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An Easy Access to 2-Oxohydrazones *via* Electrophilic α-*p*-Tolylhydrazonylation of Ketone Enolates with *tert*-Butyl *p*-Tolylazo Sulfide

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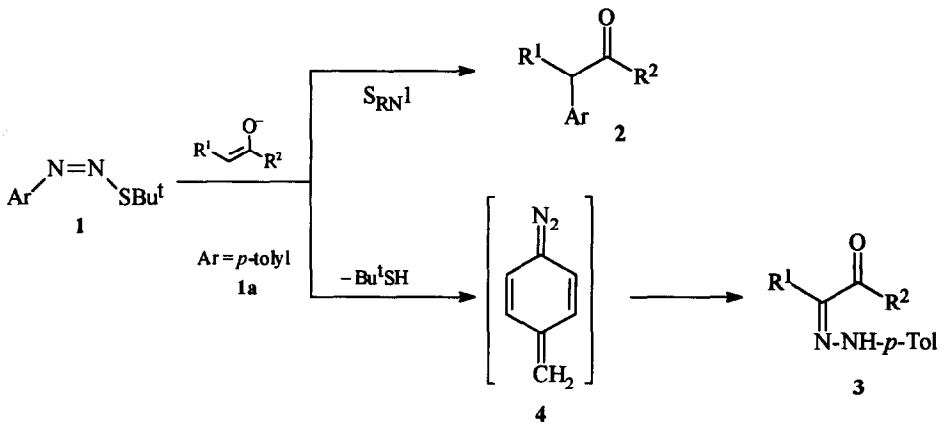
Abstract: The title reaction conveniently furnishes, as the sole or main products, α-(*p*-tolylhydrazono)ketones or their *N*-methylderivatives (H^+ or MeI quenching of the final mixture, respectively). Although the method fails with ketones having a secondary alkyl group bonded to the carbonyl, yields are otherwise more than satisfactory and particular interest is attached to the hydrazonylation of the methyl group in methyl ketones.

We have recently reported that the potassium enolates of acetone[1a] and of alkyl aryl ketones,[1b] when treated with arylazo *tert*-butyl sulfides **1** in DMSO, undergo arylhydrazonylation and/or arylation α to the carbonyl group depending on the nature of the azosulfide aryl moiety (Scheme 1). The formation of 2-oxohydrazones **3** as the sole or major products in the reactions with the *tert*-butyl *p*-tolylazo sulfide **1a** has been adequately explained[1] on the grounds of the acidity of the benzylic hydrogens of **1a**, which causes a base-promoted *tert*-butanethiol elimination followed by attack of the resulting diazocyclohexadiene intermediate **4** onto the enolate.

The hydrazonylation *via* **1a** undoubtedly provides an appealing access to monohydrazones of α–dicarbonyl compounds, through an easy $>CH_2$ to >C=N-NHAr conversion: a result whose significance is surely better understood when recalling that, although the synthetic potentialities of 2-oxohydrazones as precursors of a great variety of heterocyclic systems find numerous applications in the recent literature,[2,3] their possible transformation into likewise important intermediates such as *e.g.* α-aminoketones, β-aminoalcohols, α-ketols, azoalkenes seems to have received only scanty, non-systematic attention. This strikingly contrasts with the synthetic interest of related classes of compounds such as the hydrazones of monocarbonyl compounds or those from active-methylene derivatives:[4-7] a fact which is surely due, at least in part, to the availability of the latter two systems through classical procedures (*e.g.* condensation of carbonyl compounds with hydrazines[8] or coupling between the enolates of active-methylene compounds and arenediazonium salts,[9] respectively) which is not paralleled by a likewise straightforward access to the monohydrazones of 1,2-dicarbonyl compounds. Actually, notwithstanding a few sporadic examples relevant to glyoxal (generally as the

Scheme 1



monoacetal),[6b,7,10,11] α-ketoaldehydes[3c,12] or symmetric α–diketones,[3d,12,13] the difficulty to selectively obtain 2-oxohydrazones from α-dicarbonyl compounds and hydrazines[11c] is well recognized.[14] On the other hand, the access to compounds like **3** *via* coupling of ketone enolates with diazonium salts poses in turn some problems:[9,15] *e.g.* methyl ketones preferentially generate formazans with little chance to isolate the intermediate α-hydrazonylated compounds.[16] The most widespread synthetic route of 2-oxohydrazones is thus represented by the Japp-Klingemann coupling[15,17] of arenediazonium salts with ketones α-substituted with some activating group (*e.g.* CHO, COR) eventually cleaved in the basic medium. This of course enforces the preventive α-acylation of a ketone prior to coupling with a diazonium salt:[18] a procedure which cannot anyway be applied for the -CH_3 to -CH=N-NHAr conversion of methyl ketones.

It seemed therefore of utmost interest to better define the limits of the straightforward access to **3**[19,20] *via* α-hydrazonylation of ketone enolates with *p*-tolylazosulfide **1a**: accordingly we report herein on the extension of the reaction with **1a** to other dialkyl ketones and cycloalkanones (**5d-o**), together with some optimized results on alkyl phenyl ketones (**5a,b**) and acetone (**5c**).

5a: acetophenone	**5f**: cyclohexanone	**5k**: 3-heptanone
5b: propiophenone	**5g**: α-tetralone	**5l**: isopropyl methyl ketone
5c: propanone	**5h**: (1*R*)-(+)-camphor	**5m**: diisopropyl ketone
5d: 3-pentanone	**5i**: 2-butanone	**5n**: isopropyl phenyl ketone
5e: cyclopentanone	**5j**: 2-pentanone	**5o**: 2,6-dimethylcyclohexanone

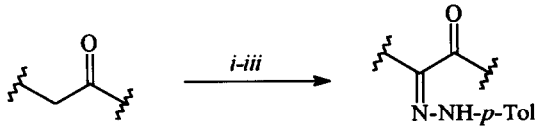
RESULTS AND DISCUSSION

Table 1 collects the results obtained from the α-hydrazonylation of alkyl phenyl ketones (**5a,b**), symmetric dialkyl ketones (**5c,d**) and cyclic ketones (**5e-h**), according to Scheme 2.

A first consideration which emerges from the data is that, with respect to previously reported[1b,c] yields of

the α-hydrazonylation of **5a** (entries 2 and 3), optimization has been reached decreasing the enolate/**1a** molar ratio to the stoichiometric 2.0 value (cf. entries 1-3). The figures suggest that a lower enolate concentration decreases the competitivity of the $S_{RN}1$ arylation pathway of Scheme 1. An analogous investigation on **5b** has on the other hand revealed that a decrease in the enolate/**1a** molar ratio, although appreciably limiting the arylation pathway, does not bring about a concomitant increase in the yield of **3b**. Anyway, the results on **5a** as well as on **5c**, where the hydrazonylation yield is again sizeably enhanced by an enolate/**1a** molar ratio only slightly higher than the stoichiometric value, have determined the successful employment of a 2.5 ratio also for the enolates of other ketones such as 3-pentanone (**5d**), cyclopentanone (**5e**) and cyclohexanone (**5f**). The very poor result of expt. 11 could find a rationale in the ascertained low stability of the enolate of α-tetralone **5g** at

Scheme 2



5 **3**

i: Bu^tOK (1 mol equiv)/DMSO (or DMF), rt, 15 min; *ii*: *p*-Tolyl-N=N-SBu^t (**1a**), rt, 40-120 min; *iii*: acidic quenching.

Table 1. α-(*p*-Tolyl)hydrazonylation of Ketones **5a-h** According to Scheme 2.[a]

Entry	5	5/1a molar ratio	3 (%)	2 (%)
1	**5a**	2.0	96	
2[b]	"	5.0	90	8
3[c]	"	10.0	71	*d*
4	**5b**	2.5	48	25
5[b]	"	5.0	47	36
6	**5c**	2.5	95	
7[e]	"	10.0	83	*d*
8	**5d**	2.5	91	
9	**5e**	2.5	≥ 98	
10	**5f**	2.5	83	
11	**5g**	2.5	30	
12	"	5.0[f]	68	
13	**5h**	2.5	62	
14	"	5.0	80	

[a]Yields refer to isolated, chromatographically pure products. [b]Ref. 1b. [c]Ref. 1c [d]Unquantified. [e]Ref. 1a. [f]Reaction carried out in DMF; $T_{enolisation}$ = -50 °C (30 min), $T_{hydrazonylation}$ = -50 °C ⇒ 20 °C.

room temperature: as a matter of fact, for such ketone a low-temperature enolisation (with the replacement of DMF for DMSO as the solvent)[21] and an enolate/**2a** molar ratio of 5 (entry 12) proved optimal for a more than satisfactory hydrazonylation yield. Finally, for (1*R*)-(+)-camphor (**5h**) best results were in turn achieved with an enolate/**1a** molar ratio of 5.

The results obtained on the hydrazonylation of the enolates of asymmetric dialkyl ketones **5i-k** are collected in Table 2, whereby experiments 1 and 2 clearly indicate that excellent chemical yields are accompanied by a high regioselectivity: the thermodynamically favoured enolates control the main reaction pathway.

Table 2. α-(*p*-Tolyl)hydrazonylation of Asymmetric Dialkyl Ketones **5i-k**.[a]

Entry	5	Yield of 3 (%)
1	**5i**	3-hydrazono-2-butanone (**3i**): 87 1-hydrazono-2-butanone (**3i'**): 9
2[b]	**5j**	3-hydrazono-2-pentanone (**3j**): 80 1-hydrazono-2-pentanone (**3j'**): 10
3	**5k**	2-hydrazono-3-heptanone (**3k**): 41 4-hydrazono-3-heptanone (**3k'**): 22

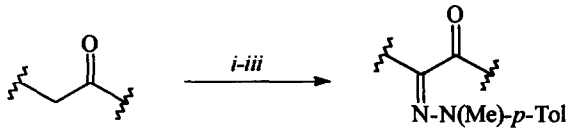
[a]Conditions: DMSO, rt, **5**/**1a** molar ratio = 2.5; reaction times were 1-4h. Yields refer to isolated, chromatographically pure products. [b]The product of arylation at C-1 was also isolated (7%).

For 3-heptanone (**5k**) the relatively low regioselectivity (2-hydrazonylation/4-hydrazonylation ca. 2) is likely governed by different steric crowding on the nucleophilic carbon of the two isomeric enolates.

Within the overall α-hydrazonylation procedure of Scheme 2, the quenching of the final mixture with MeI leads to the *N*-methylderivatives **7** of 2-oxohydrazones **3**. Compounds **7** represent in turn valuable intermediates with no acidic protons at the nitrogen atom: the *N,N*-disubstituted hydrazones are surely of relevance *e.g.* in processes involving C(α) metallation, when attack of any added electrophile onto the nitrogen is to be avoided.[3d,4-7] Yields of some *N*-methyl-*N*-*p*-tolylhydrazones **7** (Scheme 3) are generally comparable with those of the corresponding precursors **3** (Table 1), testifying an efficient methylation of the relevant anion $\mathbf{3}^-$ formed in the preliminary hydrazonylation process. It is noteworthy that the yield of **7b** (60%) is higher than that of hydrazone **3b** (48%), most likely reflecting some difficulty in the isolation of the latter from the reaction mixture.

As a preliminary example of synthetic application of hydrazones **7** we have verified the feasibility of the >C=N-N< ⇒ >C=O ozonolysis.[5c,22] The test has been run on the α-hydrazono derivative **7b** and the yield of the resulting α-diketone **8** is more than satisfactory (Scheme 4).

Scheme 3



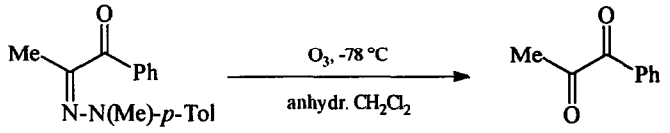
5a-d,i,j **7**

i, ii: see Scheme 2; *iii*: MeI, rt.

7a: 76%	**7d**: 90%
7b: 60%	**7i**: 70%[a]
7c: 88%	**7j**: 71%[a]

[a]Only the 3-hydrazono derivative was isolated.

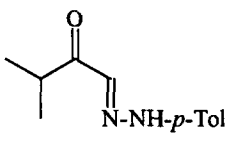
Scheme 4



7b **8**: 81%

Reaction of ***1a*** *with the enolates of isopropyl ketones* ***5l-n*** *and of 2,6-dimethylcyclohexanone* ***5o***

Quite surprisingly, the reaction of **1a** with the enolate of 3-methyl-2-butanone (**5l**) did not afford either of the expected products (**9** or **10**); as a matter of fact, the isolable main product strictly depended on the workup procedure, the hydrazone of acetone (**11**) being quantitatively isolated after aqueous quenching and immediate extraction into ether, the hexahydrotetrazine **12** being instead recovered after acidic quenching. As hexahydro-



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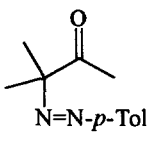

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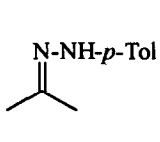

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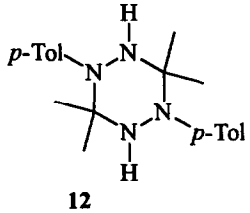
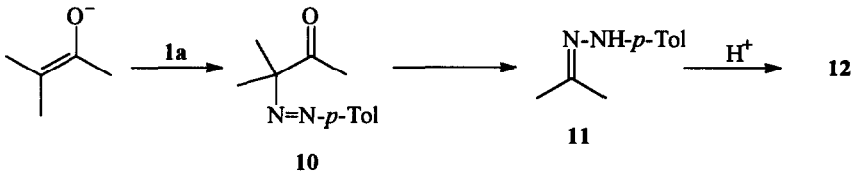


12

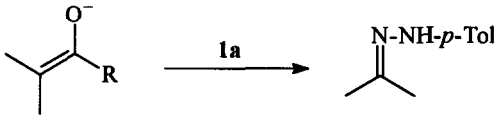
tetrazines are well-known products deriving from acid-catalyzed dimerization of hydrazones of carbonyl compounds,[23] the outcome above can be explained (Scheme 5) through an initial reaction of **1a** with the more thermodynamically favoured enolate of **5l**: the ensuing azoderivative **10** then undergoing a deacylation which is strongly reminiscent of that occurring in the Japp-Klingemann reaction.[17]

Scheme 5



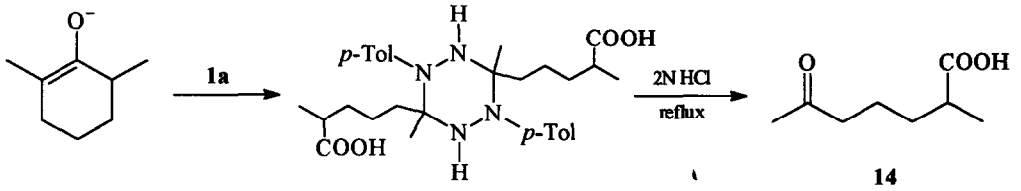
The outlined behaviour seems common to isopropyl ketones, as evidenced by the results obtained for the enolates of diisopropyl (**5m**) and isopropyl phenyl ketone (**5n**) (Scheme 6): in the latter case, the identification of PhCOOH in the final mixture undoubtedly represents a mechanistic proof.

Scheme 6



R = methyl	≥ 98%
R = isopropyl	≥ 98%
R = phenyl	91%

In agreement with the observation of a C(α)-CO bond cleavage involving ketones having a secondary alkyl group linked to the carbonyl, the same reaction, applied to the cyclic ketone **5o**, results in a ring fission eventually leading (after the necessary acidic quenching) to quantitative yields of the hexahydrotetrazine **13** as a diastereomeric mixture: the structure of **13** was confirmed through acidic hydrolysis[24] to 2-methyl-6-oxoheptanoic acid (**14**).



13, ≥ 98%

14

CONCLUSIONS

The results herein represent good evidence that, notwithstanding some limitations, pertinent to ketones with a secondary alkyl group bonded to the carbonyl, the reaction of the *tert*-butyl *p*-tolylazo sulfide **1a** with

ketone enolates is a viable and convenient access to 2-oxohydrazones **3** or **7** of potential applicative interest. The method places the synthesis of these compounds on the same level as that of hydrazones of monocarbonyl compounds or those from active-methylene derivatives; particular relevance is attached to the α-hydrazonylation of methyl ketones, a target which cannot be hit *via e.g.* the cited acylation/azocoupling procedure.[18]

EXPERIMENTAL

Melting points were determined on a Büchi 535 apparatus and are uncorrected. Distillations were performed with a Kugelröhr apparatus, the quoted boiling point referring to the oven temperature. ^{1}H-NMR spectra were taken in $CDCl_3$ (unless otherwise stated) on a Varian Gemini 200 spectrometer; TMS was used as internal standard and chemical shifts are reported as δ values (ppm). The ozonization of **7b** was performed with a Fischer Ozon-Generator.

Materials

Petroleum ether and light petroleum refer to the fractions with bp 40-60 °C and 80-100 °C, respectively. Dimethylsulfoxide (DMSO, Fluka) and dimethylformamide (DMF, Fluka) were used as received after storage over molecular sieves (4 Å). Methylene chloride for the ozonolysis test was dried by reflux over P_2O_5 and distillation before use. Potassium *tert*-butoxide (97%) was a commercial product used as received.

Column (or preparative-plate) chromatographies were performed on silica gel using petroleum ether and gradients (or appropriate mixtures) with CH_2Cl_2 or Et_2O as eluants, the solvents being distilled before use.

(*Z*)-*tert*-Butyl *p*-tolylazo sulfide (**1a**) was synthesized from commercial *p*-toluidine as previously reported.[1a]

Ketones **5a-o** were commercial products, used as received [but for the liquid samples which were dried before use].

Reactions of ketones 5a-k with azosulfide 1a: 2-oxohydrazones 3a-k

Reactions in DMSO. The general procedure has been already described.[1a,b] Usual workup involved pouring of the reaction mixture into ice/3% HCl followed by extraction with ether, washing and drying (Na_2SO_4) of the combined extracts, and solvent evaporation under reduced pressure. Column chromatography of the residue allowed separation of the reported products. It has been often possible to recover most of the excess starting ketone *via* fractional distillation (< 100 °C/1 mmHg) of the residue prior to chromatography.

Reactions in DMF. The procedure is essentially the same as that for DMSO solutions. For expt 12 of Table 1 the temperature was kept at -50 °C during enolisation; after addition of **1a**, the cooling bath was removed, allowing equilibration with room temperature to be reached. Usual workup afforded the reaction products.

The structure of all the hydrazones herein has been confirmed by ^{1}H-NMR analysis. The isolated samples were invariably characterized by an *E* geometry around the C=N double bond, although in $CDCl_3$ slow isomerization did generally occur to the *Z* isomer.

Phenyl (p-tolylhydrazono)methyl ketone (**3a**),[1b] *phenyl 1-(p-tolylhydrazono)ethyl ketone* (**3b**),[1b] and *1-(p-tolylhydrazono)-2-propanone* (**3c**)[1a] have been described elsewhere.

2-(p-Tolylhydrazono)-3-pentanone (**3d**): mp 146.7-147.6 °C (light petroleum); ^{1}H-NMR: 1.15 (3H, t, *J* 7.4 Hz), 1.99 (3H, s), 2.32 (3H, s), 2.97 (2H, q, *J* 7.4 Hz), 7.12 (4H, AA'BB', *J* 8.9 Hz), 7.69 (1H, br s). Found: C, 70.7; H, 8.0; N, 13.8% ($C_{12}H_{16}N_2O$ requires: C, 70.6; H, 7.9; N, 13.7%).

2-(p-Tolylhydrazono)cyclopentanone (**3e**): mp 227.0-228.0 °C (dec.) (EtOH); ^{1}H-NMR: 2.15 (2H, app quint), 2.30 (3H, s), 2.50 (2H, app t), 2.64 (2H, t, *J* 7.3 Hz), 7.13 (4H, AA'BB', *J* 8.8 Hz), 7.64 (1H, br s). Found: C, 71.3; H, 7.2; N, 13.7% ($C_{12}H_{14}N_2O$ requires: C, 71.3; H, 7.0; N, 13.9%).

2-(p-Tolylhydrazono)cyclohexanone (**3f**): mp 187.2-188.4 °C (EtOH); [lit.:[25] 188-189 °C (EtOH)]; ^{1}H-NMR: 1.93 (4H, m), 2.30 (3H, s), 2.57 (4H, m), 7.13 (4H, AA'BB', *J* 8.9 Hz), 7.87 (1H, br s).

2-(p-Tolylhydrazono)-1,2,3,4-tetrahydro-1-naphthalenone (**3g**): mp 91.3-91.9 °C (petroleum ether); ^{1}H-NMR: 2.32 (3H, s), 2.96 (2H, m), 3.06 (2H, m), 7.13 and 7.21 (2H each, AA'BB', *J* 8.5 Hz), 7.27 (1H, d, *J* 7.4 Hz), 7.36 (1H, td, *J* 1.3 and 7.5 Hz), 7.48 (1H, td, *J* 1.5 and 7.4 Hz), 8.05 (1H, dd, *J* 1.5 and 7.6 Hz), 14.09 (1H, br s). Found: C, 77.4; H, 6.0; N, 10.5% ($C_{17}H_{16}N_2O$ requires: C, 77.3; H, 6.1; N, 10.6%).

(1R)-(+)-3-(p-Tolylhydrazono)camphor (**3h**): mp 187.3-188.5 °C (EtOH); $[\alpha]_D^{25}$ = +401.3° (c = 0.1, $CHCl_3$); ^{1}H-NMR: 0.91 (3H, s), 1.02 (3H, s), 1.05 (3H, s), 1.54 (2H, m), 1.78 (1H, m), 2.04 (1H, m), 2.28 (3H, s), 2.88 (1H, d, *J* 4.15 Hz), 7.09 (4H, app. s), 7.66 (1H, br s). Found: C, 75.3; H, 8.1; N, 10.3% ($C_{17}H_{22}N_2O$ requires: C, 75.5; H, 8.2; N, 10.4%).

3-(p-Tolylhydrazono)-2-butanone (**3i**): mp 159.3-160.3 °C (toluene) [lit.:[26] 160 °C]; ^{1}H-NMR: 1.99 (3H, s), 2.32 (3H, s), 2.48 (3H, s), 7.13 (4H, s), 7.72 (1H, br s).

1-(p-Tolylhydrazono)-2-butanone (**3i'**): mp 112.0-114.1 °C (light petroleum); ^{1}H-NMR: 1.17 (3H, t, *J* 7.5 Hz), 2.31 (3H, s), 2.90 (2H, q, *J* 7.5 Hz), 7.06 (2H, AA' of AA'BB', *J* 8.4 Hz), 7.14 [3H in all, s and BB' of AA'BB' (*J* 8.4 Hz) partly overlapped], 8.17 (1H, br s). Found: C, 69.2; H, 7.5; N, 14.8% ($C_{11}H_{14}N_2O$ requires: C, 69.5; H, 7.4; N, 14.7%).

3-(p-Tolylhydrazono)-2-pentanone (**3j**): mp 146.7-147.6 °C (light petroleum) [lit.:[3a] 145 °C]; ^{1}H-NMR: 1.06 (3H, t, *J* 7.7 Hz), 2.32 (3H, s), 2.46 (3H, s), 2.54 (2H, q, *J* 7.7 Hz), 7.13 (4H, AA'BB', *J* 8.9 Hz), 7.88 (1H, br s).

1-(p-Tolylhydrazono)-2-pentanone (**3j'**): mp 111.5-113.1 °C (light petroleum); ^{1}H-NMR: 0.99 (3H, t, *J* 7.4 Hz), 1.72 (2H, sext, *J* 7.4 Hz), 2.31 (3H, s), 2.85 (2H, t, *J* 7.4 Hz), 6.94 (1H, s), 7.10 (4H, AA'BB', *J* 8.6 Hz), 8.2 (1H, br s). Found: C, 70.4; H, 8.0; N, 13.7% ($C_{12}H_{16}N_2O$ requires: C, 70.6; H, 7.9; N, 13.7%).

4-(p-Tolylhydrazono)-3-heptanone (**3k**): mp 76.4-76.7 °C (petroleum ether); ^{1}H-NMR: 0.98 (3H, t, *J* 7.3 Hz), 1.11 (3H, t, *J* 7.4 Hz), 1.49 (2H, sext, *J* 7.6 Hz), 2.32 (3H, s), 2.51 (2H, t, *J* 7.6 Hz), 2.95 (2H, q, *J* 7.4 Hz), 7.12 (4H, AA'BB', *J* 9.2 Hz), 7.83 (1H, br s). Found: C, 72.6; H, 8.6; N, 11.9% ($C_{14}H_{20}N_2O$ requires: C, 72.4; H, 8.7; N, 12.1%).

2-(p-Tolylhydrazono)-3-heptanone (**3k'**): mp 110.6-110.8 °C (petroleum ether); ^{1}H-NMR: 0.94 (3H, t, *J* 7.2 Hz), 1.38 (2H, sext, *J* 7.2 Hz), 1.65 (2H, m), 1.98 (3H, s), 2.32 (3H, s), 2.94 (2H, t, *J* 7.5 Hz), 7.13 (4H, AA'BB', *J* 9.5 Hz), 7.69 (1H, br s). Found: C, 72.2; H, 8.8; N, 11.9% ($C_{14}H_{20}N_2O$ requires: C, 72.4; H, 8.7; N, 12.1%).

α-(N-Methyl-N-p-tolylhydrazono)ketones 7

The final hydrazonylation mixture was quenched at room temperature with MeI (2 mol equiv with respect to the Bu^{t}OK employed for the enolization of **5**). The mixture was then poured into a saturated NaCl solution and the usual workup yielded a crude residue which was chromatographed to afford pure products.

(N-Methyl-N-p-tolylhydrazono)methyl phenyl ketone (**7a**): mp 84.0-84.9 °C (petroleum ether); ^{1}H-NMR: 2.32 (3H, s), 3.47 (3H, s), 7.14 and 7.22 (2H each, AA'BB', *J* 8.9 Hz), 7.34 (1H, s), 7.47 (3H, m), 8.06 (2H, m). Found: C, 76.5; H, 6.6; N, 11.1% ($C_{16}H_{16}N_2O$ requires: C, 76.2; H, 6.4; N, 11.1%).

1-(N-Methyl-N-p-tolylhydrazono)ethyl phenyl ketone (**7b**): mp 71.9-72.3 °C (petroleum ether); ^{1}H-NMR: 2.18 (3H, s), 2.30 (3H, s), 3.53 (3H, s), 6.98 and 7.08 (2H each, AA'BB' *J* 8.7 Hz), 7.44 (3H, m), 7.90 (2H, m). Found: C, 76.8; H, 6.7; N, 10.7% ($C_{17}H_{18}N_2O$ requires: C, 76.7; H, 6.8; N, 10.5%).

1-(N-Methyl-N-p-tolylhydrazono)-2-propanone (**7c**): mp 95.1-95.9 °C (petroleum ether); ^{1}H-NMR: 2.34 (3H, s), 2.44 (3H, s), 3.38 (3H, s), 6.94 (1H, s), 7.28 and 7.17 (2H each, AA'BB', *J* 8.6 Hz). Found: C, 69.1; H, 7.4; N, 14.4% ($C_{11}H_{14}N_2O$ requires: C, 69.5; H, 7.4; N, 14.7%).

2-(N-Methyl-N-p-tolylhydrazono)-3-pentanone (**7d**): mp 21.1-22.3 °C (pentane); ^{1}H-NMR: 1.13 (3H, t, *J* 7.4 Hz), 1.99 (3H, s), 2.32 (3H, s), 2.96 (2H, q, *J* 7.4 Hz), 3.46 (3H, s), 7.11 (4H, AA'BB', *J* 9.0 Hz). Found: C, 71.3; H, 8.2; N, 12.5% ($C_{13}H_{18}N_2O$ requires: C, 71.5; H, 8.3; N, 12.8%).

3-(N-Methyl-N-p-tolylhydrazono)-2-butanone (**7i**): mp 45.3-46.0 °C (petroleum ether); ^{1}H-NMR: 1.98 (3H, s), 2.33 (3H, s), 2.47 (3H, s), 3.49 (3H, s), 7.12 (4H, AA'BB', *J* 9.1 Hz). Found: C, 70.8; H, 7.7; N, 13.9% ($C_{12}H_{16}N_2O$ requires: C, 70.6; H, 7.9; N, 13.7%).

3-(N-Methyl-N-p-tolylhydrazono)-2-pentanone (**7j**): bp 240 °C (oven)/2 mmHg; ^{1}H-NMR: 1.04 (3H, t, *J* 7.5 Hz), 2.33 (3H, s), 2.44 (3H, s), 2.58 (2H, q, *J* 7.5 Hz), 3.54 (3H, s), 7.15 (4H, app s). Found: C, 71.3; H, 8.1; N, 12.9% ($C_{13}H_{18}N_2O$ requires: C, 71.5; H, 8.3; N, 12.8%).

Reactions of ketones 5l-o with azosulfide 1a

The structure of isolated products from **5l-n** depends on the workup procedure. Thus, the *p*-tolylhydrazone of acetone (**11**) was isolated by aqueous quenching and immediate extraction into Et_2O: after washing and drying (Na_2SO_4) of the combined extracts, solvent evaporation under reduced pressure yielded a crude residue which solidified in the cold [mp 48.2-50.1 °C after washing with petroleum ether (lit.:[27] mp 50-52 °C)].

Quenching of the reaction mixture with 3% HCl, followed by the usual workup, afforded the hexahydrotetrazines **12** and **13**, from **5l-n** and **5o** respectively. The structure of crude *3,3,6,6-tetramethyl-1,4-bis(4-methylphenyl)hexahydro-1,2,4,5-tetrazine* (**12**, yellow oil) was confirmed by NMR spectroscopy; ^{1}H-NMR: 1.58 (12H, s), 2.42 (6H, s), 7.28 and 7.64 (8H, AA'BB', *J* 8.4 Hz), 9.41 (2H, br s); ^{13}C-NMR: 21.41, 21.86, 103.37, 122.52, 129.74, 141.88, 149.11. The structure of crude *3,6-bis(4-carboxy-1-pentyl)-3,6-dimethyl-1,4-bis(4-methylphenyl)hexahydro-1,2,4,5-tetrazine* (**13**, brown oil) was confirmed by acidic hydrolysis (2N HCl, reflux, 30 min)[24] to 2-methyl-6-oxoheptanoic acid (**14**): bp 160 °C (oven)/10 mmHg (lit.:[28] 130 °C/1 mmHg); ^{1}H-NMR(CCl_4) identical to that reported in the literature.[28]

Ozonolysis of 7b

The title reaction was carried out, as described for *N,N*-dimethylhydrazones,[5c] on 0.43 mmol of **7b** in anhydrous CH_2Cl_2 (20 ml). The expected 1-phenyl-1,2-propanedione **8** was separated from *N*-methyl-*N*-nitroso-*p*-toluidine [mp 50.0-51.1 °C (lit.:[29] mp 52-53 °C)] by chromatography on a preparative plate and identified by ^{1}H-NMR comparison with a commercial sample.

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