Tetrahedron Letters,Vol.23,No.28,pp 2895-2898,1982 0040-4039/82/282895-04$03.00/0
Printed in Great Britain

REACTION OF 2-ARYLAZO-2,5-DIMETHYL-3(2H)-FURANONES WITH AMMONIA. PREPARATION OF ß-ACETYL-ß-(3-AMINO-2-BUTENOYL)ARYLHYDRAZINES.

Carlo Venturello* and Rino D'Aloisio

Istituto Guido Donegani S.p.A.

28100 Novara, Italy

Summary: Ring opening of 2-arylazo-2,5-dimethyl-3(2H)-furanones (1a-d) with ammonia leads to previously unknown ß-acetyl-ß-(3-amino-2-butenoyl)arylhydrazines (3a-d). The reaction mechanism is discussed.

2-Arylazo-2,5-dimethyl-3(2H)-furanones (1)[1,2], easily available from diazotized arylamines and 2,5-dimethyl-3(2H)-furanone (7)[3], represent a new, versatile class of intermediates. Convenient syntheses of 3-pyrazolones[2] and 4-pyridazones[4] from 1 have been previously described. We now wish to report that compounds 1a-d, in the presence of ammonia, can be converted to hitherto unknown ß-acetyl-ß-(3-amino-2-butenoyl)arylhydrazines (3a-d).

In a typical example, a solution of 2.16 g (10 mmol) of 1a[5] in methanol (50 ml) was saturated with ammonia at 0° (10-15 min), and then kept at room temperature for 30 min. After complete removal of the solvent in vacuo (<40°), the residual yellow oil was allowed to stand overnight, whereby it faded and solidified. On purification[6], it afforded 1.4 g (60%) of 3a, m.p.[7] 137-139° (from acetone/water[8])[9].

Compounds 3b-d were similarly obtained (yields: 50-68%)[9,10]. Besides the title compounds 3a-d, the corresponding ß-acetylarylhydrazines (6a-d) were formed in 10-40% yields (estimated by GLC[11]). The presence of other not yet identified by-products was also observed.

Spectral data of 3a-d, listed in the Table, show that these products have the vinylogous semicarbazide structure with strong intramolecular H-bonding. These data are in agreement with the literature values concerning acyclic cis-s-cis ß-amino α,β-unsaturated carbonyl compounds[12]. The formation of 3 can be explained by a nucleophilic attack of ammonia at the C-5 position of 1, followed by furanone-ring opening to give intermediate 2, and subsequent rearrangement of 2 to 3 (Scheme, path A). The rearrangement 2→3(slow) was found to occur mainly after removing the ammonia-containing methanol[13]. The presence of 2 could be monitored conveniently by TLC (as a yellow spot) and ^{1}H-NMR, but its isolation in an analytically pure state usually failed. However, for X = 4-CH_3, we were able to isolate[14] a yellow solid, soluble in ether, which gave analytical and spectral data consistent with the structure of 5-amino-2-hydroxy-2-(p-tolylazo)-4-hexen-3-one (2c) (Table). By standing (r.t.), 2c, as such or dissolved in methanol, gradually transformed into 3c. Further support for the intermediacy of 2 in the formation of 3 results

from the fact that, when treating the parent 2,5-dimethyl-3-furanone (7) with ammonia under the same conditions as above[15], we obtained over 90% yield of the corresponding 5-amino-2-hydroxy-4-hexen-3-one (8), m.p.[7] 67-69° [from light petroleum (40-60°)/Et_2O (1:1) at -25°][9] (Table).

It is noteworthy that, despite 3-furanone systems having been reported to undergo ring opening by nitrogen nucleophilic reagents according to the above mechanism[16], in no case was the presence of open-chain hydroxylated enamino ketones analogous to 2c and 8 observed, and new cyclic compounds were obtained exclusively.

The scope and limitations of the reaction here described have not been fully investigated. From preliminary results, however, the formation of 3 appears to be disfavoured by the presence of strongly electron-withdrawing groups in the aryl residue. Indeed, in these cases, the formation of ß-acetylarylhydrazine (6) was found to become the predominant reaction. Thus, for X = 4-NO_2 and 4-$COOCH_3$, the respective ß-acetylhydrazines (6e,f) were obtained in ca. 80% yields[17]. Intermediate 2 does not seem to be involved substantially in the formation of 6. Indeed, under the reaction conditions, the isolated product 2c did not give rise to appreciable amounts of 6c. A plausible pathway for the formation of 6 is given in the Scheme (path B). ß-Aminocrotonamide and methyl ß-aminocrotonate, presumably derived from addition of ammonia or methanol to the imino ketene (5)[18], were identified[19] in the crude material. In some cases, they were quantitatively determined, and their total amount was found to stand in an approximately 1:1 molar ratio with that of the ß-acetylarylhydrazine formed. The presence of acetamide was also observed[19]. Its formation can be explained by an alternative cleavage of intermediate 4 involving liberation of ketene.

Synthetic applications of compounds 3 are currently being explored.

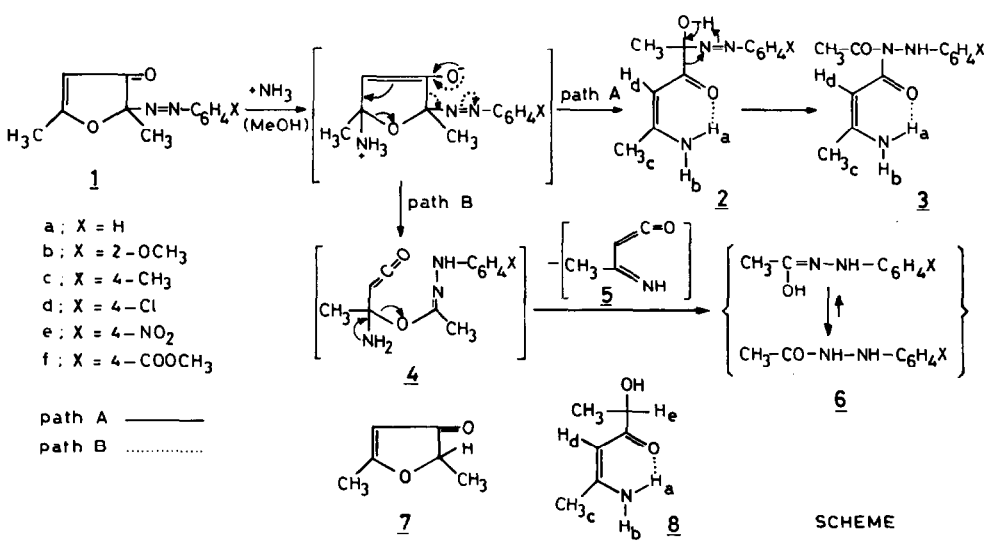

Table. Spectral data for compounds 2, 3, and 8.

Product[a]	I.R.($CDCl_3$) ν_{max} [cm^{-1}]	M.S.(70 eV) m/e (M^+)	^{1}H-N.M.R.($CDCl_3$/TMS) δ[ppm] CH_{3_c} (s^d, 1H)	H_d (brs^d, 1H)	NH_b (br, 1H)[e]	NH_a^b (br, 1H)[e]	Other signals[c]
2c	3488, 3370, 3270(sh); 1619, 1606, 1536	247[f]	1.96	5.35	5.34	9.62	1.76(s,3H); 2.40(s,3H); 5.72(s,1H)[e]
3a	3499, 3346, 3316; 1696, 1637, 1603, 1537; 1269[g]	233	1.97	5.78	4.97	8.82	2.49(s,3H); 6.67(s,1H)[e]
3b	3499, 3351, 3319; 1696, 1641, 1606, 1537; 1271[g]	263	1.94	5.77	5.03	8.83	2.48(s,3H); 3.90(s,3H); 7.09(s,1H)[e]
3c	3499, 3341, 3317; 1697, 1640, 1606, 1538; 1277[g]	247	1.96	5.78	4.94	8.84	2.25(s,3H); 2.48(s,3H); 6.63(s,1H)[e]
3d	3504, 3348, 3320; 1698, 1639, 1607, 1538; 1277[g]	267(^{35}Cl)	1.98	5.73	4.99	8.85	2.48(s,3H); 6.64(s,1H)[e]
8	3494, 3420, 3279; 1624, 1606, 1539	129	1.98	5.00	5.31	9.45	1.31(d,3H, J=6.6 Hz); 4.04(s,1H)[e,h]; 4.17(q,1H, J=6.6 Hz)[h]

[a] All products gave satisfactory microanalyses (C ± 0.25%, H ± 0.10%, N ± 0.10%, Cl - 0.30%). The U.V. spectra show a peak at λ_{max} (EtOH)=300-312 nm (ϵ =16000-22000).

[b] The NH_a resonance is essentially unaffected by stronger hydrogen-bonding solvents like acetone and dimethyl sulfoxide.

[c] Aromatic protons not given.

[d] Allylic coupling between CH_{3_c} and H_d hardly measurable.

[e] Exchangeable with D_2O.

[f] Even at 50°, the mass spectrum was essentially that of the isomer 3c. However, a peak at m/e=128, which can reasonably be attributed to the ($M^+ - ArN_2$) fragment, was observed.

[g] In Nujol.

[h] Two distinct signals in different ratio are observed for OH (at δ 3.99 and 4.04, singlets) and H_e (at δ 4.15 and 4.20, quartets). By treatment with D_2O, the two OH singlets disappear and the two H_e quartets collapse to a single quartet at δ 4.17.

Acknowledgements. We wish to thank Mr. P. Golfetto, Mr. G.C. Bacchilega and Mrs. T. Fiorani for GLC analyses, NMR and mass spectra.

REFERENCES AND FOOTNOTES

1. C. Venturello, J.C.S. Perkin I, 681 (1978).
2. C. Venturello and R. D'Aloisio, Synthesis, 283 (1979).
3. C. Venturello and R. D'Aloisio, Synthesis, 754 (1977).
4. C. Venturello and R. D'Aloisio, Synthesis, 790 (1979).
5. Starting compounds 1a-f were prepared as previously described[2,4].
6. It was chromatographed on silica gel 60 (70-230 mesh; 80 g) using acid-free Et_2O as eluent,

and the fraction R_f = 0.84 (see ref. 20) was collected. The solid isolated was spread on a porous plate, washed with n-hexane (10 ml), then with Et_2O (5-6 ml), and dried.

7. Melting points were determined by the Kofler method and are uncorrected.
8. The product was dissolved in a little acetone, water was added until turbidity was observed, and the mixture was then set aside for recrystallization.
9. For long term storage preservation in a refrigerator is advisable.
10. In the case of 3b, 150 ml instead of 50 ml of MeOH were used, and a solid was obtained directly by removing the solvent (see ref. 13). Work-up for 3b-d as in ref. 6, except that isolated 3b and 3d were washed with n-hexane (10 ml) alone.

    3b. R_f = 0.85 (see ref. 20). Yield 64%. M.P.[7] 148-150° (from acetone/water[8]; hemihydrate).

    3c. R_f = 0.86 (see ref. 20). Yield 68%. M.P.[7] 137-139° (from acetone/water[8]).

    3d. R_f = 0.85 (see ref. 20). Yield 50%. M.P.[7] 137-139° (from acetone/water[8]).

11. Glass column (2m x 2mm ID): 5% Carbowax 20 M on 60/80 Chromosorb AW; T 70° then 10°/min to 230° [for acetamide ss column (2m x 2mm ID): 5% TCEP on 30/60 Chromosorb W; T 140°] . Hewlett-Packard 5380A instrument (FID). Bibenzyl as an internal standard.
12. G.O. Dudek and R.H. Holm, J.Am.Chem.Soc., 83, 2099 (1961); G.O. Dudek and R.H. Holm, ibid., 84, 2691 (1962); G.O. Dudek and G.P. Volpp, ibid., 85, 2697 (1963); G.O. Dudek and G.P. Volpp, J.Org.Chem., 30, 50 (1965); G.O. Dudek, ibid., 30, 548 (1965); D.L. Ostercamp, ibid., 30, 1169 (1965); D.L. Ostercamp, ibid., 35, 1632 (1970).
13. The rearrangement 2b → 3b was already complete as the solvent was removed.
14. After cautious removal of the solvent in vacuo (20°), the residual yellow oil was dissolved in acid-free Et_2O. Light petroleum (40-60°) was added to the solution (filtered, if necessary) until turbidity was observed, and the mixture was then set aside for crystallization at -25°. The product, which may conveniently be stored at low temperature, melts at 80-90° with partial transformation into 3c.
15. Instead of 30 min, the reaction mixture was kept at r.t. for 24 h. The solid obtained by removing the solvent was spread on a porous plate, washed with n-hexane (3x2 ml), and dried.
16. M. Weigele, S.L. de Bernardo, J.P. Tengi and W. Leimgruber, J.Am.Chem.Soc., 94, 5927(1972); S. Gelin and D. Hartmann, J. Heterocyclic Chem., 13, 521 (1976); B. Chantagrel and S. Gelin, ibid., 15, 1215 (1978); S. Gelin, Synthesis, 291 (1978).
17. 150 ml instead of 50 ml of MeOH were used. The products were isolated from the reaction mixture chromatographically on silica gel 60 (70-230 mesh; 80 g) using MeOH/Et_2O (3:97) as eluent. For 6e, a further elution of the solid isolated, after dissolving it into MeOH (50 ml) and conc. HCl (0.2 ml) and evaporating the mixture to dryness, was required.

    6e. R_f = 0.25 (yellow spot; see ref. 20). M.P.[7] 208-210° (from EtOH) [lit.[21] a) 205-206°; b) 211-212°; c) 215-216°] .

    6f. R_f = 0.26 (see ref. 20). M.P.[7] 169-171° (from toluene).

    Satisfactory analytical and spectral data for 6e and 6f were obtained.
18. G. Kretschmer and R.N. Warrener, Tetrahedron Letters, 1335 (1975).
19. By GLC[11] and GLC-MS.
20. TLC performed on Merck pre-coated silica gel 60F-254 plates using acetone/diethyl ether (1:9) as eluent; spot detected by observation under a 254 nm source and by spraying with a potassium permanganate solution.
21. a) E. Hyde, Ber. Dtsch.Chem.Ges., 32, 1811 (1899); b) C.U. Rogers and B.B. Corson, J. Am. Chem. Soc., 69, 2910 (1947); c) P.H. Payot, Helv. Chim. Acta, 42, 1356 (1959).

(Received in UK 10 May 1982)