO	7/93	13.3	22/78	3.55
b : *p*-Me	8/92	11.5	30/70	2.33
c : H	9/91	10.1	38/62	1.63
d : *p*-Cl	11/89	8.09	67/33	0.493
e : *p*-CF_3	14/86	6.14		
f : *p*-CN	15/85	5.67	90/10	0.111
g : *p*-NO_2	16/84	5.25	92/8	0.0870
h : *m*-OMe	11/89	8.09	41/59	1.44
i : *m*-Me	9/91	10.1	32/68	2.13
j : *m*-Cl	16/84	5.25	78/22	0.282
k : *m*-CF_3	17/83	4.88		
l : *m*-NO_2	22/78	3.55	93/7	0.0753

all evident that the overall effect on K_N is, for both *para* and *meta*-substituents, rather meagre: an outcome which could be regarded as the consequence of a compensation of counteracting effects. Thus, conjugated electron-donating substituents such as the *p*-methoxy group are expected to increase the nucleophilicity of the oxygen atom in compounds **7** (contributor **C**), favouring their rearrangement into **8**, but, on the other hand, the thermodynamic stability of **7** should in turn take advantage of the same resonance contributor **C**; *vice-versa*, electron-withdrawing groups should have a balancing negative effect on both the oxygen nucleophilicity and the possibility of electron dispersal in **7**. At this regard it's worth recalling, though, that the '*internal*' conjugation (contributor **B**) generally overcomes the '*external*' one (contributor **C**) in determining the stability of the carbamoyl group of aromatic amides even in the presence of *para*-electron-releasing substituents in Ar;[17] it should anyway be also considered that, in compounds **7**, the presence of the strong electron-withdrawing 1,2,4-oxadiazol-3-yl group on the amidic nitrogen atom could appreciably modify the electronic distribution, engaging the lone pair on the nitrogen atom itself (contributor **D**) and thus lowering to some extent the relevance of the '*internal*' conjugation. A further effect to be evaluated in the overall picture is represented by any stabilizing conjugation between the aryl and the heteroaryl rings in **8** (*diaryloid effect*),[5] a factor which could well attain a primary role, due to the compensation of the two factors above, and which should effectively contribute to the stability of **8** through any electron release towards the electrophilic oxadiazolyl



C **A** **B**

D

moiety. Therefore, the increased relative stability of **7** when going from the methoxy to the nitro group could be essentially assigned to a decrease in the weight of the *diaryloid effect* in **8**.

Support to this view comes from the results relevant to the *meta*-substituted compounds, where the inductive effects of the aryl moiety obviously attain a primary role: the small but significant shift throughout of the equilibrium composition towards **7** with respect to the corresponding *para*-substituents $[(K_N)_m < (K_N)_p]$ confirms that it is mainly the acylamino structure **8** which benefits by the presence of conjugative substituents in Ar, while the higher susceptibility constant ($\rho_{meta} > \rho_{para}$) reflects a somewhat lower extent of compensation of the induced effects.

Equilibration Reactions in ^{t}BuOK/CD$_3$OD

Compounds **7** and **8** were converted into the corresponding conjugate bases (**7**$^-$ and **8**$^-$) by treatment of their methanolic solutions with ^{t}BuOK. Complete salification was obtained by the addition of increasing amounts of the base until the ^{1}H NMR analysis revealed a constant composition: although the substituent X

does affect the ^{t}BuOK/1,2,4-oxadiazole molar ratio at which the 'plateau' region is reached, the formation of the anionic species is always practically quantitative at ratios around 1.5.

A first-glance comparison of the K_A values (Table 1) with the equilibrium constants obtained in CD_3OD solutions (K_N) clearly indicates that different factors must govern the relative stability of the two heterocyclic systems in neutral and basic conditions: this is because, while **8** always prevails over **7** ($K_N > 1$ throughout), deprotonation invariably favours the stability of the 3-aroylamino structure (**7**$^-$) and K_A ranges from 0.0753 (X = *m*-NO_2) to 3.55 (X = *p*-OMe), testifying that **7**$^-$ is the major component at equilibrium (up to 92%) in the case of electron-withdrawing X groups. Such outcome, as well as the ensueing large negative substituent effect on the **7**$^-$ ⇌ **8**$^-$ equilibrium position (ρ_{para} -1.52 ± 0.07, *i* -0.08 ± 0.03, *n* 6, *r* 0.996; ρ_{meta} -1.95 ± 0.13, *i* 0.03 ± 0.05, *n* 5, *r* 0.994) can be essentially explained on the grounds of the quest for dispersion of the negative charge onto the aryl moiety: as this possibility is hampered, for the acetylamino structure **8**$^-$, by the occurrence that the charged carbamoyl function and the aryl group are separated by the heteroaromatic ring,[18] the stability advantage provided to the aroylamino structure over the acetylamino one by deprotonation finds a straightforward rationale. Accordingly, only a secondary role is at most left, in the anions, to the *diaryloid effect*, which is here again possibly responsible for the somewhat decreased susceptibility of the equilibrium constant to the *para*-substituent effect, owing to an additional stability conjugatively furnished to **8**$^-$.

CONCLUSIONS

The analysis of the results obtained shows that the position of the equilibrium for the ring-degenerate rearrangement herein is quite different whether neutral or anionic forms are involved. In the first case, 3-acetylamino-5-aryl-1,2,4-oxadiazoles **8** are more stable than the 3-aroylamino-5-methyl isomers **7** and the effect of substituents is rather meagre, possibly due to a compensation of counteracting effects. On the contrary, when the corresponding anions are in play, as the aryl group is expectedly much more efficient than a methyl in providing stabilization to the negative charge of the adjacent carbamoyl function, in every instance the equilibrium is appreciably more shifted towards the anion of the 3-aroylamino derivatives (**7**$^-$) with respect to the situation observed in neutral conditions, and, in the presence of electron-withdrawing substituents, **7**$^-$ becomes even much more stable than **8**$^-$.

Interestingly, advantage can be taken, for preparative purposes, of such different behaviour in the equilibration between neutral and anionic forms of the 1,2,4-oxadiazoles herein: thus, operating in the presence of bases, starting from **8** (especially if containing electron-withdrawing substituents) mixtures enriched in **7** can be obtained and, *vice-versa*, operating in neutral conditions, **7** in every case will afford mixtures enriched in **8**.

EXPERIMENTAL SECTION

Materials and Methods

Melting points (uncorrected) were determined with a Kofler hot-stage apparatus and IR spectra (Nujol) were registred on a Perkin-Elmer 257 instrument. Analytical determinations were carried out by ^{1}H NMR spectroscopy [Bruker AC 250 E spectrometer (tetramethylsilane as internal standard)], by integrating the

methyl singlets in the δ ranges 2.40-2.60 (characteristic of 3-aroylamino-5-methyl-1,2,4-oxadiazoles **7**) and 2.10-2.20 ppm (characteristic of 3-acetylamino-5-aryl-1,2,4-oxadiazoles **8**), respectively. Compositions at equilibrium (expressed in % of the two isomers) represent average values of three independent determinations (within 1%).

3-Aroylamino-5-methyl-1,2,4-oxadiazoles **7** were prepared by reacting 3-amino-5-methyl-1,2,4-oxadiazole[19] with the appropriate aroyl chloride according with the procedure described for **7a-c**.[5,7] Thus the aroyl chloride (0.025 moles) was added to a suspension of the amine (0.020 moles) in anhydrous benzene (200 ml) containing pyridine (0.025 moles), and the mixture was allowed to stand at room temperature (with occasional shaking) for 10-20 days, following by TLC analysis the course of the reaction. The solvent was removed under reduced pressure and the residue worked up with water, filtered off and washed with water. The crude material (60-70%) was triturated with benzene at room temperature to remove some starting material and filtered (in the case of **7f**, **7g** and **7l**, treatment with boiling benzene was most appropriate), affording almost pure **7** (final yields *ca.* 50%). Analytical samples were carefully recrystallized from a suitable solvent. The 3-acetylamino-5-aryl-1,2,4-oxadiazoles **8** were prepared by acetylation with acetic anhydride of the appropriate 3-amino-5-aryl-oxadiazole, when available (*i.e.*, **8a-d**);[20] in the other cases, the isoheterocyclic rearrangement of the corresponding 3-aroylamino compound **7** was successfully exploited. Thus, after refluxing **7** in methanol for 12 h, removal of the solvent and crystallization of the residue gave pure **8** (by ^{1}H NMR analysis) as the predominant component in the equilibration mixture. All new compounds gave satisfactory analytical data (C, H, N). Significant physical data are collected in Table 2.

***Equilibration between 3-Aroylamino-5-methyl-1,2,4-oxadiazoles* 7 *and 3-Acetylamino-5-aryl-1,2,4-oxadiazoles* 8**

a) In CD_3OD. Samples of 3-aroylamino derivatives **7** (5 mg) in CD_3OD (1 ml; 2 ml in the case of **7f**, **7g** and **7l**) were maintained in NMR tubes at 313.15 K until constant mixture composition (see Table 1). Representatively, the equilibration reaction was carried out also starting from 3-acetylamino-5-aryl-1,2,4-oxadiazoles (*i.e.*, **8a**, **8c**, **8d** and **8f**), obtaining the same equilibrium composition.

b) In CD_3OD in the presence of ^{t}BuOK. From mother CD_3OD solutions of **7** (0.02 mol dm^{-3} or 0.01 mol dm^{-3} in the case of **7f**, **7g** and **7l**) and ^{t}BuOK (0.06 mole dm^{-3}), samples were prepared so as to attain [^{t}BuOK]/[**7**]$_0$ molar ratios varying from 0.25 to 2.0. After standing for 30', NMR spectra were registered and mixture compositions calculated as above (as expected, δ values of the acetylamino C-Me singlet for **8**$^-$ are lower than that for the corresponding **8**). Plots of [**7** + **7**$^-$]% *versus* [^{t}BuOK]/[**7**]$_0$ showed a trend to limiting values corresponding to complete ionization (usually reached at around 1.5 [^{t}BuOK]/[**7**]$_0$). The [**7**$^-$]/[**8**$^-$] ratios in the plateau region are reported in Table 1: as expected, identical values were obtained when **8a-d,f,g** were representatively used as substrates.

c) On the use of the equilibration reaction as a preparative tool. As a typical procedure, ^{t}BuOK (100 mg, 2 mol equiv) was added to a solution of **8f** (100 mg) in methanol (10 ml). After standing at room temperature for 30', the solvent was removed and the residue taken up with water and neutralized with acetic acid. The collected material was **7f** containing few percents of the starting **8f**, as indicated by ^{1}H NMR analysis.

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Table 2. Physical data for 3-acylamino-1,2,4-oxadiazoles 7 and 8

Compound	X	M.p./°C[a,b]	IR/cm^{-1} ν_{CO}	^{1}H NMR δ (DMSO-d_6)
7a	*p*-MeO	145 (B)[c]		
7b	*p*-Me	137 (B)[c]		
7c	H	144 (B)[d]		
7d	*p*-Cl	162 (B)	1675	2.59 (s, 3H, Me); 7.56-8.03 (m, 4H, ArH); 11.51 (s, 1H, NH)
7e	*p*-CF_3	165 (B)	1680	2.64 (s, 3H, Me); 7.95-8.26 (m, 4H, ArH); 11.77 (s, 1H, NH)
7f	*p*-CN	182 (A)	1680	2.61 (s, 3H, Me); 8.01-8.15 (m, 4H, ArH); 11.73 (s, 1H, NH)
7g	*p*-NO_2	220 (A)[e]	1680	2.61 (s, 3H, Me); 8.19-8.38 (m, 4H, ArH); 11.82 (s, 1H, NH)
7h	*m*-MeO	145 (A)	1665	2.65, 3.89 (2s, 6H, 2Me); 7.22-7.65 (m, 4H, ArH); 11.48 (s, 1H, NH)
7i	*m*-Me	135 (B)	1660	2.44, 2.64 (2s, 6H, 2Me); 7.44-7.88 (m, 4H, ArH); 11.42 (s, 1H, NH)
7j	*m*-Cl	140 (B)	1670	2.66 (s, 3H, Me); 7.42-8.11 (m, 4H, ArH); 11.62 (s, 1H, NH)
7k	*m*-CF_3	141 (B)	1680	2.60 (s, 3H, Me); 7.76-8.37 (m, 4H, ArH); 11.74 (s, 1H, NH)
7l	*m*-NO_2	185 (A)[e]	1675	2.61 (s, 3H, Me); 7.81-8.83 (m, 4H, ArH); 11.82 (s, 1H, NH)
8a	*p*-MeO	168 (B)[c]		
8b	*p*-Me	193 (B)[c]		
8c	H	164 (B)[d]		
8d	*p*-Cl	204 (C)	1695	2.14 (s, 3H, Me); 7.70-8.08 (m, 4H, ArH); 11.25 (s, 1H, NH)
8e	*p*-CF_3	180 (C)	1695	2.20 (s, 3H, Me); 8.00-8.30 (m, 4H, ArH); 11.35 (s, 1H, NH)
8f	*p*-CN	222 (C)	1690	2.17 (s, 3H, Me); 8.10-8.23 (m, 4H, ArH); 11.33 (s, 1H, NH)
8g	*p*-NO_2	220 (C)	1700	2.23 (s, 3H, Me); 8.38-8.55 (m, 4H, ArH); 11.39 (s, 1H, NH)
8h	*m*-MeO	185 (C)	1680	2.18, 3.91 (2s, 6H, 2Me); 7.30-7.70 (m, 4H, ArH); 11.28 (s, 1H, NH)
8i	*m*-Me	152 (C)	1685	2.19, 2.45 (2s, 6H, 2Me); 7.54-7.90 (m, 4H, ArH); 11.25 (s, 1H, NH)
8j	*m*-Cl	185 (B)	1680	2.15 (s, 3H, Me); 7.37-8.04 (m, 4H, ArH); 11.27 (s, 1H, NH)
8k	*m*-CF_3	172 (B)	1685	2.15 (s, 3H, Me); 7.87-8.37 (m, 4H, ArH); 11.29 (s, 1H, NH)
8l	*m*-NO_2	185 (A)	1700	2.15 (s, 3H, Me); 7.92-8.62 (m, 4H, ArH); 11.31 (s, 1H, NH)

[a] Melting points can be affected by the thermally induced rearrangement. [b] Crystallization solvent: (A) = Ethyl Acetate, (B) = Benzene, (C) = Ethanol. [c] Lit.:[7] **7a**, m.p. 145°C; **7b**, m.p. 137°C; **8a**, m.p. 168°C; **8b**, m.p. 193°C; see also spectroscopic data therein. [d] Lit.:[5] **7c**, m.p. 144°C; **8c**, m.p. 164°C; see also spectroscopic data therein. [e] Melting point likely belonging for the corresponding **8** after thermal rearrangement.

REFERENCES AND FOOTNOTES

1) (a) Boulton, A. J.; Katritzky, A. R.; Hamid, A. M. *J. Chem. Soc. C* **1967**, 2005; (b) Boulton, A. J. *Lect. Heterocycl. Chem.* **1974,** *2*, 45; (c) Afridi, A. S.; Katritzky, A. R.; Ramsden, C. A. *J. Chem. Soc. Perkin Trans. 1* **1976**, 315; (d) Ruccia, M.; Vivona, N.; Spinelli, D. *Adv. Heterocycl. Chem.* **1981**, *29*, 141; (e) L'abbé, G. *J. Heterocycl. Chem.* **1984**, *21*, 627; (f) Vivona, N.; Buscemi, S.; Frenna, V.; Cusmano, G. *Adv. Heterocycl. Chem.* **1993**, *56*, 49.

2) See for example: van der Plas, H. C. *Ring Transformations of Heterocycles*, Blomquist, A. T., Wasserman, H. Eds.; Vol. 1, Academic Press: London and New York 1973. See also specific classes of ring transformations reviewed in *Comprehensive Heterocyclic Chemistry*, Katritzky, A. R.; Rees, C. W. Eds.; Vols. 1-8. Pergamon Press: Oxford 1984.

3) (a) Vivona, N.; Frenna, V.; Buscemi, S.; Ruccia, M. *J. Heterocycl. Chem.* **1985**, *22*, 97; (b) Vivona, N.; Buscemi, S.; Frenna, V.; Ruccia, M.; Condò, M. *J. Chem Research (M)* **1985**, 2184; (*S*) 190 (1985); (c) Andrianov, V. G.; Eremeev, A. V. *Chem. Heterocycl. Compd. (Engl Transl.)* **1990**, *26*, 1199.

4) Harsanyi, K. *J. Heterocycl. Chem.* **1973**, *10*, 957.

5) Vivona, N.; Cusmano, G.; Ruccia, M.; Spinelli, D. *J. Heterocycl. Chem.* **1975**, *12*, 985.

6) Vivona, N.; Ruccia, M.; Cusmano, G.; Marino, M. L.; Spinelli, D. *J. Heterocycl. Chem.* **1975**, *12*, 1327.

7) Buscemi, S.; Vivona, N. *Heterocycles* **1989**, *29*, 737.

8) Degenerate rearrangements are not confined to 1,2,4-oxadiazole derivatives: examples in the 1,2,5-oxadiazole,[3c,9] 1,2,4-thiadiazole[10] and isothiazole[11] series have been reported.

9) (a) Andrianov, V. G.; Semenikhina, V. G.; Eremeev, A. V.; Gaukhman, A. P. *Chem. Heterocycl. Comp. (Engl. Transl.)* 1**988**, *24*, 1410; (b) Andrianov, V. G.; Semenikhina, V. G.; Eremeev, A. V. *Chem. Heterocycl. Comp. (Engl. Transl.)* **1991**, *27*, 102.

10) (a) Akiba, K.; Kobayashi, T.; Arai, S. *J. Am. Chem. Soc.* **1979**, *101*, 5857; (b) Yamamoto, Y.; Akiba, K. *J. Am. Chem. Soc.* **1984**, *106*, 2713; (c) L'abbé, G.; Beenaerts, L.; Godts, F.; Toppet, S. *Bull. Soc. Chim. Belg.* **1987**, *96*, 827; (d) Yamamoto, Y.; Akiba, K. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 479.

11) Akiba, K.; Kashiwagi, K.; Ohyama, Y.; Yamamoto, Y.; Ohkata, K. *J. Am. Chem. Soc.* **1985,** *107*, 2721.

12) Buscemi, S.; Macaluso, G.; Vivona, N. *Heterocycles* **1989**, *29*, 1301; Buscemi, S.; Vivona, N. *J. Chem. Soc., Perkin Trans. 2* **1991**, 187.

13) La Manna, G.; Buscemi, S.; Frenna, V.; Vivona, N., Spinelli, D. *Heterocycles* **1991**, *32*, 1547.

14) Andrianov, V. G.; Makushenkov, S. V.; Eremeev, A. V. *Mendeleev Commun.* **1992**, 129.

15) Buscemi, S.; Vivona, N. *Heterocycles* **1994**, *38*, 2423.

16) Frenna, V.; Macaluso, G.; Vivona, N.; Spinelli, D.; Consiglio, G.; Mezzina, E. *Tetrahedron* **1994**, *50*, 7315 and references cited therein.

17) Dell'Erba, C.; Mele, A.; Novi, M.; Petrillo, G.; Sancassan, F.; Spinelli, D. *J. Chem. Soc., Perkin Trans. 2* **1990**, 2055; De Maria, P.; Barbieri, C.L.; Spinelli, D.; Dell'Erba, C.; Novi, M.; Petrillo, G.; Sancassan, F. *J. Chem. Soc., Perkin Trans. 2* **1991**, 373 and references cited therein.

18) In particular, the expected higher ability of a phenyl group (σ_I 0.12), with respect to a methyl group (σ_I 0.01), to stabilise the carbamoyl negative charge is measured by the large increase of the percentage of **7c**$^-$ (with respect to **7c**) at equilibrium (Table 1, K_N and K_A 10.1 and 1.63, respectively).

19) Anderson, G. W.; Faith, H. E.; Marson, H. W.; Winnek, P. S.; Roblin, R. O. Jr. *J. Am. Chem. Soc.* **1942**, *64*, 2902.

20) Eloy, F.; Deryckere, A. *Bull. Soc. Chim. Belg.* **1969**, *78*, 41 ; Westphal, G.; Schmidt, R. Z. *Chem.* **1974**, *14*, 94.

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