Tetrahedron Vol. 38, No. 17, pp. 2643 to 2652, 1982
Printed in Great Britain.

0040-4020/82/172643-10$03.00/0
Pergamon Press Ltd.

ADDITION PRODUCTS OF HYDRAZINE DERIVATIVES TO AZO-ALKENES - III.[1] α-PHENYLHYDRAZINO-PHENYLHYDRAZONES[+]

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(*Received in Germany* 13 *April* 1982)

Abstract – The addition of phenylhydrazine to phenylazo-alkenes 4 yields α-(1-phenylhydrazino)-phenylhydrazones 1. The reaction of phenylhydrazine with α-halogenated carbonyl compounds 5 affords either 1 or the isomeric α-(2-phenylhydrazino)-phenylhydrazones 2. Structures 1 and 2 (>N-NH_2 and -NH-NH- groups, respectively) can be differentiated by ^{1}H NMR in DMSO-D_6 solution. Possible pathways of the reactions leading to either 1 or 2 are discussed. Compounds 1 are found to be precursors of phenylosazones 6.

In previous reports on α-phenylhydrazino-phenylhydrazones the structure of α-(2-phenylhydrazino)-phenylhydrazones 2 has been assumed rather arbitrarily. Thus, the products from the reaction of phenylhydrazine with α-negatively substituted carbonyl compounds 5 (X=Cl, Br, CH_3COO);[2-9] with negatively substituted oxiranes;[6,10] and with the phenylazo-alkene 4g[5] have been assigned structure 2. Also the addition of Grignard reagents to the aldehydic phenylhydrazone moiety of the 1,2-bis-phenylhydrazone 6[1] has been reported to yield compounds of structure 2.[11] Furthermore, compounds 2 have been postulated to be the precursors of phenylosazones 6.[5-8,12]

On the other hand, the isomeric structure of α-(1-phenylhydrazino)-phenylhydrazones 1 represents a novel type of compounds.

RESULTS

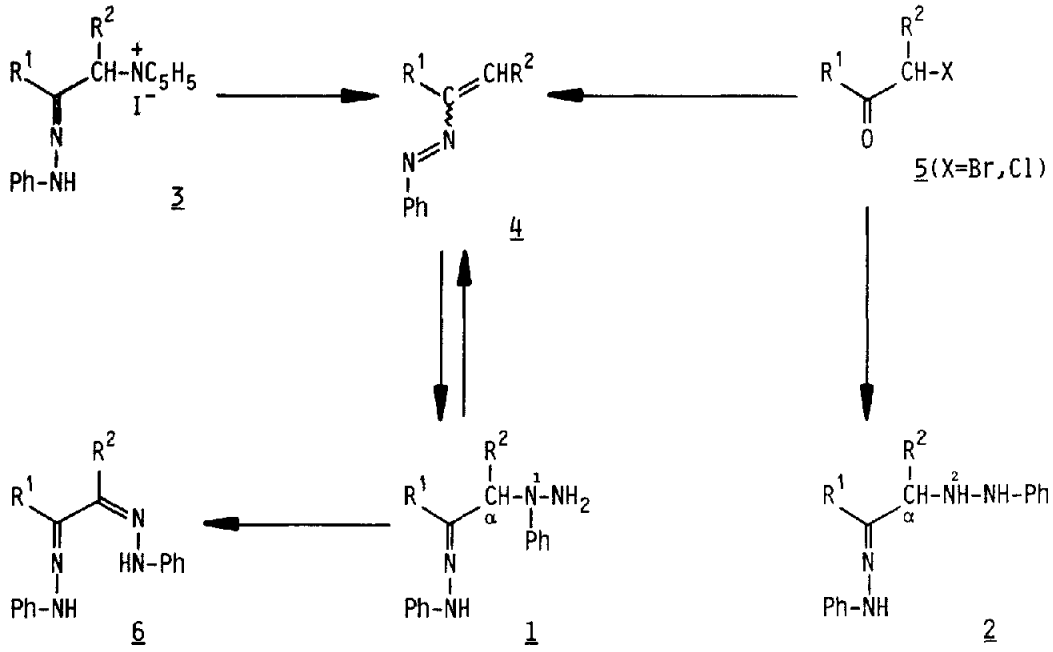
Syntheses. The conversion of phenylhydrazones into 1-(2-phenylhydrazono-alkyl)-pyridinium iodides 3 and the subsequent base induced elimination of pyridine.HI provides a convenient method for the preparation of phenylazo-alkenes 4.[13] The heterodienic system of phenylazo-alkenes 4 adds nucleophiles in a 1,4-manner affording α-substituted phenylhydrazones.[1,5,14] Phenylhydrazine reacted accordingly and α-(1-phenylhydrazino)-phenylhydrazones 1 were obtained (Scheme 1, Table 1).

These products 1 have to be handled with care: Catalytic amounts of acids or elevated temperatures (in solution already below m.p. temperature) readily reconverted compounds 1 into their components 4 and phenylhydrazine. An excess of phenylhydrazine may lead to phenylosazones 6 (see below). Therefore, the preparation of compounds 1 required equimolar portions of phenylhydrazine and phenylazo-alkene 4 to be mixed at low temperature (at or below -20°C). The addition reaction was then started by allowing the mixture to warm up slowly. For the purification of compounds 1 a reprecipitation procedure rather than recrystallization was preferred.

Two exceptions of this reaction were noted: The synthesis of 1c by the addition of phenylhydrazine to 4c failed: At low temperature no reaction occurred, and raising the temperature caused the formation of several unidentified products (tlc). Similarly, starting from 4l the expected addition product 1l was not found,

[+] A preliminary report was presented at the 1st European Symposium on Organic Chemistry (ESOC I), Cologne, Germany, August 1979.

Scheme 1.



R^1, R^2 see Table 1.
Reaction conditions see text.

and the phenylosazone 6l was isolated instead; this may conform with the assumption of a reactive intermediate 11 (see below).

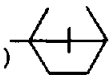
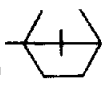
α-Phenylhydrazino-phenylhydrazones were also formed in the reaction of α-halogenated carbonyl compounds 5 with three molar equivalents phenylhydrazine (Scheme 1, Table 1): 5a, 5b, 5d, 5e, 5f, 5g, 5j and 5k(X as given in Table 1) were converted to the respective α-(1-phenylhydrazino)-phenylhydrazones 1; these products 1 (except 1j and 1k which were synthesized only following this latter route) were identical with the addition products 1 obtained as described above.

Very remarkably, in a few instances this reaction proceeded in a different way: When phenylhydrazine reacted with compounds 5c, 5h and 5l only the isomeric α-(2-phenylhydrazino)-phenylhydrazones 2c, 2h and 2l were isolated (Table 1). – When 5i(X=Br or Cl) was reacted, neither 1i nor 2i were obtained: At -50°C no reaction occurred (tlc), and at -10°C merely the known cyclodimerization of the intermediate 4i took place.[15]

Structures. As it has been demonstrated for model compounds ^{1}H NMR properly differentiates 1,1- (as) and 1,2- (sym) substituted phenylhydrazine derivatives in dimethylsulphoxide-D_6 (DMSO-D_6) solutions.[16] Accordingly, the as-substituted hydrazine structure 1 was revealed by one signal (range of δ 3.8 - 4.3) observed for the two protons of the NH_2-group. (There is also chemical evidence for the NH_2-group of 1.[17]) On the other hand, the two nonequivalent protons of the hydrazo moiety (-NH-NH-) of the isomeric structure 2 give rise to two clearly separated resonances (range of δ: 4.5 - 5.1 and 6.5 - 7.2). This assignment receives further support by the vicinal coupling between the 2-NH (high field NH-signal) and the adjacent α-methine proton, as shown by the simplification of the methine resonance pattern after D-exchange of the NH-groups. Occasionally, the coupling between both NH-protons can also be observed. Since the NH-signal of the phenylhydrazone group appears farther downfield (δ 8.3 - 9.6), it does not interfere with the NH-signal(s) of the phenylhydrazino moiety (Table 2).

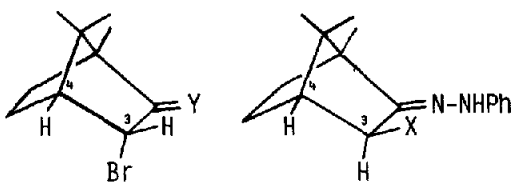
The camphor system h allows to follow configurational changes at C-3 by evaluation of the coupling of H-3 and H-4 (Figure 1).

Table 1. α-(Phenylhydrazino)-phenylhydrazones 1 and 2 from 4 and/or 5.

Compound	R^1	R^2	Isolated yield (%) from 4	from 5(X=)	M.p. (°C)	solvent of recrystalln	Found (%) C	H	N	(Required) Molecular formula	weight
1a	H	H	55	62 (Cl)	102-107	benzene	69.71 (69.97	6.79 6.71	23.60 23.31)	$C_{14}H_{16}N_4$	240.3
1b	H	Me	60	62 (Cl)	73- 75	EtOH (40°C); Et_2O/hexane	71.07 (70.84	7.27 7.13	22.08 22.03)	$C_{15}H_{18}N_4$	254.3
1c	H	Ph	0	0 (Cl)	---						
1d	Me	H	30	17 (Cl)	88- 93	Et_2O	70.55 (70.84	7.25 7.13	22.27 22.03)	$C_{15}H_{18}N_4$	254.3
1e	Me	Me	45	24 (Cl)	95- 98	MeOH	71.79 (71.61	7.99 7.51	20.98 20.88)	$C_{16}H_{20}N_4$	268.4
1f	Me	Ph	49	53 (Cl)	92- 95	Et_2O/hexane	76.69 (76.33	6.85 6.71	17.33 16.96)	$C_{21}H_{22}N_4$	330.4
1g	$(CH_2)_4$		61	47 (Cl)	124-134	MeOH				$C_{18}H_{22}N_4$	294.4
1h(1R)			17	0 (Br)	foam						
1h(rac.)			62	0 (Br)	126-129	EtOH	75.96 (75.82	8.10 8.10	16.11 16.08)	$C_{22}H_{28}N_4$	348.5
1i	Ph	H	-	0 (Br,Cl)	---						
1j	Ph	Me	-	67 (Br)	132-133	MeOH	76.39 (76.33	6.78 6.71	17.17 16.96)	$C_{21}H_{22}N_4$	330.4
1k	Ph	Et	-	44 (Br)	98-100	EtOH	76.29 (76.71	7.03 7.02	16.16 16.27)	$C_{22}H_{24}N_4$	344.5
1l	Ph	Ph	0	0 (Cl)	---						
2c	H	Ph	0	23 (Br)	100-106	pentane	76.23 (75.92	6.66 6.37	17.60 17.71)	$C_{20}H_{20}N_4$	316.4
2h(1R)			0	50 (Br)	128-132	MeOH	76.05 (75.82	8.37 8.10	16.14 16.08)	$C_{22}H_{28}N_4$	348.5
2h(rac.)			0	51 (Br)	125-127	MeOH; hexane					
2l	Ph	Ph	0	84 (Cl)	121-126	MeOH	79.30 (79.56	6.29 6.16	14.30 14.27)	$C_{26}H_{24}N_4$	392.5

Thus the ^{1}H NMR spectra indicate an inversion at C-3 when (1R)- or (rac.)-3endo-bromocamphor 5h(X=Br) or the 2,2-bis-(2-phenylhydrazino) derivatives 8h are converted to the (1R)-/(rac.)-3exo-(2-phenylhydrazino)-camphor phenylhydrazone 2h suggesting a nucleophilic substitution at C-3 of the precursor. In the same way, the thermodynamically favored 3exo-configuration was established for the addition product 1h.

Figure 1.



3endo-Br 3exo-X

$J_{3,4} \sim 4.5$ Hz $J_{3,4} < 1$ Hz

5h: Y = O 1h: X = N(Ph)-NH_2

8h: Y = $(NH\text{-}NH\text{-}Ph)_2$ 2h: X = NH-NH-Ph

Similarly, the equatorial orientation of the 2-(1-phenylhydrazino) group of 1g was confirmed by the vicinal coupling constants of H-2, indicative of an axial proton (Figure 2). Also the configuration of the phenylhydrazone group is evident from the ^{1}H NMR spectrum: The signal at δ = 3.09 is distinctly shifted downfield from the other cycloaliphatic protons (H-3 to H-5 including H-6_{ax}) and has been assigned to H-6_{eq} as being syn to the phenylhydrazone group (Figure 2), in agreement with studies on 6-ring hydrazones.[18] Further support is obtained from the coupling pattern: Besides the observed geminal coupling the width of the multiplets at

Table 2. ^{1}H NMR[a] of 1 and 2.

Compound	R^1	R^2	R^2-CH-N< (α)	C-N-NH$_2$ (α, Ph[b])	=N-NH-Ph[b]
1a	[b]	→	4.14 (d 5.5)	4.28	9.69
1b	[b]	1.32 (d 6.4)	4.58 (d 4, q 6.4)	3.89	9.56
1d	1.83 (s)	→	4.10 (s)	4.25	8.63
1e	1.83 (s)	1.30 (d 6.5)	4.51 (q 6.5)	3.83	8.59
1f	1.86 (s)	[b]	5.63 (s)	4.06	8.76
1g	1.0-2.2 (m), 3.09[c]		4.43[c]	4.07	8.74
1h(1R) 1h(rac.)	0.7-2.1 (s,s,s,m)		3.96 (s)[d]	4.58	9.26
1j	[b]	1.37 (d 6)	4.95 (q 6)	3.78	8.28
1k	[b]	0.93 (t 7) 1.97 (dq 7, 7)	4.65 (t 7)	3.83	8.24

Compound	C-NH- (α)	-NH-Ph[b]	=N-NH-Ph[b]
2c	4.60 (dd 6, 4.5)	[b]	9.68
2h(1R) 2h(rac.)	3.49 (d 4.5)[d]	4.55 (dd 4.5, 2)	7.2 (d 2) 9.59
2l	4.78 (A 7.6)	5.07 (B 7.6)	[b] 8.49

[a] In DMSO-D_6, δ = ppm from TMS, (coupling pattern, J in Hz)

[b] Aromatic proton region 6.3 - 7.4 ± 0.1 ppm

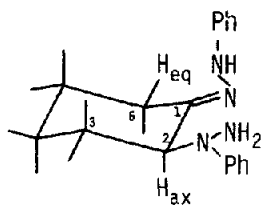
[c] See Figure 2 and text

[d] See Figure 1 and text

half heigt (W_H)[19] is characteristic of an equatorial proton.

Figure 2.

1g



$H\text{-}2_{ax}$: δ = 4.43,
dd $J_{2ax,3a}$ = 9 Hz, $J_{2ax,3eq}$ = 5 Hz

$H\text{-}6_{eq}$: δ = 3.09,
dm $J_{6ax,6eq}$ = 15 Hz, $W_H \sim 8$ Hz.

DISCUSSION

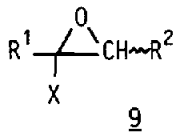
These findings necessitate to comment on some literature reports of α-phenylhydrazino-phenylhydrazones:

The product obtained from 2-chloroacetaldehyde 5a(X=Cl) and phenylhydrazine has been assigned structure 2a by Freer[3] and later by Simon et al.[7] However, the ^{1}H NMR spectrum in DMSO-D_6 as well as the ability to form hydrazones with carbonyl compounds[17] evidently prove structure 1a. – The product from the reaction of chloroacetone 5d(X=Cl) and phenylhydrazine, first obtained by Bender[20] and later claimed by Bodforss[4] to be 2d, has been shown to be the addition product of methylglyoxal bisphenylhydrazone 6d to 4d.[1a] – The product of the reaction of phenylhydrazine with phenylazo-cyclohexene 4g[5] or with 2-chlorocyclohexanone 5g(X=Cl)[8] has been assigned structure 2g, but by the same spectroscopic arguments structure 1g is the correct one.[21]

It has been reported by Giumanini et al.[9] that 3-bromocamphor (no configuration given) reacted with phenylhydrazine to afford 2h at 100°C (and 6h at 150°C). When this reaction was repeated with (1R)-3endo-bromocamphor 5h (X=Br) using three molar equivalents of phenylhydrazine (without solvent at 100°C), a mixture of (1R)-3exo-(2-phenylhydrazino)-camphor-phenylhydrazone 2h, (1R)-3endo-bromo-2,2-bis-(2-phenylhydrazino)-bornane 8h(X=Br), phenyl-

hydrazine.HBr and starting material 5h(X=Br) was obtained. The reaction of (rac)-5h(X=Br) gave a similar result. The ^{1}H NMR spectra of (1R)- and (rac)-2h are identical but differ from the data given for 2h in the lit.[9]

The reaction of 3-methyl-2-methoxy-2-phenyl-oxirane 9j(X=OCH_3) with phenylhydrazine in EtOH



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and a trace of AcOH has been reported by Temnikowa and Kropachewa[10] to give 2j. Referring to this, Bloink and Pausacker[23] have denied the formation of any α-phenylhydrazino-phenylhydrazone. When this reaction was repeated under the conditions originally reported, an α-phenylhydrazino-phenylhydrazone was obtained indeed: The product was not 2j but the isomer 1j, as was proved by comparison with the product 1j obtained from 5j(X=Br).

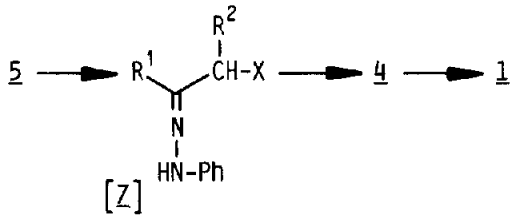
The addition of the Grignard reagents EtMgBr and PhMgBr to the aldehydic carbon of the phenylosazone 6i, as reported by Grammaticakis[11] should provide an unambiguous access to 2k and 2l, respectively, but our attempts to reproduce this procedure failed.

Diverging results have been recorded about the products obtained from 2-chloro-1,2-diphenyl-ethan-2-one (desylchloride) 5l(X=Cl) and phenylhydrazine: Bodforss[12a] has reported the formation of benzil bisphenylhydrazone 6l (EtOH, room temp, 3 d), whereas Brodka and Simon[24] have isolated phenylazo-stilbene 4l (THF, 48 hr at room temp followed by refluxing for 5 hr). [Notably, we obtained the osazone 6l when 4l was reacted with phenylhydrazine (MeOH, N_2, 25°C, 6 d)]. But surprisingly, in our hands 5l(X=Cl) and phenylhydrazine afforded 2l in high yield (refluxing MeOH, N_2, 3 hr).[22]

Mechanism. The reaction of phenylhydrazine with phenylazo-alkenes 4 afforded α-(1-phenylhydrazino)-phenylhydrazones 1 and evidently, the N-1 of phenylhydrazine acts as the nucleophilic site in this 1,4-addition reaction.

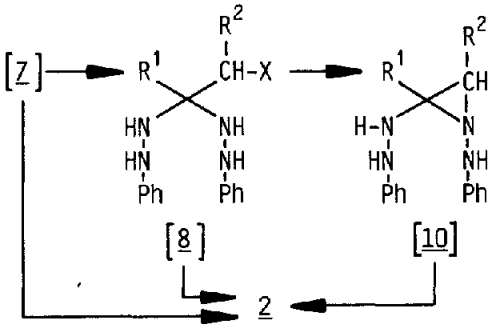
Most likely, the same addition occurs as the last step of the reaction of α-halogenated carbonyl compounds 5 with phenylhydrazine (three molar equivalents required) to yield compounds 1. In fact, phenylazo-alkenes 4 were detected (by tlc) or isolated, and obviously, 4 derives from the probable primary reaction intermediate 7 by HX elimination (Scheme 2).

Scheme 2.



Conversely, no intermediate phenylazo-alkene 4 appears to be involved as precursor of α-(phenylhydrazino)-phenylhydrazones 2. Conceivable intermediates of this reaction 5 → 2 are 7 and 8. A nucleophilic displacement of the α-X by phenylhydrazine (or intramolecularly by the phenylhydrazino group of 8 via 10) may possibly account for the formation of 2, the N-2 of phenylhydrazine (or the N-2 of the phenylhydrazino group of 8) acting as the nucleophilic site in this case (Scheme 3).

Scheme 3.



The few examples investigated do not allow to draw conclusions as to the structural prerequisites of 5 to direct the reaction with phenylhydrazine to either 1 or 2. But evidently, phenylhydrazine shows an ambident nucleophilic reactivity.

Simple HMO calculations[25] show close energy levels for the LUMO of phenylazo-ethene 4a and the HOMO of phenylhydrazine. Thus, an orbital controlled addition reaction (soft-soft interaction) at the centers with largest coefficient, i.e. at the terminal olefinic carbon atom of 4a and at N-1 of phenylhydrazine appears to be favored and explains the forma-

tion of compounds 1.

By contrast, the presumed displacement reaction in the course of the conversion 5 → 2 can be visualized as a charge controlled (hard-hard) reaction: A σ^*_{C-X} orbital of the conceived intermediate electrophile (7 or 8, X=Br,Cl) is estimated to be higher in energy (as compared with the LUMO of 4a), thereby rendering it a harder electrophile to interact with the HOMO of phenylhydrazine (or the phenylhydrazino moiety of 8 to give 10, respectively). The greater charge at N-2 determines this atom as the nucleophilic site in the substitution reaction.

Osazone precursors. 1,2-Bisphenylhydrazones 6 (phenylosazones) and besides aniline and ammonia are formed when α-negatively substituted carbonyl compounds 5 (X = halide, O-, N<) react with an excess of phenylhydrazine at ambient or elevated temperatures and commonly under acid catalysis.[26] This parallels the classical Fischer osazone reaction originally discovered with monosaccharides.[27]

Several pathways have been discussed to explain the formation of phenylosazones 6 from α-negatively substituted carbonyl compounds 5.[28] In some cases there is convincing evidence that phenylazo-alkenes 4 are true intermediates in this reaction.[5,6,12f,14a,29,30] It has been postulated, that in a subsequent step α-(2-phenylhydrazino)-phenylhydrazones 2 are formed as the precursors of phenylosazones 6, cf lit.[5-8,12]

However, it seems reasonable to accept 1 rather than 2 as the precursors of phenylosazones 6 (in the course of the reaction sequence 5 → 4 → 1 → 6), since we have shown that the addition of phenylhydrazine to phenylazo-alkenes 4 affords α-(1-phenylhydrazino)-phenylhydrazones 1.

EXPERIMENTAL

Dried and distilled solvents were used, petroleum ether (PE) refers to the fraction of b.p. 40-60°C. The reactions with phenylhydrazine were run under N_2. Column chromatography was performed on SiO_2 (70-230 mesh; Merck) which was deactivated by addition of 10% (w/w) H_2O. Analytical thin layer chromatography (tlc) was carried out on SiO_2 precoated sheets (0.25 mm thick; Sil G/UV_{254}, Machery & Nagel). M.ps were determined on a Kofler hot stage microscope (Reichert) and are uncorrected. ^1H NMR spectra were recorded at 60 MHz with either a JEOL C-60-HL (26°C) or PMX 60 (40°C) instrument.

Starting compounds: α-Halogeno carbonyl compounds 5 were either purchased or prepared according to literature procedures. - Phenylazo-alkenes 4 except those described below were prepared from the corresponding 1-(2-phenylhydrazino-alkyl)-pyridinium iodides 3 as reported.[13]

1-Phenyl-2-phenylazo-propene 4f: A soln of I_2 (2.26 g, 8.9 mmole) in pyridine (10 ml) was added dropwise to a soln of freshly prepared and recrystallized (EtOH) 1-phenyl-2-propanone phenylhydrazone (2 g, 8.9 mmole) in pyridine (5 ml) at such a rate that the mixture was discolored before the next drop was added. After 2 days standing at room temp the reaction mixture was alkalized with 2 N NaOH and extracted several times with Et_2O. The organic phase was successively washed with 2 N HCl, $NaHCO_3$ aq and H_2O, dried over $MgSO_4$ and evaporated in vacuo. The residual red oil consisted of a mixture of E,E- and E,Z-4f (1.34 g, 68%), but was free of the isomeric E-3-phenyl-2-phenylazo-1-propene as shown by ^1H NMR and tlc.[13c]

(rac)-2-Phenylazo-bornene 4h:

(a) (rac)-Camphor-phenylhydrazone: A soln of phenylhydrazine (21.6 g, 0.2 mole) in EtOH (10 ml) was added dropwise to a soln of (rac)-camphor (30.4 g, 0.2 mole) in EtOH (50 ml). After addition of AcOH (1 ml) the mixture was refluxed for 3 hr and then freed of most of the solvent by evaporation. Cooling in an icebath afforded colorless crystals of (rac)-camphor-phenylhydrazone (28.2 g, 58%), m.p. 63°C. ^1H NMR (CCl_4): 0.5-2.5 (16 H, m, 3 CH_3, 3 CH_2, and CH); 6.35 (1 H, s, NH); 6.4-7.3 (5 H, m, C_6H_5).

(b) (rac)-Camphor-2-phenylhydrazono-3-pyridinium iodide 3h: A soln of I_2 (10.17 g, 40 mmole) in pyridine (50 ml) was added dropwise (very slowly) to a boiling soln of (rac)-camphor-phenylhydrazone (9.7 g, 40 mmole) in pyridine (20 ml). After refluxing for 5 hr the mixture was diluted with H_2O (70 ml) and extracted several times with PE (to remove unreacted phenylhydrazone and a little (rac)-2-phenylazo-bornene 4h) until further addition of PE induced crystallization. Cooling to 0°C and filtration of the crystals afforded 3h (7.9 g,

44%), m.p. 194-6°C (from MeOH). (Found: C 56.47; H 5.81; N 9.46; $C_{21}H_{26}IN_3$ requires: C 56.38; H 5.86; N 9.40%). ^{1}H NMR (DMSO-D_6): 0.3-2.4 (13 H, m, 3 CH_3, 3 CH_2); 2.62-2.85 (1 H, m, H-4); 6.07 (1 H, d, J=5 Hz, H-3); 6.5-7.3 (5 H, m, C_6H_5), 7.7-9.5 (6 H, m, $^+NC_5H_5$ and NH).

(c) (rac)-2-Phenylazo-bornene 4h: A soln of 3h (2.32 g, 5.2 mmole) in DMSO (15 ml) in a separatory funnel was thoroughly mixed with H_2O (25 ml), PE (75 ml) and 2 N NaOH (10 ml). The organic layer was separated and the aqueous layer was further extracted twice with PE (50 ml). The combined orange-red PE extracts were washed three times with H_2O (25 ml) and then dried over $MgSO_4$. The solvent was removed and the residue chromatographed: The first fractions afforded a red oil 4h (150 mg, 12%). ^{1}H NMR (CCl_4): 0.82, 0.92, 1.32 (9 H, 3 s, 3 CH_3); 1.0-2.2 (4 H, m, CH_2-CH_2); 2.5 (1 H, m, H-4); 6.57 (1H, d, J=3 Hz, H-3); 7.15-7.85 (5 H, m, C_6H_5).

(1R)-2-Phenylazo-bornene 4h was obtained accordingly.

α-(1-Phenylhydrazino)-phenylhydrazones 1:

2-(1-Phenylhydrazino)-1-ethanone phenylhydrazone 1a.

(a) From phenylazo-ethene 4a:[31] Phenylhydrazine (230 mg, 2.1 mmole) was added to a soln of 4a (280 mg, 2.1 mmole) in MeOH (10 ml) at -40°C. The temp of the orange mixture was allowed to warm up to room temp during 12 hr. Subsequent cooling to -40°C completed precipitation of 1a (280 mg).

(b) From 2-chloroacetaldehyde 5a(X=Cl): The product obtained from 5a(X=Cl) and phenylhydrazine following the literature procedure[7] [erroneously quoted as 2a, m.p. 96°C and 110°C (Et_2O)] was identical by m.p., IR, NMR and tlc with the product 1a obtained by the foregoing procedure.

2-(1-Phenylhydrazino)-1-propanone phenylhydrazone 1b:

(a) From 1-phenylazo-1-propene 4b:[31] A soln of 4b (260 mg, 1.8 mmole) in MeOH (3 ml) at -20°C was combined with a soln of phenylhydrazine (192 mg, 1.8 mmole) in MeOH (2 ml). The temp was allowed to rise to room temp during 20 hr. After evaporation of the solvent the remaining orange oil was dissolved in a few ml Et_2O and crystallization was induced by dropwise addn of hexane to afford 1b (270 mg).

(b) From 2-chloropropanal 5b(X=Cl): A soln of 5b(X=Cl) (5.55 g, 60 mmole) in MeOH (20 ml) at -20°C was slowly combined with a soln of phenylhydrazine (19.46 g, 180 mmole) in MeOH (35 ml). The temp was kept for 13 hr, and after the precipitated phenylhydrazine.HCl was filtered off the filtrate was diluted with benzene (200 ml), washed with H_2O, dried over $MgSO_4$. The yellow oil left after evaporation of the solvent was dissolved in a few ml Et_2O and brought to crystallization upon addn of hexane to give 1b (9.42 g), identical (m.p., IR, NMR, tlc) with the product from the preparation described above.

1-(1-Phenylhydrazino)-2-propanone phenylhydrazone 1d.

(a) From 2-phenylazo-1-propene 4d:[13a] To a soln of 4d (890 mg, 6.1 mmole) at -20°C in MeOH (5 ml) a soln of phenylhydrazine (658 mg, 6.1 mmole) in MeOH (5 ml) was added dropwise. The mixture was allowed to warm up to 20°C during 8 hr and kept at this temp for 12 hr. After evaporation of the solvent the residual oil was triturated with pentane (30 ml) and then treated with MeOH (3 ml) at -20°C to yield colorless crystals 1d (460 mg).

(b) From chloroacetone 5d(X=Cl): A soln of phenylhydrazine (13.5 g, 125 mmole) in MeOH (15 ml) was combined dropwise at -60°C with a stirred soln of 5d(X=Cl) (3.85 g, 41.6 mmole) in MeOH (25 ml). The mixture was kept at -50°C for 7 hr and then diluted with benzene (300 ml) to precipitate phenylhydrazine.HCl. The salt was filtered off, the filtrate washed three times with 0.2 N HCl and subsequently with H_2O and dried over $MgSO_4$. After evaporation of the solvent the oily residue was chromatographed and crystallized from pentane to give 1d (1.82 g).

3-(1-Phenylhydrazino)-2-butanone phenylhydrazone 1e.

(a) From 2-phenylazo-2-butene 4e:[13b] To a soln of 4e (40 mg, 0.25 mmole) in MeOH (1.5 ml) at -60°C phenylhydrazine (27 mg, 0.25 mmole) was added. The temp was allowed to rise to 20°C during 15 hr. After evaporation of the solvent the residue crystallized from pentane to give 1e (30 mg).

(b) From 3-chloro-2-butanone 5e(X=Cl): A soln of phenylhydrazine (7.83 g, 72.4 mmole) in MeOH was added slowly to a soln of 5e(X=Cl) (2.57 g, 24.1 mmole) at -20°C and the mixture was kept at this temp for 15 hr. The precipitated phenylhydrazine.HCl was filtered off and the filtrate

was reduced to about 15 ml by evaporation and then diluted with benzene (200 ml). This soln was washed several times with 0.1 N HCl and with H_2O, dried over $MgSO_4$ and evaporated. The oily residue was crystallized with pentane to give 1e (1.57 g).

1-Phenyl-1-(1-phenylhydrazino)-2-propanone phenylhydrazone 1f.

(a) From E,E- and E,Z-1-phenyl-2-phenylazopropene 4f: The cooled (0°C) solns of 4f (400 mg, 1.8 mmole) in MeOH (5 ml) and phenylhydrazine (194 mg, 1.8 mmole) in MeOH (3 ml) were combined and kept at room temp for 24 hr. After evaporation of the solvent the residual oil was chromatographed. The fractions of R_f = 0.4 (PE/Et_2O 1:1) were evaporated and reprecipitated from Et_2O/hexane to yield colorless crystals 1f (290 mg).

(b) From 1-bromo-1-phenyl-2-propanone 5f(X=Br): A methanolic soln (20 ml) of phenylhydrazine (9.73 g, 90 mmole) was dropped into a soln of 5f(X=Br) (6.39 g, 30 mmole) in MeOH (20 ml). From this mixture phenylhydrazine.HBr began to precipitate and was filtered off after dilution with benzene (100 ml). The filtrate was washed with H_2O, dried over $MgSO_4$ and evaporated. The residue was chromatographed: The fractions eluted first contained E,E- and E,Z-4f (140 mg, 2%, ratio 4:1 by ^1H NMR). The following fractions (R_f 0.4, PE/Et_2O) afforded pure 1f (5.3 g) after crystallization from pentane.

2-(1-Phenylhydrazino)-1-cyclohexanone phenylhydrazone 1g.

(a) From 1-phenylazo-cyclohexene 4g:[13b] Phenylhydrazine (540 mg, 5 mmole) was mixed with a soln. of 4g (930 mg, 5 mmole) in MeOH (2 ml). After 4 hr standing at room temp PE (20 ml) was added to induce the precipitation of slightly yellow crystals 1g (890 mg).

(b) From 2-chloro-cyclohexanone 5g(X=Cl): A soln of phenylhydrazine (17.2 g, 159 mmole) in EtOH (50 ml) was slowly dropped (2 hr) to a cooled (-60°C) soln of 5g(X=Cl) (7 g, 52.8 mmole) in EtOH (70 ml). After standing overnight at -20°C the precipitated crystals were filtered off and washed with precooled EtOH (further workup of the filtrate see below). Subsequently, the crystals were washed with little H_2O and after sucking dry they were triturated with warm Et_2O to give colorless crystals 1g (4 g); another crop of 1g (3.3 g) was obtained by dilution of the Et_2O filtrate with the same volume of hexane. Further purification was accomplished by recrystallization from MeOH or better by reprecipitation from benzene/hexane.

The EtOH mother liquor of the crude product was evaporated and the residue was treated with Et_2O to remove insoluble phenylhydrazine.HCl. The filtrate was washed with H_2O, dried over $MgSO_4$ and evaporated. The residual oil crystallized upon addition of little MeOH to give yellow 1,2-cyclohexanedione bisphenylhydrazone 6g (2 g, 13%), identical with an authentic sample prepared from 1,2-cyclohexanedione.[32]

(rac)- and (1R)-3-(1-Phenylhydrazino)-campher-phenylhydrazone (rac)-1h and (1R)-1h.

From (rac)- and (1R)-2-phenylazo-bornene (rac)-4h and (1R)-4h: A soln of 4h (480 mg, 2 mmole) and phenylhydrazine (216 mg, 2 mmole) in MeOH (0.5 ml) was warmed to 50°C for 1 hr. After cooling to 0°C PE (3 ml) was added to precipitate 1h: (rac)-1h (430 mg) was obtained as slightly yellow crystals. (1R)-1h (120 mg) did not crystallize and was obtained as a foam after chromatography (R_f = 0.3, PE/Et_2O 4:1).

1-Phenyl-2-(1-phenylhydrazino)-1-propanone-phenylhydrazone 1j.

(a) From 2-bromo-1-phenyl-1-propanone 5j (X=Br): The mixture of phenylhydrazine (9.72 g, 90 mmole) and 5j(X=Br) (6.39 g, 30 mmole) in MeOH (80 ml) was allowed to stand at 20°C for 4 hr and was then cooled to 0°C to complete crystallization of 1j (6.6 g).

(b) From 2-methyl-1-methoxy-1-phenyl-oxirane 9j: To a soln of 9j(X=OCH_3)[10] (55 mg, 0.3 mmole) in EtOH (2 ml) phenylhydrazine (150 mg, 1.38 mmole) and one drop of AcOH were added. This mixture was refluxed for 30 min and then allowed to stand at room temp for 12 hr. Subsequent cooling yielded colorless crystals 1j (40 mg, 36%), identical (IR, ^1H NMR) with the product obtained from 5j(X=Br).

1-Phenyl-2-(1-phenylhydrazino)-1-butanone phenylhydrazone 1k from 2-bromo-1-phenyl-1-butanone 5k(X=Br): A soln of 5k(X=Br) (2.27 g, 10 mmole) and phenylhydrazine (3.24 g, 30 mmole) in MeOH (15 ml) was allowed to stand at 20°C for 3 hr and was then cooled to 0°C to give crystalline 1k (1.5 g).

α-(2-Phenylhydrazino)-phenylhydrazones 2:

2-Phenyl-2-(2-phenylhydrazino)-1-ethanone-phenylhydrazone 2c. Phenylhydrazine (570 mg, 5.3 mmole) was added to a soln of 2-bromo-2-

phenylacetaldehyde 5c(X=Br) (350 mg, 1.8 mmole) in EtOH (10 ml). After 13 hr standing at room temp phenylhydrazine.HBr was precipitated by diluting the reaction mixture with toluene/PE (1:1, 100 ml) and filtered off. The filtrate was concentrated in vacuo. Upon addition of pentane (20 ml) and a few drops of EtOH followed by cooling to 0°C crystallization was induced. Column chromatography (PE/Et_2O 1:1) afforded colorless crystals 2c (130 mg).

(rac)- and (1R)-3exo-(2-phenylhydrazino)-campher phenylhydrazone (rac)- and (1R)-2h. The mixture of 5h(X=Br) (3.92 g, 18 mmole) and phenylhydrazine (5.83 g, 54 mmole) was heated to 100°C for 3 hr. After evaporation of H_2O formed in the reaction, addition of Et_2O caused precipitation of phenylhydrazine.HBr which was filtered off. The filtrate was evaporated and the residual glassy mass (6.3 g) was subjected to column chromatography (PE/Et_2O 4:1). The first fraction (tlc R_f = 0.6, PE/Et_2O 4:1) afforded a yellow oil which consisted of a 2:1-mixture of unreacted 5h(X=Br) and 2,2-bis-(2-phenylhydrazino)-3endo-bromobornane 8h [(rac)- and (1R), respectively] according to ^1H NMR (DMSO-D_6): 0.7-2.4 (m, aliphatic portions of 5h and 8h); 4.2 (broad s, HN-2 of 8h); 4.7 (d, J=4.5 Hz, H-3 of 8h); 4.94 (d, J=4.5 Hz, H-3 of 5h); 6.4-7.4 (m, 2 C_6H_5 of 8h); 7.86 (broad s, HN-1 of 8h). The following fraction (tlc R_f = 0.35, PE/Et_2O 4:1) crystallized upon addition of a few ml PE and afforded (rac)-2h (3.17 g) and (1R)-2h (3.11 g), respectively.

1,2-Diphenyl-2-(2-phenylhydrazino)-1-ethanone phenylhydrazone 21. The mixture of 2-chloro-1,2-diphenyl-1-ethanone 51(X=Cl) (3 g, 13 mmole) and phenylhydrazine (4.22 g, 39 mmole) dissolved in MeOH (30 ml) was refluxed for 3 hr, then kept at room temp for 12 hr and finally cooled to -20°C. The separated crystals were filtered off, washed with H_2O and dried over P_4O_{10} yielding 21 (4.3 g).

1,2-Diphenyl-1,2-ethanedione-bisphenylhydrazone (benzil phenylosazone) 61 from E,Z-1,2-diphenyl-1-phenylazo-ethene (phenylazo-stilbene) 41. Phenylhydrazine (60 mg, 0.6 mmole) and 41[13c] (160 mg, 0.6 mmole) were dissolved in MeOH (2 ml). After 6 d standing at room temp the yellow crystals formed were filtered off, washed and dried: The product 61 (30 mg, 14%), m.p. 234°C (EtOH), was identical (m.p., IR) with an authentic sample.[33] No α-phenylhydrazino-phenylhydrazone 11 or 21 was isolated.

Acknowledgement — Thanks are due to the Fonds zur Förderung der wissenschaftlichen Forschung for instrumental support and to the Verein Österreichischer Chemiker for providing a dissertation grant (to P.K.). We also thank Dr.H. Egg, Dr.P. Hebeisen, Dr.R.Hohlbrugger and H. Lindner for microanalyses.

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