The Reaction of Aroylhydrazines with *N*-Phenylsulfonylarenehydrazonoyl Chlorides. A Route to Substituted 4-Amino-(4*H*)-1,2,4-triazoles and 1,3,4-Oxadiazoles

Ahmad S. Shawali (1) and Abdel-Gawad A. Fahmi

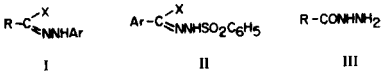
Department of Chemistry, Faculty of Science, University of Kuwait, State of Kuwait

Received April 13, 1977

Treatment of *N*-phenylsulfonylarenehydrazonoyl chlorides (II) with equivalent amounts of aroylhydrazines (III) in ethanol gave 3,5-diaryl-4-phenylsulfonylamino-1,2,4-triazoles (IV). Reaction of II with two equivalents of III in tetrahydrofuran gave 2,5-diaryl-1,3,4-oxadiazoles (V), in addition to IV. Addition of triethylamine to II or its mixture with III yielded only the tetrazenes (VIII). The possible pathways leading to IV-V and VIII are discussed.

J. Heterocyclic Chem., 14, 1089 (1977)

In connection with our investigation (2) on the reactions of *N*-arylhydrazonoyl halides (I), it was of interest to examine the reactions of their *N*-arylsulfonyl analogs, II. As hydrazonoyl halides are a kind of imidoyl halide and the arylsulfonyl group can be eliminated (3), compounds II can be utilized as starting materials for synthesis of heterocycles.



I II III

X = Cl or Br
R = alkyl, aryl, EtOOC, or C_6H_5NHCO
Ar = phenyl, or substituted phenyl

The present paper describes new route for synthesis of 4-amino-(4*H*)-1,2,4-triazoles (IV) and 1,3,4-oxadiazoles (V) through the reaction of II (X = Cl) with aroylhydrazines (III). The reactions studied are outlined in Scheme 1.

IV V

a, Ar = R = C_6H_5
b, Ar = *p*-ClC_6H_4; R = C_6H_5
c, Ar = C_6H_5; R = *p*-$CH_3C_6H_4$
d, Ar = C_6H_5; R = 2-thienyl
e, Ar = C_6H_5; R = *p*-BrC_6H_4
f, Ar = R = *p*-ClC_6H_4
g, Ar = C_6H_5; R = *p*-$CH_3OC_6H_4$

Results and Discussion.

When *N*-phenylsulfonylbenzenecarbohydrazonoyl chloride (II, X = Cl, Ar = C_6H_5) was refluxed with an equivalent amount of benzoyl hydrazine (III, R = C_6H_5) in ethanol, 4-phenylsulfonylamino-3,5-diphenyl-(4*H*)-1,2,4-triazole (IV, R = Ar = C_6H_5) was obtained. Other aroylhydrazines react similarly with II to give the corresponding triazole derivatives, IVb to IVg. The results are summarized in Table I. The identity of the materials was confirmed by elemental analyses and spectral data.

Thus, all compounds, IVa to IVg show C=N stretching absorption at 1605 ± 3 cm^{-1}, consistent with a similar absorption by the triazole ring (4). Also, a group of three bands between 1320-1250 cm^{-1}, which appear in the ir spectra of all these compounds, have been assigned to the C-N vibrations of the triazole ring (5). Furthermore, all compounds exhibit strong and sharp bands at 1360 and 1170 cm^{-1} and a broad weak band in the region 3120-3050 cm^{-1} assignable to the $C_6H_5SO_2NH$- group. The electronic absorption pattern was characterized, in each case, by the presence of an intense maximum ($\log \epsilon > 4$) in the 240 to 300 nm region.

The assigned triazole structure for the compounds IV was also consistent with the following chemical evidences: (1) all compounds dissolve in potassium hydroxide solution and precipitate on acidification. (2) The product IVa (R = Ar = C_6H_5) was identical in all respects with an authentic sample prepared from 3,5-diphenyl-(4*H*)-1,2,4-triazole (6) and benzenesulfonyl chloride in pyridine. (3) Reactions of II (Ar = C_6H_5; X = Cl) with III (R = *p*-ClC_6H_4) and of II (Ar = *p*-ClC_6H_4; X = Cl) with III (R = C_6H_5) gave in both cases the same product IVb (R = *p*-ClC_6H_4; Ar = C_6H_5). This finding excludes the isomeric structure of 1-phenylsulfonyl-3,6-diaryl-1,4-dihydro-1,2,4,5-tetrazene (XI) or its tautomeric form (XII). This was further indicated by the fact that compound IVa was recovered unchanged after being refluxed in ethanolic sodium ethoxide for 8 hours. Structures of type XI and XII are expected to eliminate benzenesulfinic acid upon base treatment (7) to yield the corresponding tetrazine, XIII (Scheme 1).

Clearly, the triazole products IV can be considered as arising from the hydrazidine intermediates (IX) that result from the nucleophilic substitution of the chlorine atom by acylhydrazine. The tautomeric form, X, of IX readily cyclizes by loss of water under the catalytic influence of hydrogen chloride liberated in the first step (Scheme 1).

When II (X = Cl, Ar = C_6H_5) was refluxed with two equivalent amounts of III (R = C_6H_5) in tetrahydrofuran, the triazole IV (R = Ar = C_6H_5) precipitated during reflux. After the removal of the latter by filtration and distilling of the solvent in the filtrate, 2,5-diphenyl-1,3,5-oxadiazole (V, R = Ar = C_6H_5) was isolated. Similar treatment of II with other aroylhydrazines in tetrahydrofuran gave, in each case, the corresponding triazole (IV) and oxadiazole (V) products. The ratio of the percent yields of IV to V obtained seems to depend on the structure of the R group

Table I

4-Phenylsulfonylamino-3,5-diaryl-(4*H*)-1,2,4-triazoles, IV

Compound No.	M.p. °C	Molecular formula	C, %		H, %		N, %		S, %		λ max nm (log ε) (a)
			Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	
IVa	303-305	$C_{20}H_{16}N_4O_2S$	63.81	63.81	4.34	4.28	15.09	14.88	8.74	8.52	260 (4.636)
IVb	287-288	$C_{20}H_{15}ClN_4O_2S$	58.51	58.46	3.70	3.68	13.64	13.63	7.64	7.80	263 (4.340)
IVc	284-285	$C_{21}H_{18}N_4O_2S$	64.35	64.59	4.69	4.64	14.29	14.32	8.19	8.21	265 (4.591)
IVd	279-281	$C_{18}H_{14}N_4O_2S_2$	56.62	56.53	3.70	3.69	14.51	14.65	16.58	16.77	290 (4.248)
IVe	305	$C_{20}H_{15}BrN_4O_2S$ (b)	52.97	52.75	3.39	3.32	12.19	12.30	6.99	7.04	271 (4.420)
IVf	320-322	$C_{20}H_{14}Cl_2N_4O_2S$	53.60	53.94	3.22	3.17	12.50	12.58	7.18	7.20	267 (4.442)
IVg	277-278	$C_{21}H_{18}N_4O_3S$	61.88	62.05	4.40	4.46	13.69	13.78	7.90	7.89	270 (4.389)

(a) In ethanol containing 1% by volume dioxane. (b) Br Calcd.: 17.55, Found: 17.47.

Scheme - 1

Scheme - 2

in the hydrazide, III, used. Electron withdrawing substituents in group R increases the yield of IV. Addition of triethylamine to the reaction mixture of II and III (either in 1:1 or 1:2 ratio) to trap the liberated hydrogen

chloride resulted in the formation of 3,6-diphenyl-1,4-bis-(phenylsulfonyl)-1,4-dihydro-1,2,4,5-tetrazene (VIII, Ar = C_6H_5) as the only isolable product.

Identification of the oxadiazoles, V, prepared was carried out by their elemental and spectral data and, in the case of known compounds, by comparison with authentic samples (8). Thus, the electronic absorption pattern of V in ethanol is of typical oxadiazole derivatives; in each oxadiazole derivatives; in each case, there is an intense maximum (log $\epsilon > 4$) in the 250-320 nm region. An examination of the infrared spectra of V shows bands at 1600, 1550, 1438 and 1050 cm^{-1} attributable to oxadiazole ring (9).

To account for the formation of V, two alternative pathways are proposed in Scheme 2. We base such sequences on the following facts. First, it is known that hydrazonoyl halides react with arylhydrazines to form the corresponding hydrazidines, and air oxidation of the latter gives formazans (10). Hence we feel that acid hydrazides should do likewise; hence the steps IX to XV. Secondly, 5-arylsulfonylformazans are known to undergo readily elimination of benzenesulfinic acid (13) and give arylazoaryldiazomethane that cyclizes into the corresponding tetrazole product (3b). In the present case, such elimination and the subsequent cyclization would lead to the formation of 2-acyltetrazole (XVI), (Scheme 2). The latter intermediate can loose nitrogen upon heating to give the 1,5-dipolar ion (XVII) that cyclizes into V (11). Alternatively, concurrent elimination of benzenesulfinate ion and nitrogen, followed by 1,5-cyclization of the resulting azocarbonium ion (XVIII) and loss of a proton would yield V.

EXPERIMENTAL

Melting points were determined with a Gallenkamp electrothermal melting point apparatus Model MF 550 and are uncorrected. The microanalyses were performed by Alfred Bernhardt Mikroanalytisches Laboratorium, West Germany. The infrared (potassium bromide) and ultraviolet (ethanol) spectra were measured with Pye-Unicam SP1000 and SP8000 spectrophotometers, respectively.

Aroylhydrazines, III, were prepared from the corresponding ethyl aroate and hydrazine hydrate in the usual way. 1-Aroyl-2-phenylsulfonylhydrazines were prepared in a rigorously similar manner from benzenesulfonyl chloride and aroylhydrazine as previously described (12). The latter hydrazides were converted into II by refluxing them with excess thionyl chloride following the procedure of Ito, *et al.*, (3b). The properties of II prepared corresponded to data reported (3b).

Reaction of II with III.

Method A.

A mixture of equivalent amounts of II and III (0.005 mole each) in ethanol (50 ml.) was refluxed for 4 hours, and cooled. The white solid that precipitated was filtered and washed with ethanol twice and finally crystallized from dimethylformamide-ethanol mixture to give the respective 4-phenylsulfonylamino-3,5-diaryl-1,2,4-triazoles (IV) in 80 to 90% yield. All products dissolve in aqueous potassium hydroxide solution and precipitate upon acidification. The results are summarized in Table I.

Method B.

A mixture of II (0.005 mole) and III (0.01 mole) in tetrahydrofuran (40 ml.) was refluxed for 4 hours, and cooled. The white solid precipitated during reflux was filtered and washed with tetrahydrofuran (10-20 ml.) (filtrate A). The collected solid was dissolved in 40 ml. of aqueous potassium hydroxide (10%) and the unreacted aroylhydrazine was removed by filtration. Acidification of the filtrate with dilute sulfuric acid precipitated the corresponding triazoles, IV, (40-45%). The latter products were identical with those obtained by method A above.

The solvent in filtrate A combined with tetrahydrofuran washings was distilled off, and the residue left solidified on trituration with dilute methanol. The crude solid was collected and crystallized from methanol to give the corresponding 2,5-diaryl-1,3,4-oxadiazoles, V, in 35-45% yield.

Compound Va.

This compound had m.p. 140° (Lit. m.p. 138°), m.mp with an authentic sample (14) showed no depression; λ max (ethanol): (log ϵ) 280 (4.527) nm.

Compound Vb.

This compound had m.p. 155-157° (methanol); λ max (ethanol): (log ϵ) 285 (4.389).

Anal. Calcd. for $C_{14}H_{19}ClN_2O$: C, 65.51; H, 3.53; N, 10.91. Found: C, 65.53; H, 3.70; N, 10.98.

Compound Vc.

This compound had m.p. 115-116° (Lit. m.p. 115° (15)); λ max (ethanol): (log ϵ) 285 (4.161) nm.

Compound Vd.

This compound had m.p. 109-110° (cyclohexane), Lit. m.p. 118° (8); λ max (ethanol): (log ϵ) 300 (4.347) nm.

Anal. Calcd. for $C_{12}H_8N_2OS$: C, 63.14; H, 3.53; N, 12.27. Found: C, 63.19; H, 3.66; N, 12.30.

Compound Ve.

This compound had m.p. 160° (methanol); λ max (ethanol): (log ϵ) 285 (3.419) nm.

Anal. Calcd. for $C_{14}H_9BrN_2O$: C, 55.83; H, 3.01; N, 9.30. Found: C, 56.57; H, 2.98; N, 9.37.

Compound Vf.

This compound had m.p. 242° (ethanol), Lit. m.p. 243° (8); λ max (ethanol): (log ϵ) 288 (4.583).

Compound Vg.

This compound had m.p. 150-151° (methanol); λ max (ethanol (log ϵ) 295 (4.368).

Anal. Calcd. for $C_{15}H_{12}N_2O_2$: C, 71.42; H, 4.79; N, 11.10. Found: C, 71.68; H, 4.80; N, 10.99.

Reaction of II with III in Presence of Triethylamine.

To a mixture of equivalent amounts of II (Ar = C_6H_5; X = Cl) (0.005 mole) and benzoylhydrazine (0.005 mole) in tetrahydrofuran (40 ml.) was added dropwise a solution of triethylamine (0.005 mole) in the same solvent (10 ml.) at room temperature while stirring. The addition took 30 minutes and stirring continued for 4 hours. The reaction mixture was filtered and the solvent in the filtrate was evaporated. The residue left solidified on triutration with methanol. It was collected and crystallized from ethanol to give the tetrazene VIII (Ar = C_6H_5) in 88% yield,

m.p. 190°; λ max (ethanol): (log ε) 252 (4.385) nm.

Anal. Calcd. for $C_{26}H_{20}N_4O_4S_2$: C, 60.45; H, 3.90; N, 10.84; S, 12.41. Found: C, 60.34; H, 3.78; N, 10.90; S, 12.40.

Repetition of the above experiment without using benzoylhydrazine gave the same tetrazene, identical in all respects with the sample obtained above.

REFERENCES AND NOTES

(1) To whom all correspondence should be addressed. Present address: Department of Chemistry, Faculty of Science, University of Cairo, Giza, Egypt.

(2) A. S. Shawali and A. O. Abdelhamid, *J. Heterocyclic Chem.*, **13**, 45, 989 (1976); A. S. Shawali and H. M. Hassaneen, *Tetrahedron*, **29**, 21 (1972); A. S. Shawali, H. M. Hassaneen, M. Sami and H. M. Fahham, *J. Heterocyclic Chem.*, **13**, 1137 (1976).

(3a) W. Paterson and G. R. Proctor, *J. Chem. Soc.*, 485 (1965); (b) S. Ito, Y. Tanaka, A. Kakehi and K. Kondo, *Bull. Chem. Soc. Japan*, **49**, 762, 1920 (1976).

(4) E. Lieber, D. R. Levering and L. J. Patterson, *Anal. Chem.*, **23**, 1594 (1951).

(5) M. Dziewonska, *Spectrochim. Acta*, **23A**, 1195 (1967).

(6) R. M. Herbst and J. A. Garrison, *J. Org. Chem.*, **18**, 872 (1953).

(7) M. L. Sreter and K. Lempert, *Tetrahedron*, **31**, 1677 (1975).

(8) F. N. Hayes, B. S. Rogers and D. G. Ott, *J. Am. Chem. Soc.* **77**, 1850 (1955).

(9) M. Milone and E. Borello, *Gazz. Chim. Ital.*, **81**, 368 (1951).

(10) H. von Pechmann, *Ber.*, **27**, 320 (1894); F. D. Chattaway and A. J. Walker, *J. Chem. Soc.*, **127**, 975 (1925).

(11) R. Huisgen, J. Sauer and H. J. Sturm, *Angew. Chem.*, 273 (1958).

(12) S. Wawzonek and J. N. Kellen, *J. Org. Chem.*, **38**, 3627 (1973).

(13) H. Reimlinger, *Chem. Ber.*, **103**, 1900 (1970).

(14) A. O. Fitton and R. K. Smalley, "Practical Heterocyclic Chemistry", Academic Press, New York, N. Y., 1968, pp. 37-39.

(15) E. C. Gilbert, *J. Am. Chem. Soc.*, **49**, 286 (1927).