

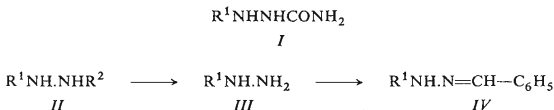
PREPARATION AND CYANOETHYLATION  
OF SOME HYDRAZINE DERIVATIVES

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Received August 28th, 1969\*

We determined earlier<sup>1,2</sup> that on reaction of some urea or thiourea derivatives with acylating agents the splitting off of the carbonyl or thiocarbonyl group, resp., takes place. An analogous cleavage was observed later during the cyanoethylation of some urea derivatives<sup>3</sup>. As we needed for further cyanoethylation N,N'-dibenzoylhydrazine and certain diarylsulfonyl derivatives of hydrazine, we tried to prepare them by an analogous cleavage of corresponding semicarbazides. Boiling of 1-benzoylsemicarbazide (*Ia*) with benzoyl chloride in pyridine gave N,N'-dibenzoylhydrazine (*Ila*). In contrast to this 1-(*p*-toluenesulfonyl)- and 1-(*p*-acetamidobenzenesulfonyl)-semicarbazides (*Ib,c*) do not react under these conditions either with benzoyl chloride or *p*-toluenesulfonyl chloride, or *p*-acetamidobenzenesulfonyl chloride. These results confirm older results<sup>2,4</sup> on the greater stability of the carbamoyl group in arylsulfonylsemicarbazides. The splitting off of the carbamoyl group in 1-benzoylsemicarbazide (*Ia*) also takes place on boiling with acetic acid, pyridine, and dimethylformamide. In no case is the expected benzoylhydrazine formed after the splitting off of the carbamoyl group, but N,N'-dibenzoylhydrazine (*Ila*) is formed instead. As it is known<sup>5</sup> that benzoylhydrazine on heating at 180°C gives N,N'-dibenzoylhydrazine, it is very probable that in this case too the reaction takes place *via* benzoylhydrazine as the intermediate. This view is supported by the reaction of 1-benzoylsemicarbazide (*Ia*) with acetic acid in the presence of benzaldehyde, giving rise to N-benzoyl-N'-benzylidenehydrazine (*Iva*). Under these conditions a disproportionation of the temporarily formed benzoylhydrazine to N,N'-dibenzoylhydrazine (*Ila*) is prevented. In contrast to this, it was impossible to obtain by an analogous method N-arylsulfonyl-N'-benzylidenehydrazines *Ivb,c*, because under the given conditions arylsulfonylsemicarbazides do not split off the carbamoyl group. These substances were prepared from corresponding arylsulfonylhydrazines on reaction with benzaldehyde in acetic acid, making use of an analogous, well-known procedure<sup>6</sup>.



In formulae I–IV

a, R<sup>1</sup> = R<sup>2</sup> = C<sub>6</sub>H<sub>5</sub>CO

b, R<sup>1</sup> = CH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>, R<sup>2</sup> = C<sub>6</sub>H<sub>5</sub>CO

c, R<sup>1</sup> = CH<sub>3</sub>CONH.C<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>, R<sup>2</sup> = C<sub>6</sub>H<sub>5</sub>CO

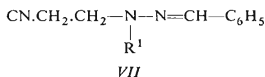
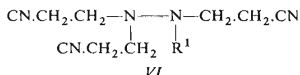
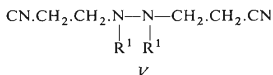
d, R<sup>1</sup> = R<sup>2</sup> = CH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>

e, R<sup>1</sup> = R<sup>2</sup> = CH<sub>3</sub>CONH.C<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>

f, R<sup>1</sup> = C<sub>6</sub>H<sub>5</sub>, R<sup>2</sup> = C<sub>6</sub>H<sub>5</sub>CO

\* The revised manuscript was received on July 30th, 1970.

Compounds *Iib-d* were prepared from corresponding arylsulfonylhydrazines *IIIb,d* on reaction with benzoyl chloride, or the corresponding arylsulfonyl chloride, or else on reaction of arylsulfonyl chlorides with hydrazine hydrate. Analogously, *N*-phenyl-*N'*-benzoylhydrazine (*IIf*) or *N*-phenyl-*N'*-(*p*-toluenesulfonyl)hydrazine (*IIf*) were prepared from phenylhydrazine (*IIIc*) and benzoyl chloride or *p*-toluenesulfonyl chloride, respectively. In contrast to this we could not obtain the corresponding *N,N'*-di(*p*-acetamidobenzenesulfonyl)hydrazine (*IIf*) on reaction of *p*-acetamidobenzenesulfonyl chloride with hydrazine hydrate or with *p*-acetamidobenzenesulfonylhydrazine (*IIIc*). From the reaction mixture, only *p*-acetamidobenzenesulfonylhydrazine (*IIIc*) was isolated.



in formulae V–VII

a,  $\text{R}^1 = \text{C}_6\text{H}_5\text{CO}$

b,  $\text{R}^1 = \text{CH}_3 \cdot \text{C}_6\text{H}_4 \cdot \text{SO}_2$

c,  $\text{R}^1 = \text{CH}_3 \cdot \text{CO} \cdot \text{NH} \cdot \text{C}_6\text{H}_4 \cdot \text{SO}_2$

d,  $\text{R}^1 = \text{C}_6\text{H}_5$

As we mentioned earlier<sup>3</sup> 1-benzylidene-semicarbazide may be cyanoethylated in aqueous triethylamine on the nitrogen atom in position 2. On the other hand, 1-benzoyl-semicarbazide (*Ia*) does not react under analogous conditions either in pyridine or triethylamine, or under catalysis with alkalis. Under the mentioned conditions the expected splitting off of the carbamoyl group does not take place. In contrast to this, it is known<sup>3</sup> that 1-(*p*-toluenesulfonyl)semicarbazide (*Ib*) splits off the carbamoyl group smoothly during cyanoethylation, giving rise to *N,N,N'*-tris(2-cyanoethyl)-*p*-toluenesulfonylhydrazine (*VIIb*). An analogous cleavage of 1-(*p*-acetamidobenzenesulfonyl) semicarbazide (*Ic*) gave *N,N,N'*-tris(2-cyanoethyl)-*p*-acetamidobenzenesulfonylhydrazine (*VIIc*). Hence, during cyanoethylation the stability of the carbamoyl group in arylsulfonylsemicarbazides is less than in 1-benzoylsemicarbazides, which contrasts with the reactions with acylating agents, acetic acid or pyridine, where the opposite is true.

On boiling *N,N'*-dibenzoylhydrazine (*IIf*) with acrylonitrile in aqueous triethylamine *N,N'*-bis(2-cyanoethyl)-*N,N'*-dibenzoylhydrazine (*VIIa*) is formed. In contrast to this cyanoethylation of *N,N'*-di(*p*-toluenesulfonyl)hydrazine (*IIIc*) gives substance *VIIb* instead of the expected *N,N'*-bis(2-cyanoethyl)-*N,N'*-di(*p*-toluenesulfonyl)hydrazine (*VIIc*). It was proved by cyanoethylation of *p*-toluenesulfonylhydrazine (*IIIc*) under analogous conditions that the compound *VIIb* is *N,N,N'*-tris(2-cyanoethyl)-*p*-toluenesulfonylhydrazine<sup>3</sup>. Hence, during the cyanoethylation of compound *IIIc* the splitting off of one *p*-toluenesulfonyl group took place. In the presence of alkali in dilute triethylamine and dioxan cyanoethylation takes place in this way even at room temperature. However, during the cyanoethylation of *N-p*-toluenesulfonyl-*N'*-benzoylhydrazine (*IIf*) the benzoyl group is split off preferentially, giving rise again to compound *VIIb*.

On boiling *N*-benzoyl-*N'*-benzylidenehydrazine (*VIa*) with acrylonitrile in aqueous triethylamine *N*-(2-cyanoethyl)-*N*-benzoyl-*N'*-benzylidenehydrazine (*VIIa*) is formed. *N*-(*p*-Acetamidobenzenesulfonyl)-*N'*-benzylidenehydrazine (*IVc*) may be cyanoethylated in aqueous triethylamine only in the presence of alkali and at room temperature, giving rise to *N*-(2-cyanoethyl)-*N*-*p*-acet-

amidobenzenesulfonyl-N'-benzylidenehydrazine (*VIIc*). On cyanoethylation at boiling temperature the starting compounds were regenerated in both cases. Hence, at elevated temperatures decyanoethylation takes place simultaneously. A similar course was also observed with N-phenyl-N'-benzylidenehydrazine (*IVf*).

#### EXPERIMENTAL

Melting points were determined on a Kofler block. The samples for analysis were dried at 40–60°C/20 Torr.

#### N,N'-Dibenzoylhydrazine (*IIa*)

To a solution of 1-benzoylsemicarbazide (*Ia*; 5.37 g; 0.03 mol) in pyridine (50 ml) benzoyl chloride (4.2 g; 0.03 mol) was added and the solution was refluxed for 6 hours and then evaporated *in vacuo* to dryness. Ethanol (30 ml) was added to the residue and evaporated again twice, and the residue was crystallised from ethanol (50 ml). Yield, 3.6 g (50%), m.p., 236–238°C. Lit.<sup>7</sup> gives m.p. 237–239°C. Analogously, boiling of 1-benzoylsemicarbazide (5.37 g) in acetic acid (50 ml) or dimethylformamide (30 ml) for 8 hours gave 68.5% and 66.8% of compound *IIa*, resp., which melted undepressed on admixture of the compound obtained above.

#### N-(*p*-Toluenesulfonyl)-N'-benzoylhydrazine (*IIb*)

To a stirred suspension of *p*-toluenesulfonylhydrazine (*IIIb*; 18.6 g; 0.1 mol) in water (100 ml) benzoyl chloride (14 g; 0.1 mol) and sodium hydroxide (4 g) solution in water (25 ml) were added simultaneously over one hour. The mixture was heated at 60°C for 8 hours and then allowed to stand at room temperature overnight. The separated compound was filtered off under suction and recrystallised from ethanol (100 ml). Yield, 16 g (55%), m.p., 162–164°C. Lit.<sup>8</sup>, describing a synthesis from *p*-toluenesulfonyl chloride and benzoylhydrazine, gives m.p. 163–164°C. By an analogous procedure N-(*p*-acetamidobenzenesulfonyl)-N'-benzoylhydrazine (*IIc*) (10 g; 60%), m.p. 226–228°C, was obtained from *p*-acetamidobenzenesulfonylhydrazine (*IIIc*) (11.45 g; 0.05 mol). For C<sub>15</sub>H<sub>15</sub>N<sub>3</sub>O<sub>4</sub>S (333.3) calculated: 54.05% C, 4.54% H, 12.61% N; found: 54.30% C, 4.40% H, 12.29% N.

#### N,N'-Di-(*p*-toluenesulfonyl)hydrazine (*IId*)

A suspension of hydrazine sulfate (13 g; 0.1 mol) in water (20 ml) was neutralised to pH 9 with a solution of sodium hydroxide (8 g; 0.2 mol in 30 ml of water) at a temperature not exceeding 5°C. *p*-Toluenesulfonyl chloride (38 g; 0.2 mol) and sodium hydroxide solution (8 g; 0.2 mol) in water were added simultaneously in order to keep the pH value of the solution within the 9–10 interval. After 24 hours standing at room temperature the separated compound was filtered off, washed with water, dried at 70°C and crystallised from ethanol (120 ml). Yield, 20.5 g (60%); m.p., 183–185°C. For C<sub>14</sub>H<sub>16</sub>N<sub>2</sub>O<sub>4</sub>S<sub>2</sub> (340.3) calculated: 49.41% C, 4.74% H, 8.23% N; found: 49.23% C, 4.91% H, 8.09% N.

N-Phenyl-N'-benzoylhydrazine (*IIf*) and N-Phenyl-N-(*p*-toluenesulfonyl)hydrazine (*IIg*) were prepared by a known procedure from benzoyl chloride or *p*-toluenesulfonyl chloride, resp., and phenylhydrazine<sup>8,9</sup>.

#### N-Benzoyl-N'-benzylidenehydrazine (*IVa*)

A mixture of 1-benzoylsemicarbazide (*Ia*; 8.95 g; 0.05 mol), benzaldehyde (18 ml), and acetic acid (60 ml) was refluxed for 4 hours, evaporated to dryness, and the residue crystallised from ethanol

(50 ml). Yield, 6.72 g (60%); m.p., 204–206°C. Lit.<sup>10</sup> (from benzoylhydrazine and benzaldehyde) gives m.p. 206°C.

*N,N,N'*-Tris(2-cyanoethyl)-*N'*-*p*-acetamidobenzenesulfonylhydrazine (*VIc*)

*A.* A mixture of 1-(*p*-acetamidobenzenesulfonyl) semicarbazide (*Ic*; 2.72 g; 0.01 mol), acrylonitrile (10 ml), triethylamine (20 ml), and water (20 ml) was refluxed for 5 hours, then evaporated *in vacuo* to dryness, and the residue crystallised from 50% ethanol (40 ml). Yield, 2.78 g (71.5%); m.p., 213–215°C. For  $C_{17}H_{20}N_6O_3S$  (388.4) calculated: 52.57% C, 5.19% H, 21.64% N, 8.24% S; found: 52.31% C, 5.04% H, 21.28% N, 8.05% S.

*B.* A mixture of *p*-acetamidobenzenesulfonylhydrazine (*IIIc*; 2.29 g; 0.01 mol), acrylonitrile (10 ml), triethylamine (20 ml), and water (20 ml) was refluxed for 5 hours, evaporated *in vacuo* to dryness, and the residue crystallised from 50% ethanol (40 ml). Yield, 2.98 g (77%); m.p., 212–214°C, undepressed on admixture of the substances obtained under *A*.

*N,N'*-Bis(2-cyanoethyl)-*N,N'*-dibenzoylhydrazine (*Va*)

A mixture of *N,N'*-dibenzoylhydrazine (*IIa*; 2.4 g; 0.01 mol), acrylonitrile (5 ml), triethylamine (10 ml), and water (10 ml) was refluxed for 6 hours, then evaporated *in vacuo* to dryness, and the residue crystallised from 70% ethanol (160 ml). Yield, 2.49 g (72%); m.p., 162–164°C. For  $C_{20}H_{18}N_4O_2$  (346.4) calculated: 69.35% C, 5.24% H, 16.18% N; found: 69.01% C, 5.05% H, 16.02% N.

*N,N,N'*-Tris(2-cyanoethyl)-*p*-toluenesulfonylhydrazine (*VIb*)

*A.* A mixture of *N,N'*-di-*p*-toluenesulfonylhydrazine (*IIb*; 2.4 g; 0.01 mol), acrylonitrile (5 ml), triethylamine (10 ml), and water (10 ml), was refluxed for 6 hours, evaporated *in vacuo* to dryness, and the residue crystallised from 70% ethanol (160 ml). Yield, 2.36 g (68.5%); m.p., 91–93°C. For  $C_{16}H_{19}N_5O_2S$  (345.3) calculated: 55.64% C, 5.55% H, 20.28% N, 9.26% S; found: 55.34% C, 5.38% H, 20.01% N, 9.04% S.

*B.* Analogously, using *p*-toluenesulfonylhydrazine (*IIIb*; 3.72 g; 0.02 mol) as starting material, the yield was 4.5 g (70%), m.p. 90–92°C, undepressed on admixture of substance *VIb* obtained under *A*.

*C.* A mixture of *N,N'*-di-*p*-toluenesulfonylhydrazine (*IIb*; 3.4 g; 0.01 mol), acrylonitrile (10 ml), triethylamine (10 ml), dioxan (10 ml), and a sodium hydroxide solution (0.4 g in 10 ml of water) was stirred at room temperature for 7 hours, then allowed to stand overnight, neutralised with acetic acid (2.5 ml), and evaporated to dryness. Crystallisation from ethanol (20 ml) gave 2.20 g (64%) of product, m.p. 92–94°C, undepressed on admixture of the substance obtained under *A* and *B*.

*N*-(2-Cyanoethyl)-*N*-benzoyl-*N'*-benzylidenehydrazine (*VIIa*)

A mixture of *N*-benzoyl-*N'*-benzylidenehydrazine (*IVa*; 2.24 g; 0.01 mol), acrylonitrile (10 ml), triethylamine (20 ml), and water (20 ml) was refluxed for 6 hours and evaporated to dryness. The residue was crystallised from ethanol (15 ml). Yield, 1.86 g (67%); m.p., 118–120°C. For  $C_{17}H_{15}N_3O$  (277.3) calculated: 73.63% C, 5.45% H, 15.15% N; found: 73.21% C, 5.90% H, 15.02% N.

N-(2-Cyanoethyl)-N-*p*-acetamidobenzenesulfonyl-N'-benzylidenehydrazine (*VIIc*)

A mixture of N-*p*-acetamidobenzenesulfonyl-N'-benzylidenehydrazine (*IVc*; 1.58 g; 0.005 mol), acrylonitrile (5 ml), triethylamine (5 ml), dioxan (10 ml), and a sodium hydroxide solution (0.05 g in 5 ml of water) was allowed to stand overnight, then neutralised with acetic acid (0.9 ml), and the solution was evaporated to dryness *in vacuo*. The residue was crystallised from 50% ethanol (10 ml). Yield, 1.2 g; m.p., 143–145°C. For  $C_{18}H_{18}N_4O_3S$  (370.4) calculated: 58.37% C, 4.90% H, 15.13% N; found: 58.05% C, 4.71% H, 15.02% N.

Applying the above procedure N-phenyl-N'-benzylidenehydrazine (*IVf*; 1.96 g; 0.01 mol) gave 1.65 g (66.5%) of compound *VII*, m.p. 120–122°C. For  $C_{16}H_{15}N_3$  (249.3) calculated: 77.08% C, 6.06% H, 16.86% N; found: 76.92% C, 6.05% H, 16.69% N.

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Translated by Ž. Procházka.