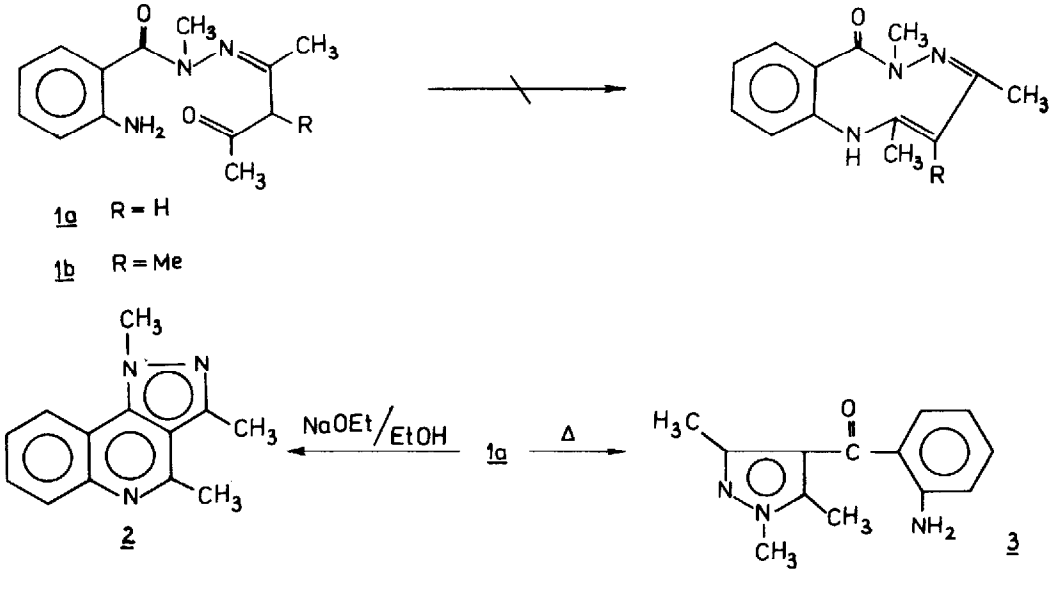
Tetrahedron Letters Vol. 21, pp 1567 - 1570 0040-4039/80/0415-1567/$02.00/0

THE RING CLOSURE AND REARRANGEMENT OF 1-(2-AMINO)-BENZOYL-1-METHYLHYDRAZONES OF β-DICARBONYL COMPOUNDS: ON THE FORMATION AND CRYSTAL STRUCTURE OF 3a,9a-DIHYDRO--1,3,3a,9a-TETRAMETHYL-4*H*-PYRAZOLO[3,4-*b*]QUINOLIN-4-ONE

Melinda Gál*, Ödön Fehér, Endre Tihanyi, Gyula Horváth and Gyula Jerkovich
Institute for Drug Research, H-1325-Budapest, P.O.B. 82., Hungary,
Gyula Argay and Alajos Kálmán*
Central Research Institute of Chemistry, Hungarian Academy of Sciences, H-1525 Budapest, P.O.B., 17., Hungary

The conversion of 1-(2-amino)-benzoyl-1-methylhydrazones of β-dicarbonyl compounds into heterocyclic derivatives yielded in addition to the already known type of product 2 further three novel pyrazole derivatives 3, 4 and 5. The structures of these products have been established by chemical and spectroscopic (MS) methods. The crystal structure of 5 has been determined by X-ray diffraction.

Our original aim of converting 1-(2-amino)-benzoyl-1-methylhydrazones of β-dicarbonyl compounds 1 into a nine-membered 1,5,6-benzotriazonin-7-one ring system (*via* ring closure) has failed so far. Instead, depending on the procedure applied (reaction media, temperature) and the substituent R (H for 1a[1], mp[2]: 409-411 K, Me for 1b, mp: 415-421 K) the following four pyrazole derivatives were obtained: 2 (mp: 423-425 K), 3 (mp: 393-395 K), 4 (mp: 480-481 K) and 5 (mp: 440-443 K).



1a R = H

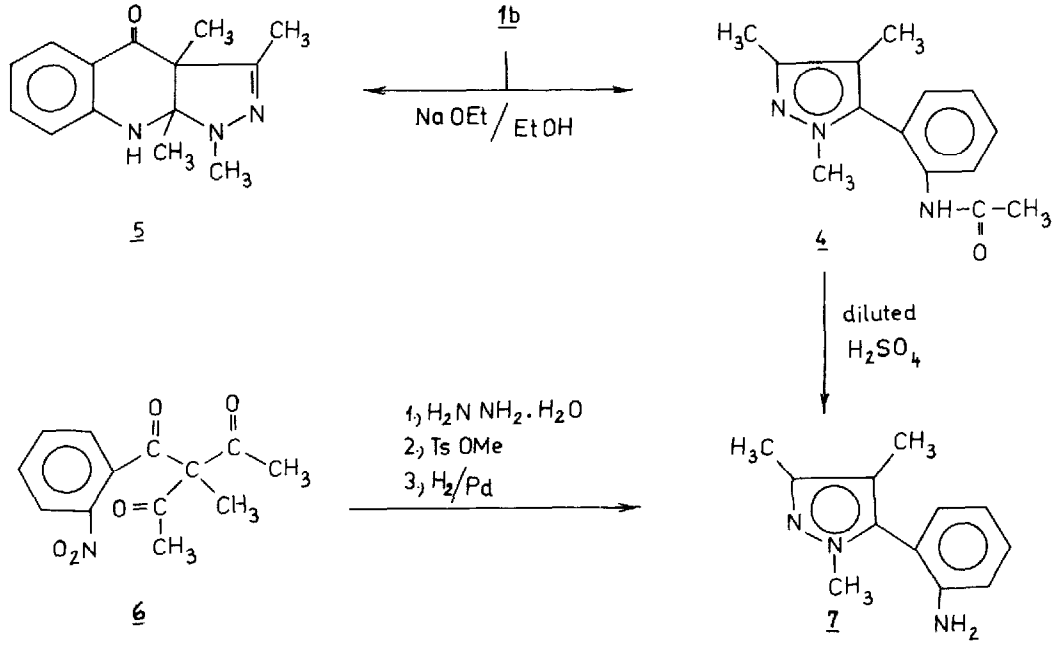
1b R = Me

2 3

As has been known since 1927[3] the cyclization of some 1-aroyl-1-phenylhydrazones of β-keto-aldehydes in alkaline media yields 4-acyl pyrazoles. Accordingly, compound 2 could be readily produced from 1a in NaOEt/EtOH *via* double condensation. On dry heating we have found that 1a produced a novel compound 3 by losing only one molecule of water.

The chemical formula of 3 (2-amino)-phenyl-[1,3,5-trimethyl-4-(1*H*)-pyrazolyl]-methanone could be inferred from mass spectra[2] [*m/z*(%) 229(100)M^+, 137(23) $C_7H_9N_2O$, 120(35) C_7H_6NO, 56(3,3) C_3H_6N]. The fragment ions *m/z* 137 and 120 indicate that a C=O group forms a linkage between the phenyl and the hetero rings. It is worth noting that 3 could also be synthesized from 3-(2-nitro)-benzoyl-2,4-pentanedione[4].

In order to avoid the undesirable conversions of 1a (i.e. 1a → 2 ring closure and 1a → 3 reaction) we have attempted the synthesis of the nine-membered ring by boiling 1b in NaOEt/EtOH and in dry benzene as well. Contrary to expectations, these procedures resulted, however, in a mixture[5] of two isomeric products 4 and 5.



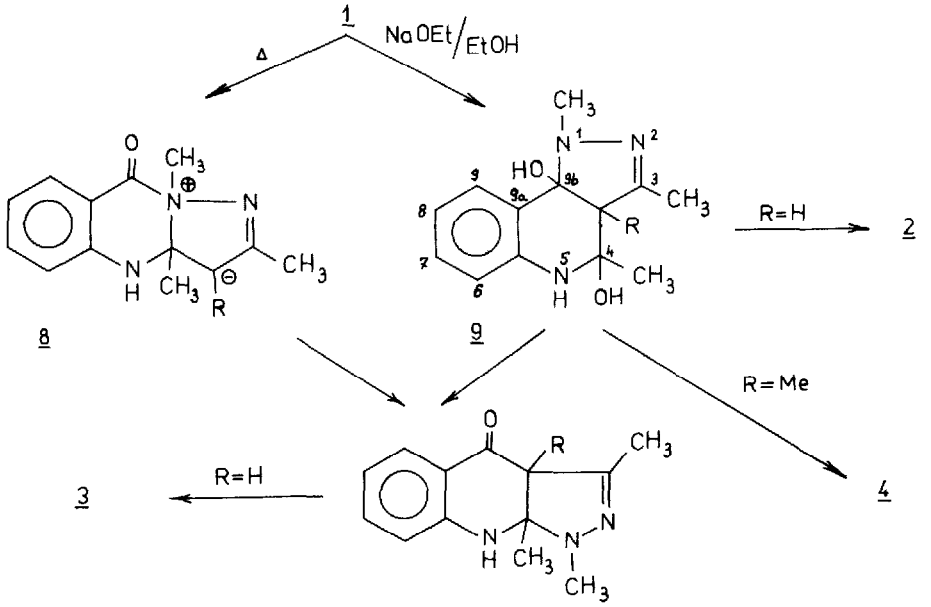
5 4 6 7

The structure of 4 [5-(2-acetylamino)-phenyl-1,3,4-trimethyl-1*H*-pyrazole] proposed on the basis of mass spectral data [*m/z*(%): 243(100)M^+, 242(4,8), 228(9), 201(13), 200(28), 186(4,3), 159(7), 130(1,8)] was also proved by an independent synthesis[6] while that of 5 deduced also from MS spectra [*m/z*(%): 243(29)M^+, 228(36), 174(14) $C_{11}H_{12}NO$, 125(100) $C_7H_{13}N_2$, 124(60), 123(43), 119(70), 109(10)] had to be corroborated by X-ray analysis.

The crystal structure of 5 [3a,9a-dihydro-1,3,3a,9a-tetramethyl-4*H*-pyrazolo(3,4-*b*)quinolin-4-one] was solved in the orthorhombic space group $P2_12_12_1$ and refined with program *SHELX* to a final R of 0.072 for 1484 independent counter diffractometer data[7]. The bond distances (pm) and valency angles along with the atomic numbering[8] are given in Fig. 1. As shown by the puckering parameters

(Q = 37.6 pm, Θ = 49.6°, φ = 227°)[9,10] the hetero ring of the quinolin-4-one moiety assumes an almost perfect half-chair conformation (the lowest asymmetry parameter[11] ΔC_2(C6-C11) = 2.5°) while the pyrazole ring (Q = 42.2 pm, φ = 179° at C(13) is of an envelope conformation with C(13) on the flap [ΔC_s(C13) = 2.3°]. The hetero ring junction is of *cis* configuration [torsion angle C(16)-C(4)-C(13)-C(17) = -44.8°]. The methyl groups bound to N(1) and C(3) are *pseudo-equatorial*. The symmetry related molecules are linked together by N(12)-H...N(2) hydrogen bond helices [N...N = 309.0, H...N = 204.6 pm, ∢NH..N = 160.2°].

The mechanism of reaction *1a* → *3* may be explained by assuming an *8* type intermediate[12] which converts into *10* *via* 1,3-acyl migration. This reaction path, if R = H gives *3* by ring-opening, or the reaction terminates at *10* in case R = Me (i.e. *10* = *5*). But the formation of *4* cannot be explained by this reaction path. More attractive, therefore, is the hypothesis that in alkaline solution a common intermediate *9* (by which *1a* is readily converted into *2*) may also undergo two types of dehydration if R = Me (*1b*). The formation of *4* may then be attributed to dehydration at 9b followed by ring-opening. The somewhat less favourable dehydration at 4 accompanied by rearrangement may lead to *10* = *5*. This assumption seems to be supported by the fact that the electron-withdrawing substituents in position 5 of *1b* increased the yield of *5* type products. This substitution may induce deprotonation at 9b-OH of *9* which hinders reaction into *4*.



Notes and references

1. All tautomeric forms of the hydrazones are intended to be implied.
2. All compounds have correct analytical data; mp.'s are not corrected.
   Mass spectra were taken on a Varian MAT SM-1 instrument at 70 eV and R = 1250.

High resolution mass measurements were made at R = 10 000 using PFK as reference standard.

3. K.v. Auwers and H. Mauss, *J. Pract. Chem.* 117, 311 (1927).
4. J.D. Loudon and I. Wellings, *J. Chem. Soc.*, 3470 (1960).
5. *4* and *5* were produced in NaOEt/EtOH in yields of 60% (*4*) and 40% (*5*). In dry benzene they were produced in rather poor yield.
6. 5-(2-Amino)-phenyl-1,3,4-trimethyl-1*H*-pyrazole *7* synthesised from 3-methyl-3-(2-nitro)--benzoyl-2,4-pentanedione *6* was identical with the hydrolysis product of *4*.
7. Intensities were collected on a semi-automatic two-circle Stoe-Güttinger diffractometer using Ni-filtered $CuK_{\bar{\alpha}}$ (λ=154.18 pm) radiation (cf. A. Kálmán, K. Simon, J. Schawart and G. Horváth, *J. Chem. Soc., Perkin Trans. 2.* 1849 (1974)). The lattice parameters, a = 976.6(6), b = = 1077.0(1), c = 1271.0(2) pm [Z = 4, F(000) = 520] were refined from precession photographs.
8. Listing of positional parameters for non-hydrogen and hydrogen atoms together with the anisotropic vibrational parameters for non-hydrogen atoms of *5* may be obtained from the Cambridge Crystallographic Data Centre, University Laboratory, Lensfield Road, Cambridge CB2 1EW, (England) [see *Tetrahedron Letters.*, 3081 (1978)].
9. D. Cremer and J.A. Pople, *J. Amer. Chem. Soc.*, 97, 1354 (1975).
10. J.C.A. Boeyens, *J. Cryst. Mol. Struct.* (1978) still in the press.
11. W.L. Duax, C.M. Weeks and D.C. Rohrers in *Topics in Stereochemistry* Vol. 9. edited by N.L. Allinger and E.L. Eliel, pp. 271-383, New York: John Wiley and Sons, 1976.
12. Similar to the mechanism postulated for the thermal rearrangement of 2,4-diphenyl-2,3-benzodiazocin-1(2*H*)-one by N. Dennis, A.R. Katritzky, E. Lunt and M. Ramaiah, *Tetrahedron Letters.* 1569 (1976).

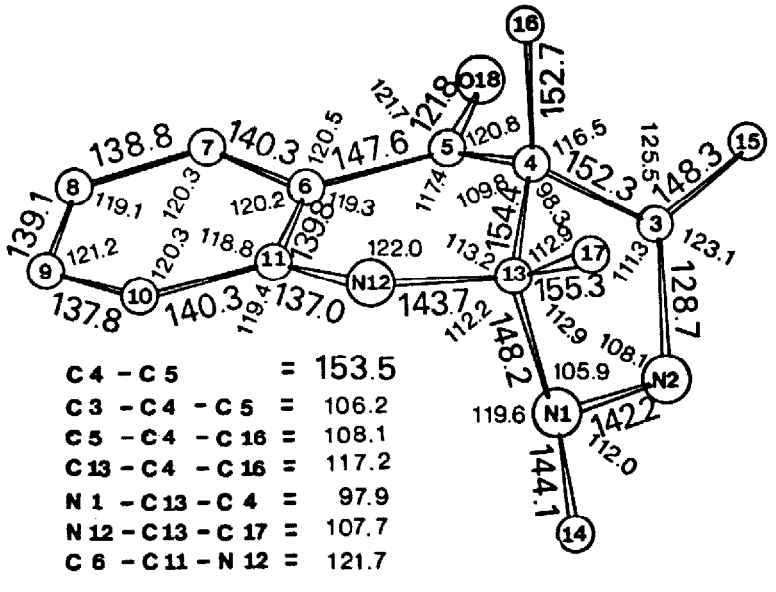


Fig. 1. A schematic view of the structure of 5 showing atomic numbering (the bare numbers are for carbon atoms unless indicated otherwise) bond distances (pm) and bond angles (°). E.s.d's are numerically in the range of 0.3-0.5, for lengths (pm) and angles (°).

(Received in UK 22 February 1980)