Monatshefte für Chemie 124, 299–308 (1993)

Monatshefte für Chemie
Chemical Monthly

Addition Products of Hydrazine Derivatives to Azo-Alkenes, Part V [1]: The Reaction of α-(1-Phenylhydrazino)alkanone Phyenylhydrazones with Acids and Acid Derivatives

J. G. Schantl* and **M. Prean**

Institut für Organische und Pharmazeutische Chemie, Universtät Innsbruck, A-6020 Innsbruck, Austria

Summary. The bifunctional title compounds **2** react with acylating, carbamoylating and sulfonylating reagents mostly at the primary amino group of the hydrazine function. Both functional groups of **2** are attacked by N,N′-carbonyldiimidazole converting it into 1*H*-1,2,4,5-tetrazepin-3-one derivatives **8**. The acid-induced 1,4-elimination of phenylhydrazine from **2** gives rise to the formation of phenylosazones **3**. In the presence of thiocyanic acid the intermediately formed phenylazo-alkenes **1** undergo [3 + 2]-cycloaddition furnishing 1-anilino-imidazoline-2-thiones **13**.

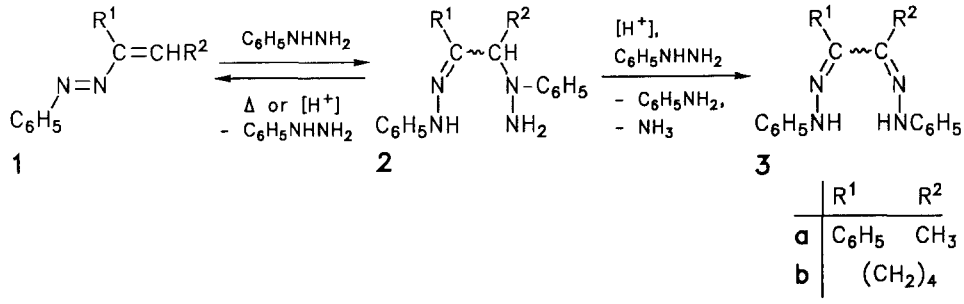
Keywords. α-(1-Phenylhydrazino)alkanone phenylhydrazones; α-(1-Phenylhydrazido)alkanone phenylhydrazones; Phenylosazones; 1*H*-1,2,4,5-Tetrazepin-3-ones; 1-Anilinoimidazo-line-2-thiones.

Additionsprodukte von Hydrazin-Derivaten an Phenylazo-alkene, 5. Mitt. [1]:
Umsetzung von α-(1-Phenylhydrazino)alkanon phenylhydrazonen mit Säuren und Säurederivaten

Zusammenfassung. Die bifunktionellen Titelverbindungen **2** reagieren mit Acylierungs-, Carbamoylierungs- und Sulfinylierungs-Reagenzien meist an der primären Amino-Gruppe der Hydrazin-Funktion. N,N′-Carbonyldiimidazol greift beide funktionelle Gruppen von **2** an und bedingt die Umwandlung in 1*H*-1,2,4,5-Tetrazepin-3-on-Derivate **8**. Die säureinduzierte 1,4-Eliminierung von Phenylhydrazin aus **2** führt zur Bildung der Phenylosazone **3**. In Gegenwart von Thiocyansäure erfolgt [3 + 2]-Cycloaddition an die intermediär gebildeten Phenylazo-alkene **1**, sodaß 1-Anilino-imidazolin-2-thione **13** entstehen.

Introduction

The 1,4-addition of phenylhydrazine to phenylazo-alkenes **1** yields α-(1-phenylhydrazino)alkanone phenylhydrazones **2** (Scheme 1) [2]. A noteworthy structural feature of these adducts **2** is the unsymmetrically N,N-disubstituted hydrazine moiety which has been substantiated both by spectroscopic means (^{1}H-NMR) [2] and by chemical evidence: Condensation with carbonyl compounds furnishes the corresponding hydrazones [3]. Furthermore, a rather intriguing reaction of compounds **2** is the facile conversion into phenylosazones [i.e. 1,2-alkanedione



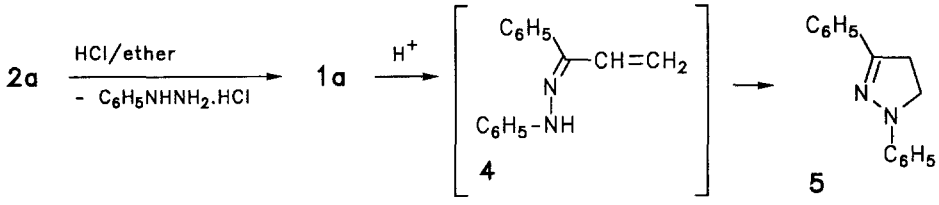
Scheme 1

bis(phenylhydrazones)] **3**: This is brought about by weak acids (e.g. acetic acid) or by catalytic amounts of a mineral acid in the presence of phenylhydrazine (added or liberated in the course of the acid catalyzed 1,4-elimination of phenylhydrazine from **2**) [2]. This result has established α-(1-phenylhydrazino)alkanone phenylhydrazones **2** as true precursors [3] of phenylosazones **3** [4].

In order to further explore the reactivity of α-(1-phenylhydrazino)alkanone phenylhydrazones **2** with respect to both functional groups present in the molecule, the reaction with several acid derivatives has been investigated in a model study.

Results

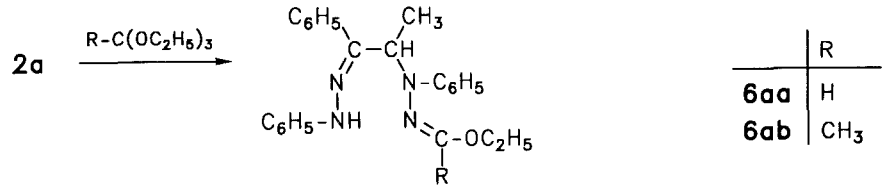
Contrary to the acid induced conversion of α-(1-phenylhydrazino)alkanone phenylhydrazone **2a** into the phenylosazone **3a** (*vide supra*), the addition of **2a** to an ether solution of hydrogen chloride gave a different result: The attempt to obtain the salt **2a**·HCl resulted in the formation of phenylhydrazine hydrochloride beside mainly polymeric material from which a small amount of 4,5-dihydro-1,3-diphenyl-1*H*-pyrazole **5** was extracted (Scheme 2). Presumably, the formation of **5** is due to the known facile acid induced 1,4-elimination of phenylhydrazine: In the absence of a nucleophile the intermediately formed azo-alkene **1a** tautomerizes and the conceivable intermediate **4** undergoes ring-closure to yield the heterocyclic product **5**.



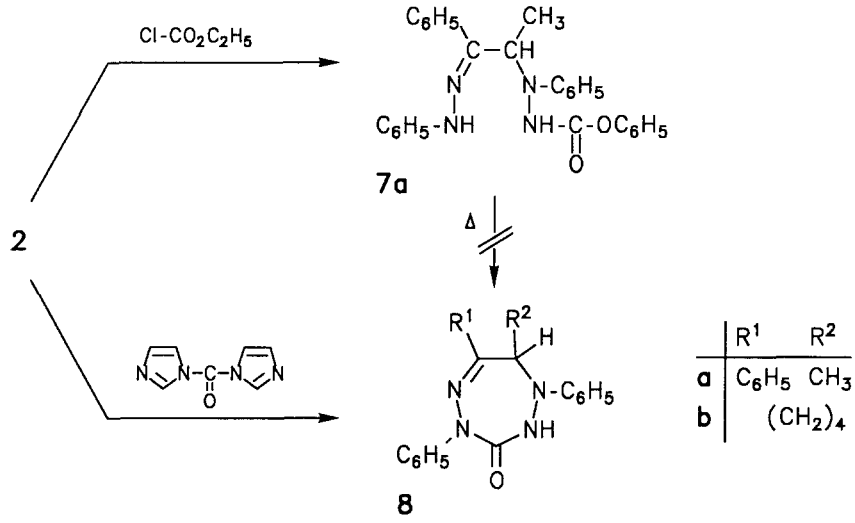
Scheme 2

The reaction of **2a** with ortho-esters gives rise to the formation of the corresponding hydrazonoates **6** (Scheme 3). An attempt to induce thermal cyclization of compounds **6a** failed.

Similarly, phenyl chloroformate reacts with **2a** and furnishes the phenoxycarbonyl derivative **7a** (Scheme 4). No cyclization occurred upon heating, only unidentified products were formed beside phenol. However, the reaction of **2** with



Scheme 3

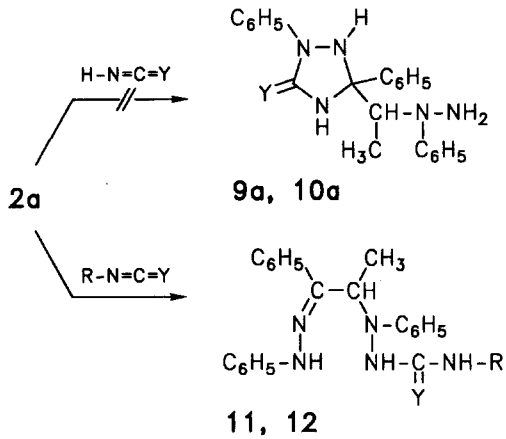


Scheme 4

N,N′-carbonyldiimidazole provided the cyclization products, the tetrazepinone derivatives **8** (Scheme 4).

Both functional groups of **2a**, the hydrazone and the hydrazino functions are expected to react with cyanic acid (generated *in situ* from potassium cyanate in acetic acid): The hydrazone function may be anticipated to undergo [3 + 2]-cycloaddition [5] to yield the 1,2,4-triazolidin-3-one derivative **9a** (Scheme 5). On the other hand, the hydrazine moiety of **2a** is disposed to give the corresponding semicarbazide derivative **11aa**; in fact, only the latter adduct was isolated from this reaction. Arylisocyanates provide the corresponding N-4-substituted semicarbazides **11ab** and **11ac**.

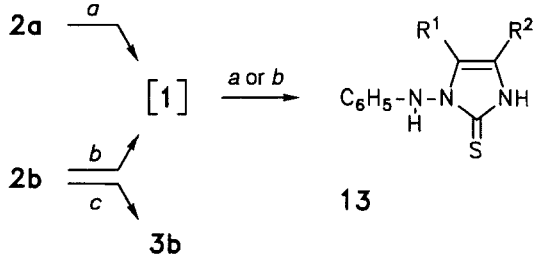
Similarly, the reaction of **2a** with alkylisothiocyanates yields the N-4-substituted thiosemicarbazides **12ab** and **12ac**. By contrast, the reaction with thiocyanic acid (generated *in situ* from potassium thiocyanate in acetid acid) took an unexpected different course. Neither the 1,2,4-triazolidine-3-thione derivative **10a** [5] nor the thiosemicarbazide **12aa** (Scheme 5) were obtained. Instead, the isolated product is lacking the elements of phenylhydrazine which have been replaced by those of thiocyanic acid; the structure turned out to be that of the 1-anilino-imidazoline-2-thione derivative **13a** [6, 7] (Scheme 6). Likewise, **2b** was converted into **13b** upon reaction with potassium thiocyanate and trimethylsilylchloride in dimethylformamide [6, 7], whereas the reaction of a benzene solution of **2b** with potassium thiocyanate and followed by addition of acetic acid gave the phenylosazone **3b**;



	Y
9a	O
10a	S

	Y	R
11aa	O	H
11ab	O	4-Cl-C_6H_4
11ac	O	4-H_3CO-C_6H_4
12aa	S	H (not formed)
12ab	S	CH_3OCH_2
12ac	S	C_6H_{11}

Scheme 5



	R^1	R^2
a	C_6H_5	CH_3
b	$(CH_2)_4$	

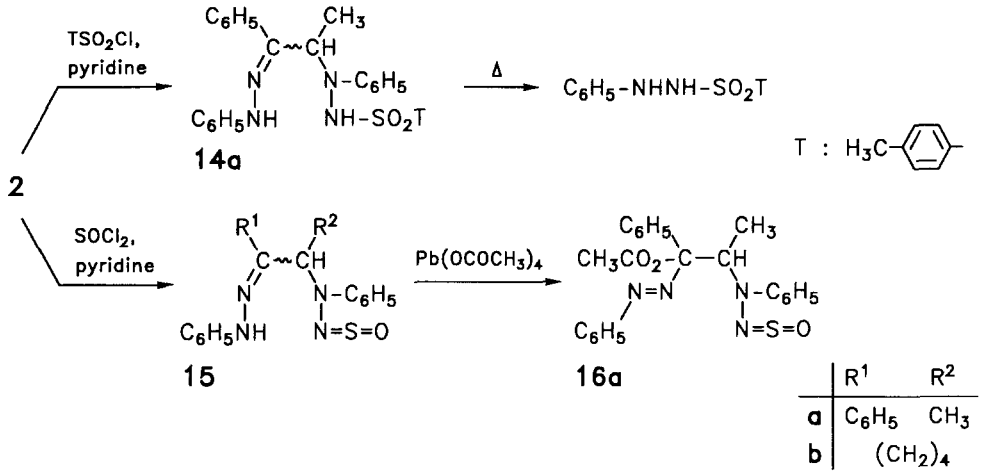
a KNCS, CH_3CO_2H. *b* KNCS, $(CH_3)_3SiCl$, DMF. *c* KNCS, benzene; CH_3CO_2H.

Scheme 6

obviously, in the latter reaction some part of **2a** undergoes acid catalysed 1,4-elimination of phenylhydrazine, which in turn, reacts with **2a** yielding the phenylosazone **3a** as outlined in Scheme 1 [3].

The formation of the heterocycles **13** is well explained by the 1,4-elimination of phenylhydrazine followed by the reaction of the phenylazo-alkene intermediate **1** with thiocyanic acid (or its tautomeric form, isothiocyanic acid) [7]. In fact, 1-phenylazo-cyclohexene **1b** reacts with potassium thiocyanate both in acetic acid and in dry dimethylformamide in the presence (but not so in the absence) of chlorotrimethylsilane to give the adduct **13b** [7].

Usually, the reaction of phenylhydrazones with 4-methyl-benzenesulfonyl-chloride turns them into N-phenyl-N-(4-methyl-benzenesulfonyl)hydrazone derivatives [8]; this conversion has not been observed to occur with **2a**. The ambident nucleophile **2a** reacts at the primary amino group of the hydrazine moiety furnishing the sulfonylhydrazide derivative **14a** (Scheme 7). Compound **14a** is thermally labile, recrystallization from boiling methanol induces 1,4-elimination giving rise to the formation of 1-(4-methyl-benzenesulfonyl)-2-phenylhydrazine.



Scheme 7

The reaction of **2** with thionylchloride in the presence of pyridine yields the N-sulfinylhydrazino derivatives **15**; again, the hydrazone group of **2** is not involved in the reaction. The derivatization of the primary amino group of compounds **2** (like hydrazone formation [3] or tosylation, *cf.* **14a**) increases the tendency to eliminate the derivatized phenylhydrazine moiety. By contrast, the N-sulfinyl group appears to provide additional stabilization, and **15a** can be subjected to a reaction taking place at the hydrazone group: Oxidation with lead tetraacetate [9] yields a mixture of diastereomeric azo-compounds **16a** (Scheme 7).

The oxidation of 1,1-disubstituted hydrazine derivatives has been reported to result in the formation of tetrazene derivatives [10]. Contrary to the oxidation of **15a**, attempts to oxidize **2a** with a number of reagents (benzoquinone in benzene, nitrosobenzene in benzene and ethanol, N-chlorosuccinimide in dichloromethane, lead tetraacetate in dichloromethane, silveroxide in benzene, iodine in pyridine) all failed to give a single major product, only complex product mixtures were obtained.

Experimental Part

The α-(1-phenylhydrazino) alkanone phenylhydrazones **2** are available as reported [2]. Dried and freshly distilled solvents were used. Evaporation of solvents was carried out at ca. 20 mbar: Rotatory evaporator Vapsilator [Chemophor]. The following instruments were used: M.p.: Kofler hot-stage microscope [Reichert]. IR: Beckman AccuLab 4. ^{1}H-NMR: JEOL JNM-PMX-60 (60 MHz). ^{1}H-NMR (300 MHz) and ^{13}C-NMR: Bruker AM-300. MS: Varian MAT 44S (70 eV). Elemental analyses were made by Dr. J. Zak, University of Vienna.

4,5-Dihydro-1,3-diphenyl-1H-pyrazole (**5**) *from* **2a** *with HCl/Ether*

A mixture of 3.30 g (10 mmol) **2a** and 100 ml ether saturated with gaseous hydrogen chloride was stirred for 12 h at ambient temperature. The resultant crystalline precipitate was filtered off to give 1.40 g (97%) phenylhydrazine·HCl. The filtrate was evaporated and the glassy residue gave a dark colored crystalline product upon addition of little ethanol. The crystals were repeatedly extracted with petroleum ether, and from the combined extracts 0.09 g (4%) yellowish crystals **5** were obtained, m.p. 152 °C (ethanol), identical with an authentic sample [11].

Ethyl 1-(1-methyl-2-phenyl-2-phenylhydrazonoethyl)-1-phenylhydrazono Formate (**6aa**)

A solution of 0.33 g (1 mmol) **2a** and 0.01 g 4-methyl-benzenesulfonic acid in 2.50 g (16.9 mmol) triethyl orthoformate was kept for 2 h at 22 °C. The excessive reagent was distilled off *in vacuo* at 50 °C and the residue was kept at 0.01 mbar for 30 min. Addition of 15–30 ml pentane at −20 °C induced crystallisation of the product: 0.18 g (47%) slightly yellow crystals **6aa** were isolated, m.p. 93–96 °C (ethanol). IR (KBr): $\nu = 3325\,cm^{-1}$ (NH), 1240, 1110 (C–O). ^{1}H-NMR (*DMSO-d*$_6$): δ (ppm) = 1.24 (t, $J = 7$ Hz, CH_3–CH_2), 1.40 (d, $J = 6$ Hz, CH_3–CH), 4.18 (q, $J = 7$ Hz, OCH_2–CH_3), 5.06 (q, $J = 6$ Hz, CH–CH_3), 6.4–7.6 (m, $3C_6H_5$), 7.44 (s, =CH–), 8.54 (s, NH, exchangeable with D_2O). $C_{24}H_{26}N_4O$ (386.50): calcd. C 74.58, H 6.78, N 14.50; found C 74.63, H 7.00, N 14.52.

Ethyl-1-(1-methyl-2-phenyl-2-phenylhydrazonoethyl)-1-phenylhydrazono Acetate (**6ab**)

As described above, 0.33 g (1 mmol) **2a** and 3.20 g (19.7 mmol) triethyl orthoacetate were kept at 80 °C for 4.5 h yielding 0.23 g (58%) of colorless crystals **6ab**, m.p. 103 °C (ethanol). IR (KBr): $\nu = 3320\,cm^{-1}$ (NH), 1240, 1110 (C–O). ^{1}H-NMR (*DMSO-d*$_6$): δ (ppm) = 1.06 (s, CH_3–C=), 1.22 (t, $J = 7.5$ Hz, CH_3–CH_2), 1.41 (d, $J = 6.5$ Hz, CH_3–CH), 4.14 (q, $J = 7.5$ Hz, OCH_2–CH_3), 5.07 (q, $J = 6.5$ Hz, CH–CH_3), 6.3–7.7 (m, $3C_6H_5$), 8.48 (s, NH, exchangeable with D_2O). $C_{25}H_{28}N_4O$ (400.53): calcd. C 74.97, H 7.05, N 13.99; found C 74.86, H 7.24, N 14.24.

Phenyl 1-(1-methyl-2-phenyl-2-phenylhydrazonoethyl)-1-phenylhydrazido Carbonate (**7a**)

To a solution of 0.47 g (3 mmol) phenyl chloroformate in 5 ml benzene was added a solution of 0.3 g (3 mmol) triethylamine in 3 ml benzene. This mixture was vigorously stirred, and a solution of 0.99 g (3 mmol) **2a** in 15 ml benzene was added dropwise. After stirring of the mixture was continued for 1 h, 20 ml water were added, and the organic phase was separated and repeatedly washed with water (4 times 20 ml each), dried ($MgSO_4$) and evaporated. The residue was an orange foam which crystallized upon treatment with pentane: 0.88 g (65%) colorless crystals **7a**, m.p. 144–146 °C (methanol). IR (KBr): $\nu = 3340\,cm^{-1}$ (NH), 1766, 1725 (C=O), 1250, 1210 (C–O, C–N). ^{1}H-NMR (*DMSO-d*$_6$): δ (ppm) = 1.47 (d, $J = 6$ Hz, CH_3–CH), 5.00 (q, $J = 6$ Hz, CH–CH_3), 6.5–7.7 (m, $4C_6H_5$), 8.53 (s, HN–N=, exchangeable with D_2O), 9.33 (s, NH–CO, exchangeable with D_2O). $C_{28}H_{26}N_4O_2$ (450.54): calcd. C 74.64, H 5.82, N 12.43; found C 75.11, H 6.23, N 12.42.

*7-Methyl-2,3,4,7-tetrahydro-1,4,6-triphenyl-1*H*-1,2,4,5-tetraazepine-3-one* (**8a**)

The mixture of 2.70 g (8.2 mmol) **2a**, 50 ml tetrachloromethane, and 1.62 g (10 mmol) N,N′-carbonyldiimidazole was refluxed for 2 h. After evaporation of the solvent the residue was distributed between 50 ml each of ether and water; part of the product, separated as colorless crystals and was filtered off. The two phases of the filtrate were separated, the ether phase was repeatedly washed with water (3 times 50 ml), dried ($MgSO_4$), and evaporated. The residual yellow oil was brought to crystallization with ethanol to give 2.01 g (66%) **8a**, m.p. 225–227 °C (methanol). IR (KBr): $\nu = 3280$, $3210\,cm^{-1}$ (NH), 1660 (C=O). ^{1}H-NMR (*DMSO-d*$_6$): δ (ppm) 1.50 (d, $J = 6.5$ Hz, CH_3–CH), 5.48 (q, $J = 6.5$ Hz, CH–CH_3), 6.6–7.6 (m, 13 arom. H), 7.6–8.0 (m, 2 arom. H), 9.98 (s, NH, exchangeable with D_2O). MS: *m/z* (%) 356 (< 1) [M^+]; 355 (7.4) [$M - 1$], 250 (100) [$M - C_6H_6N_2$]. $C_{22}H_{20}N_4O$ (356.43) + 0.2 CH_4O (as indicated by ^{1}H NMR): calcd. C 73.49, H 5.78, N 15.44; found C 73.45, H 5.68, N 15.41.

3,6-Diphenyl-2,3,5,6-tetraaza-bicyclo[5.4.0]undec-1(2)-en-4-one (**8b**)

As described in the preceding experiment, 3.50 g (11.9 mmol) **2b** dissolved in 80 ml tetrachloromethane and 2.3 g (14.1 mmol) N,N′-carbonyldiimidazole were converted into 2.8 g (74%) **8b**, m.p. 205 °C. IR (KBr): $\nu = 3200\,cm^{-1}$ (NH), 1600 (C=O). ^{1}H NMR ($CDCl_3$): δ (ppm) = 1.72–2.10 (mm, 2 H), 2.25–2.45

(mm, 4 H), 2.45–2.65 (m, 1 H), 2.89 (d, $J = 13.5$ Hz, 1 H), 4.56 (dd, $J = 8.8$ Hz, CH–N), 7.15–7.65 (mm, 2 C_6H_5, NH). ^{13}C-NMR ($CDCl_3$): δ (ppm) = 25.47, 27.89, 34.51, 37.66 (4 CH_2), 59.93 (CHN), 114.19, 121.18, 125.12, 126.09, 128.49, 129.54 (10 arom. CH), 143.96, 148.90 (2 arom. C_{quart}), 159.43, 161.15 (C=N, C=O).

1-(1-Methyl-2-phenyl-2-phenylhydrazonoethyl)-1-phenylsemicarbazide (**11aa**)

To 15 ml acetic acid were added under stirring 2.00 g (24.7 mmol) potassium cyanate, and subsequently 2.00 g (6.1 mmol) **2a**. After 2 h the reaction mixture was poured dropwise into 400 ml water to precipitate the product. Stirring was continued for 30 min, then the precipitate was filtered, washed with water and dried *in vacuo*. The crude amorphous product turned cystalline upon boiling in diisopropylether for 15 min to yield 1.60 g (71%) slightly yellow crystals **11aa**, m.p. 173–176 °C (methanol). IR (KBr): $\nu = 3500$, 3460, 3390, 3320, 3180 cm^{-1} (NH); 1675, 1650 (amide I), 1595, 1560 (amide II), 1250, 1230 (N–CO). ^{1}H-NMR (*DMSO-d*$_6$): δ (ppm) = 1.38 (d, $J = 6.5$ Hz, CH_3–CH), 4.96 (q, $J = 6.5$ Hz, CH–CH_3), 5.98 (br s, H_2NCO, exchangeable with D_2O), 6.4–7.5 (m, 3 C_6H_5, NH–CO, 1 H exchangeable with D_2O), 8.30 (br s, HN–N= exchangeable with D_2O). MS: *m/z* (%): 373 (1) [M^+], 372 (4.1) [$M - 1$], 222 (45.8) [C_6H_5–N=N–C(C_6H_5)=CH–CH_3], 207 (4), 151 (10.4) [$C_6H_5NHNHCONH_2$], 117 (100) [C_9H_9], 105 (29) [$C_6H_5N_2$], 77 (94) [C_6H_5]. $C_{22}H_{23}N_5O$ (373.46): calcd. C 70.76, H 6.21, N 18.75; found C 70.44, H 6.26, N 18.59.

4-(4-Chlorophenyl)-1-(1-methyl-2-phenyl-2-phenylhydrazonoethyl)-1-phenylsemicarbazide (**11ab**)

A slurry of 0.99 g (3 mmol) **2a** in 50 ml ether was stirred and combined with a solution of 0.46 g 4-chlorophenylisocyanate in 10 ml ether. After 15 min the reactants were completely dissolved, and after 4 h the separated colorless crystals were filtered off, washed with ether and dried *in vacuo* to give 1.41 g (97%) **11ab**, m.p. 205–208 °C (acetonitrile). IR (KBr): $\nu = 3360$, 3320, 3200 cm^{-1} (NH), 1685 (C=O) 1520 (amide II), 1250, 1225 (N–CO). ^{1}H-NMR (*DMSO-d*$_6$): δ (ppm) = 1.40 (d, $J = 6.5$ Hz, CH–CH_3), 5.09 (q, $J = 6.5$ Hz, CH–CH_3), 6.45–7.7 (m, 19 arom. H), 7.7–9.3 (several broad signals, NH–N=, NH–CONH, 3 H exchangeable with D_2O). $C_{28}H_{26}ClN_5O$ (484.00): calcd. C 69.48, H 5.41, N 14.47; found C 69.25, H 5.40, N 14.55.

4-(4-Methoxyphenyl)-1-(1-methyl-2-phenyl-2-phenylhydrazonoethyl)-1-phenylsemicarbazide (**11ac**)

As described in the preceding experiment, 0.99 g (3 mmol) **2a** and 0.45 g (3 mmol) 4-methoxyphenylisocyanate were converted into 1.38 g (97%) colorless crystals **11ac**, m.p. 185–190 °C (methanol). IR (KBr): $\nu = 3365$, 3325, 3200 cm^{-1} (NH), 2820 (OCH_3), 1680 (C=O), 1530 (NH) 1250, 1230 (N–CO). ^{1}H-NMR (*DMSO-d*$_6$): δ (ppm) = 1.43 (d, $J = 6.5$ Hz, CH–CH_3), 3.62 (s, OCH_3), 5.06 (q, $J = 6.5$ Hz, CH–CH_3), 6.4–7.6 (m, 19 arom. H), 7.56–9.19 (several broad signals, HN–N=, NH–CO–NH, 3 H exchangeable with D_2O). $C_{29}H_{29}N_5O_2$ (479.58): calcd. C 72.63, H 6.09, N 14.06; found C 72.55, H 6.26, N 14.59.

4-Methoxymethyl-1-(1-methyl-2-phenyl-2-phenylhydrazonoethyl)-1-phenylthiosemicarbazide (**12ab**)

To a solution of 0.99 g (3 mmol) **2a** in 50 ml ether was added 0.31 g (3 mmol) methoxymethylisothiocyanate; the mixture was refluxed for 10 h, and then left at ambient temperature for 48 h. The separated crystals were filtered off; after evaporation of the filtrate 0.33 g of unchanged **2a** was recovered. The crystalline product was washed with cold ether and dried *in vacuo* to give 0.35 g (40%, with respect to consumed **2a**), **12ab**, m.p. 169–172 °C (methanol). IR (KBr): $\nu = 3320$, 3140 cm^{-1} (NH), 2815 (OCH_3), 1520, 1250 (N–C=S), 1080 (C–O). ^{1}H-NMR (*DMSO-d*$_6$): δ (ppm) = 1.36, 1.40 (2 d, $J = 6.5$ Hz, CH–CH_3, *E*- and *Z*-hydrazone), 2.93, 3.14 (2 s, ratio 1:2.4, OCH_3, *E*- and *Z*-hydrazone), 4.1–5.3 (superimposed and unresolved mm, CH–CH_3, N–CH_2–O), 6.45–7.65 (m, 15 arom. H), 7.66–9.76 (broad signals, NH–N=, NHCSNH, 3 H exchangeable with D_2O).

4-Cyclohexyl-1-(1-methyl-2-phenyl-2-phenylhydrazonoethyl)-1-phenylthiosemicarbazide (**12ac**)

A mixture of 0.73 g (2.21 mmol) **2a** and 5.00 g (35.4 mmol) cyclohexylisothiocyanate was heated to 120 °C for 3.5 h. After cooling to ambient temperature, petroleum ether (boiling range 40–60 °C) was added until the mixture became turbid. Further cooling to 0 °C for 10 h induced crystallization. 0.24 g yellowish crystals were filtered off, and from the mother liquor – upon addition of more petroleum ether – another crop was obtained, in total 0.44 g (45%) **12ac**, m.p. 185–188 °C (methanol). IR (KBr): $\nu = 3320, 3130\,cm^{-1}$ (NH), 1530, 1250 (N–C=S). ^{1}H-NMR (*DMSO-d*$_6$): δ (ppm) = 0.47–2.19 (m, 13 H, $(CH_2)_5$, CH–CH_3), 4.0 (m, **CH**–N), 4.81, 4.92 (2 q, $J = 6.5$ Hz, **CH**–CH_3, *E*- and *Z*-hydrazones), 6.37–7.76 (m, 15 arom. H), 7.76–9.30 (several broad s HN–N=, NHCSNH, 3 H exchangeable with D_2O). $C_{28}H_{33}N_5S$ (471.67): calcd. C 71.30, H 7.05, N 14.85; found C 71.40, H 7.20, N 14.89.

1-Anilino-2,3-dihydro-4-methyl-5-phenyl-1 H-*imidazole-2-thione* (**13a**)

A mixture of 3.30 g (10 mmol) **2a**, 2.50 g (25.7 mmol) potassium thiocyanate, and 20 ml acetic acetic acid was stirred and heated to 90 °C for 10 min. After cooling to ambient temperature the colorless crystals separated were filtered off; from the filtrate upon addition of water another crystalline crop was isolated: The combined fractions were recrystallized from methanol to yield 2.2 g (78%) **13a**, m.p. (dec.) 210–212 °C (methanol). IR (KBr): $\nu = 3250\,cm^{-1}$ (NH), 3060 br, 2905 br, (NH, CH, NH^+), 2705, 2500 (HN^+). ^{1}H-NMR (*DMSO-d*$_6$): δ (ppm) = 2.12 (s, CH_3), 6.3–7.5 (C_6H_5, **HN**–C_6H_5, 1 H exchangeable with D_2O) 12.2 (broad s, HN–C=S, exchangeable with D_2O). MS: *m/z* (%) 281 (68.5) [M^+], 189 (11.4) [$M - C_6H_5NH$], 131 (100) [$M - C_6H_5NHNCS$], 93 (65.7) [$C_6H_5NH_2$], 77 (17.1) [C_6H_5]. $C_{16}H_{15}N_3S$ (281.38): calcd. C 68.30, H 5.37, N 14.93, S 11.40; found C 68.13, H 5.39, N 15.02, S 11.39.

Cyclohexane-1,2-dione Bis (phenylhydrazone) (**3b**)

To a solution of 1.30 g (4.42 mmol) **2b** in 50 ml benzene was added 1.0 g (10.3 mmol) finely ground potassium thiocyanate; the resulting mixture was stirred at ambient temperature for 30 min after addition of 3 ml acetic acid. To the heterogeneous mixture was added 50 ml water. After 48 h of stirring the mixture was filtered, the organic phase was separated and evaporated (20 °C, 15 mm). The oily residue – upon addition of little methanol – turned crystalline and 0.4 g (31%) yellow crystals **3b** were isolated, m.p. 152–153 °C (methanol). This product proved to be identical with an authentic sample [12].

1-Anilino-2,3,4,5,6,7-hexahydro-1 H-*benzimidazole-2-thione* (**13b**)

A stirred mixture of 0.295 g (1 mmol) **2b**, 0.1 g (1 mmol) potassium thiocyanate and 5 ml dimethylformamide was cooled to 0 °C, and under a nitrogen atmosphere a solution of 0.12 g (1 mmol) chlorotrimethylsilane in 2 ml dimethylformamide was added dropwise. The reaction mixture immediately turned yellow, and after 5 min it was transferred into a separating funnel. Upon dilution with 50 ml ether the solution was repeatedly washed with water (3 times 20 ml). The ether phase was dried ($MgSO_4$), and evaporated. The residual oil was dissolved in tetrachloromethane; addition of *n*-hexane precipitated 0.07 g (29%) colorless crystals **13b**, m.p. 204–205 °C (methanol) [6].

1-Phenyl-2-[1-phenyl-2-(4-methylbenzenesulfonyl)hydrazino]-1-propanone Phenylhydrazone (**14a**)

To a stirred solution of 3.30 g (10 mmol) **2a** at – 20 °C were added 1.90 g (10 mmol) 4-methyl-benzenesulfonylchloride. The reaction mixture was allowed to warm up to 0 °C, and after dilution with 200 ml chloroform it was extracted with 18% hydrochloric acid (3 times 100 ml). The organic layer was washed with H_2O, dried ($MgSO_4$) and evaporated. The residual foam crystallized upon addition of 15 ml methanol yielding 2.30 g (48%) beige crystals **14a** (pure by tlc), m.p. (dec.) 131–133 °C

(methanol/water). To obtain an analytical sample, **14a** was dissolved in methanol (< 50 °C); water was added to the warm methanolic solution until it became turbid; recrystallization at higher temperature or prolonged heating furnished 1-(4-methyl-benzenesulfonyl)-2-phenylhydrazine, m.p. 150–153 °C (Ref. [13] 154 °C), identical (by ^{1}H-NMR) with an authentic sample. The analytical sample of colorless **14a** (after 18 h drying at 60 °C, 0.02 mbar) still contained 0.2 mol of methanol: IR (KBr): $\nu = 3320$, 3230 cm^{-1} (NH), 1340, 1260 (SO_2). ^{1}H-NMR (*DMSO-d_6*): δ (ppm) = 1.33 (d, $J = 6.5$ Hz, CH–CH_3), 2.20 (s, CH_3–C_6H_4), 3.38 (CH_3OH, solvent), 4.68 (q, $J = 6.5$ Hz, CH–CH_3), 6.37–7.51 (m, 19 arom. H), 8.22 (s, HN–N=, exchangeable with D_2O), 9.28 (s, NH–SO_2, exchangeable with D_2O). $C_{28}H_{28}N_4O_2S$ (400.53) with 0.2 CH_4O: calcd. C 69.98, H 5.91, N 11.41, S 6.53; found C 68.70, H 5.96, N 11.39, S 6.54.

1-Phenyl-2-(1-phenyl-2-sulfinylhydrazino)-1-propanone Phenylhydrazone (**15a**)

To a vigorously stirred mixture of 3.30 g (10 mmol) **2a**, 1.58 g (20 mmol) pyridine and 10 ml benzene was slowly added a solution of 1.19 g (10 mmol) thionylchloride in 3 ml benzene at a temperature below 10 °C. The resultant viscous reaction mixture was diluted with benzene to permit stirring for another 1 h. The precipitated crystals were filtered off and washed with 5 ml ethanol and twice with 5 ml water. The filtrate was evaporated, and the brownish crystals were treated in the same way. Both fractions were dried *in vacuo* giving 2.36 g (62%) of yellow crystals **15a**, m.p. 137–140 °C (acetone). IR (KBr): $\nu = 3290$ cm^{-1} (NH), 1245, 1100 (N=S=O). ^{1}H-NMR (*DMSO-d_6*): δ (ppm) = 1.66 (d, $J = 6.5$ Hz, CH–CH_3), 5.59 (q, $J = 6.5$ Hz, CH–CH_3), 6.36–7.70 (m, 3 C_6H_5), 8.73 (s, NH, exchangeable with D_2O). $C_{21}H_{20}N_4OS$ (376.48): calcd. C 66.99, H 5.35, N 14.88; found C 66.49, H 5.44, N 14.87.

2-(1-Phenyl-2-sulfinylhydrazino)-1-cyclohexanone Phenylhydrazone (**15b**)

As described in the preceding experiment, the solutions of 1.30 g (4.41 mmol) **2b**, 0.60 g (8.86 mmol) pyridine in 6 ml toluene and 0.52 g (4.41 mmol) thionylchloride in 3 ml toluene were combined to give 0.30 g (20%) **15b**, m.p. 133–134 °C (acetone). IR (KBr): $\nu = 3280$ cm^{-1} (NH), 1599 (C=N), 1245, 1096 (N=S=O). ^{1}H-NMR ($CDCl_3$): δ (ppm) = 1.35–2.30 (mm, 3CH_2, CH), 2.70 (broad d, $J = 15.6$ Hz, CH), 4.92 (m, CH–N), 6.6–7.3 (mm, 2 C_6H_5, NH). ^{13}C-NMR ($CDCl_3$): δ (ppm) = 23.29, 23.69, 24.25, 31.38 (4 CH_2), 68.14 (CH–N), 112.91, 119.83, 121.57, 126.03, 128.65, 129.14, (10 arom. CH), 142.24, 145.55, 146.05 (2 arom. C_{quart}, C=N).

1-Acetoxy-1-phenyl-1-phenylazo-2-(1-phenyl-2-sulfinylhydrazino)-propane (**16a**)

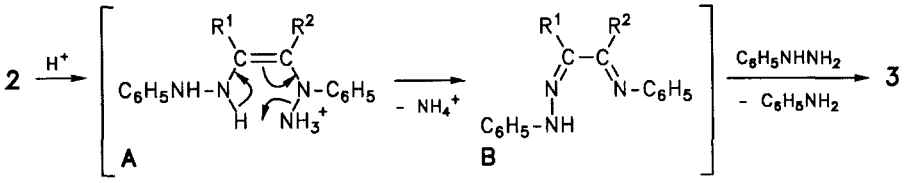
To a stirred solution of 0.376 g (1 mmol) **15a** in 20 ml dichloromethane was added dropwise at − 20 °C a solution of 1.0 g lead tetraacetate in 10 ml dichloromethane (ca. 1.89 mmol). After 2 h the mixture had warmed up to ambient temperature, and 0.1 ml ethyleneglycol was added. Subsequently, the dichloromethane solution was repeatedly washed with water, dried ($MgSO_4$) and evaporated. The residual viscous red oil was dissolved in ether and chromatographed on silica (deactivated with 10% water) with ether: The first 50 ml of colored eluate fractions were collected and evaporated. The resultant 0.26 g orange foam was treated with 30 ml pentane to induce crystallization yielding 0.14 g (32%) yellow crystals **16a**, m.p. 128–130 °C (ethanol). The product **16a** appeared to be pure by tlc, but the ^{1}H-NMR revealed a 9:1 mixture of diastereomeric racemates. IR (KBr): $\nu = 1750$ cm^{-1} (C=O), 1215, 1100 (N=S=O). ^{1}H-NMR (CCl_4): δ (ppm) = 1.36 (2.7 H, d, $J = 6.5$ Hz, CH–CH_3), 1.47 (0.3 H, d, CH–CH_3), 1.92 (0.3 H, s, CO–CH_3), 2.01 (2.7 H, s, $COCH_3$), 4.65 (3 H, m, CH–CH_3), 6.68–7.84 (15 H, mm, 3 C_6H_5). $C_{23}H_{22}N_4O_3S$ (434.52): calcd. C 63.58, H 5.10, N 12.89; found C 62.93, H 5.29, N 12.78.

Acknowledgement

Compounds **8b** and **15b** have been prepared by S. Masselter and M. Wilfinger.

References and Notes

[1] Part IV: Schantl J. G., Karpellus P., Prean M. (1987) Tetrahedron **43**: 5807–5814
[2] Schantl J. G., Karpellus P., Prean M. (1982) Tetrahedron **38**: 2643–2652
[3] Several mechanisms [4] have been forwarded to explain the formation of phenylosazones **3** in the course of the reaction of carbonyl compounds with an electronegative substituent in α-position with phenylhydrazine, but none has considered α-(1-phenylhydrazino)alkanone phenylhydrazones **2** as the precursors of phenylosazones **3**. The conversion of **2** into **3** is envisaged to be initialized by the acid catalysed isomerization of **2** giving rise to the protonated en-dihydrazine tautomer **A**, followed by 1,4-elimination of ammonium ion to form the anil-hydrazone derivative **B** which eventually reacts with phenylhydrazine by undergoing an anil-phenylhydrazone exchange to yield the phenylosazone **3**. Work is in progress to further investigate the mechanism of osazone formation from α-(1-phenylhydrazino)alkanone phenylhydrazones **2**



Scheme 8

[4] Simon H., Heubach G., Wacker H. (1967) Chem. Ber. **100**: 3106–3120. Simon H., Moldenhauer W. (1969) Chem. Ber. **102**: 1191–1197. Ref. cited therein
[5] Schantl J. G., Hebeisen P. (1983) Sci. Pharm. **51**: 379–390
[6] Chemical and spectroscopic structure proofs of compounds **13** together with a mechanism of the formation will be reported in a separate paper
[7] Prean M. (1981) Doctoral Thesis. University of Innsbruck
[8] Schantl J. G., Hebeisen P., Karpellus P. (1989) Synth. Commun. **19**: 39–48
[9] Iffland D. C., Salisbury L., Schafer W. R. (1961) J. Am. Chem. Soc. **83**: 747–749
[10] Thesing J., Willersinn C. H. (1956) Chem. Ber. **89**: 1195–1203
[11] Young G. W., Roberts J. D. (1946) J. Am. Chem. Soc. **68**: 649–652
[12] Bloink G. J., Pausacker K. H. (1950) J. Chem. Soc. 1328–1331
[13] Dutt P. K., Whitehead H. R., Wormall A. (1921) J. Chem. Soc. **119**: 2098–2094

Received April 24, 1992. Accepted May 15, 1992