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VINYLAMINES—VII[1]

MORE SUBSTITUTED ALKYLATED ENAMINES FROM CYCLOHEXANONE ENAMINES AND PHENYL VINYL SULFONE

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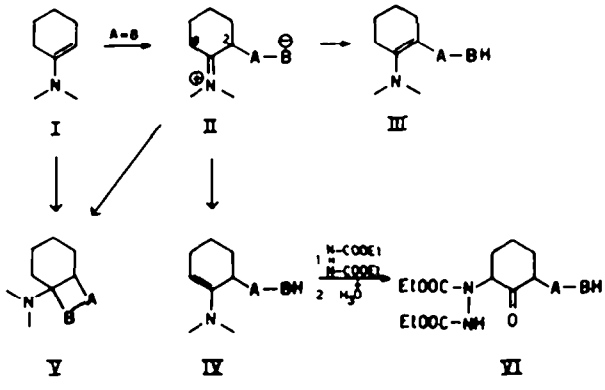
Abstract—The morpholine and piperidine enamines of cyclohexanone reacted with phenyl vinyl sulfone to give mainly the more substituted alkylated enamines. The structure of the products was determined by spectral and/or chemical evidence. Different results were found for the pyrrolidine enamine. The possible mechanism and the factors affecting the stereochemistry of the reactions are discussed.

INTRODUCTION

IN THIS report we describe our results of the reaction of cyclohexanone enamines with phenyl vinyl sulfone.[2] The Stork's C-alkylation[3] of enamines (I) with electrophilic olefins and the analogous reaction with other dienophiles (simply indicated as A=B) are generally considered to be two step processes, involving a dipolar intermediate (II). The rearrangement of the latter can generate different products: the more substituted III or the less substituted enamine IV, by proton transfer from the 2 and 6 position of the ring, respectively, or compounds like V by cycloaddition.[4]

CHART 1



[1] Part VI. A. Risaliti, L. Marchetti and M. Forchiassin, *Ann. Chim. Rome* **56**, 317 (1966).

[2] A preliminary account of this work has been published: A. Risaliti, S. Fatutta, M. Forchiassin and E. Valentin, *Tetrahedron Letters* 1821 (1966).

[3] G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz and R. Terrel, *J. Am. Chem. Soc.* **85**, 207 (1963).

[4] Adducts like V can be formed also by direct cycloaddition to the enaminic double bond: I. Fleming and J. Harley-Mason, *J. Chem. Soc.* 2165 (1964); K. C. Brannock, A. Bell, R. D. Burpitt and C. A. Kelly, *J. Org. Chem.* **29**, 801 (1964); K. C. Brannock, R. D. Burpitt, V. W. Goodlet and J. G. Thweatt, *Ibid.* 813, 818 (1964).

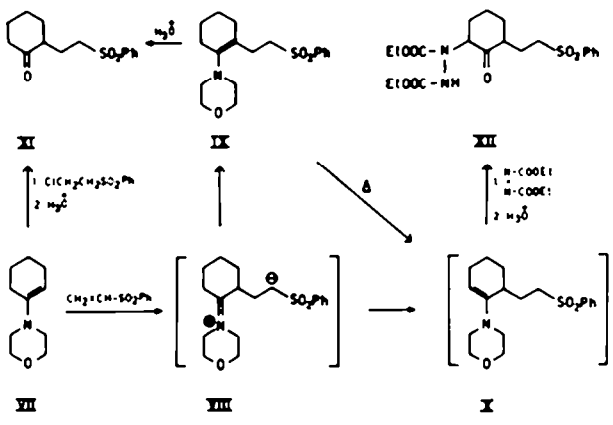
In such a reaction several factors may contribute to the preferred formation of one of the three possible isomers III, IV and V. Important determining factors may be the particular structure and conformation of the intermediate II and the nature of the electrophilic reagent. For instance, when the reagent A=B, such as ethyl azodicarboxylate[5] and β-nitrostyrene,[1] bears hindering groups at the electrophilic center, only the less substituted enamine IV is formed. Its structure follows from NMR spectral data (one vinyl hydrogen) and from the reaction with ethyl azodicarboxylate yielding 2,6-disubstituted derivatives VI (Chart 1) in almost quantitative yield (85–95%).

In connection we have investigated the reaction of phenyl vinyl sulfone, a reagent bearing no substituent at the electrophilic carbon atom, with cyclohexanone enamines.

RESULTS

The reaction of 1-N-morpholino-cyclohexene (VII) with phenyl vinyl sulfone (Chart 2) in refluxing ether, benzene or cyclohexane gave by concentration of the solution, 1-N-morpholino-2-(β-phenylsulfonylethyl)cyclohex-1-ene (IX) as major product. The structure of more substituted enamine for IX was demonstrated as follows. On hydrolysis in aqueous acetic acid IX gave 2-(β-phenylsulfonylethyl) cyclohexanone (XI) which was identical with that obtained from the reaction of VII with phenyl β-chloroethyl sulfone and subsequent hydrolysis. The NMR spectrum of IX showed a two-proton signal at 6·78 τ corresponding to the —CH_2SO_2— group and

CHART 2



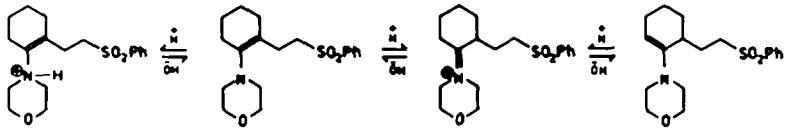
therefore a cyclic structure like V (Chart 1) could be ruled out.[6] Moreover no signal was seen in the region of 4–6 τ, as would be expected if vinyl protons were present. Finally, IX did not react with ethyl azodicarboxylate under the conditions in which all the less substituted enamines gave 2,6-disubstituted derivatives VI (Chart 1). In fact it was recovered quantitatively unchanged even after several days.

[5] A. Risaliti and L. Marchetti, *Ann. Chim. Rome* **55**, 635 (1965).

[6] Cyclobutane adducts are obtained, on the contrary, from methyl vinyl sulfone and divinyl sulfone with isobutyraldehyde and propionaldehyde enamines: K. C. Brannock, A. Bell, R. D. Burpitt and C. A. Kelly, *J. Org. Chem.* **29**, 801 (1964).

The alkylated enamine IX gave a sparingly water soluble hydrochloride from which by treating with diluted ammonia, just the starting material was reformed (92%). This seems to indicate that the conjugate acid of the salt exists in the N-protonated (XIIIa) rather than in the C-protonated form (XIIIb), because in the latter case on treatment with alkali two isomeric alkylated enamines, IX and X, would be expected.[7]

CHART 3



XIIIa IX XIIIb X

According to the structure XIIIa, the above mentioned hydrochloride gave with LAH the enamine IX, whereas the corresponding saturated tertiary amine was not formed.[7c]

In the reaction of VII with phenyl vinyl sulfone, beside the enamine IX also the less substituted isomer X was formed as minor product. We were unable to isolate the latter but it could be detected in the following way. The solution of reaction, without separating the compound IX, was cooled, treated with excess ethyl azodicarboxylate and allowed to stand at room temperature for several days. By acidic hydrolysis 2-(β-phenylsulfonylethyl)cyclohexanone (XI) and 2-(β-phenylsulfonylethyl)-6-(N,N'-dicarbethoxyhydrazino)cyclohexanone (XII) were obtained from the reaction mixture, in 68% and 23% yield respectively, calculated on the starting enamine. Considering that alkylated enamine IX does not react with ethyl azodicarboxylate, whereas the less substituted enamines react almost quantitatively, the XI:XII ratio represents approximatively the IX:X ratio in the reaction mixture of 1-N-morpholino-cyclohexene with phenyl vinyl sulfone.

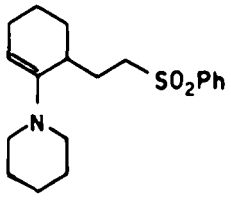
The compound XII was obtained in two isomeric forms, m.p. 138–140° (XIIa) and m.p. 105–107° (XIIb). The isomer XIIa was found to be stable in acidic medium at room temperature, but it was converted into XIIb on heating in acetic solution. The IR and NMR spectra of both compounds were alike. In the IR spectrum NH absorption bands at 3310 cm^{-1} (XIIa) and at 3280 cm^{-1} (XIIb) were evident. The NMR spectrum (chf) revealed signals at 6·93 τ (XIIa) and 6·82 τ (XIIb) for the $—CH_2—SO_2—$ protons and at 5·25 τ (XIIa) and 5·19 τ (XIIb) for the proton attached to the ring carbon atom bearing the dicarbethoxy hydrazinic group. The two isomers gave *p*-nitro phenylhydrazones which, after recrystallization, were found to be identical, probably because isomerization had occurred. From these data XIIa and XIIb appeared to be *cis–trans* 2,6-disubstituted isomeric cyclohexanones.

As regards the formation of enamine X we believe it was formed in part by re-

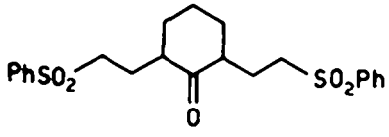
[7] As regards the N- and C-protonation of enamines see: [a] J. Elguero, R. Jacquier and G. Tarrago, *Tetrahedron Letters* 4719 (1965); [b] E. J. Stamhuis and W. Maas, *J. Org. Chem.* **30**, 2156 (1965); [c] G. Opitz and A. Griesinger, *Liebig's Ann.* **665**, 101 (1963).

arrangement of enamine IX, during the reaction with phenyl vinyl sulfone in refluxing benzene. Actually, when pure IX was refluxed in benzene for 24 hr and treated, after cooling, with ethyl azodicarboxylate, XII was obtained in about 38% yield. This indicates a thermal partial conversion of IX to X.[8]

Such a conversion was evident when 1-N-piperidino-cyclohexene and phenyl vinyl sulfone were heated in benzene under reflux. Concentration of the reaction solution yielded 1-N-piperidino-2-(β-phenylsulfonylethyl)cyclohex-6-ene (XIV). It was unstable and measurement of its NMR spectrum was not possible. Its structure, however, was proved by hydrolysis to XI and by reaction with ethyl azodicarboxylate, yielding 2,6-disubstituted cyclohexanone XII in 90% yield. Compound XIV was the major product when the reaction with phenyl vinyl sulfone was carried out under reflux, whereas at room temperature it was the minor product. This was demonstrated by treatment of the reaction mixtures, without isolating XIV, with ethyl azodicarboxylate and subsequent hydrolysis. In the former case, XI and XII were obtained in 18% and 65% yield respectively. In the latter case, in contrast 65% of XI and only 21% of XII were formed.



XIV



XV

No difference was observed for the reaction of 1-N-pyrrolidino-cyclohexene with the same olefin in benzene either at room temperature or under reflux. In fact the less substituted alkylated enamine was found to be always the main product (65–80%). In this case none of the two isomeric enamines could be isolated. However their relative amounts in the reaction mixtures were established as above mentioned, i.e. from the percentages of XI and XII obtained after treatment with ethyl azodicarboxylate.

When to the reaction mixture of pyrrolidine enamine with phenyl vinyl sulfone a second equivalent of the same electrophilic reagent was added, a dialkylated cyclohexanone was obtained after hydrolysis. Therefore the structure of 2,6-bis-(β-phenylsulfonylethyl)cyclohexanone (XV) was assigned to this product. According to this assignment, two isomers of XV, regarded as *cis* and *trans* forms, were obtained. Actually, when the acidic hydrolysis was carried out at room temperature, a derivative m.p. 108–110° was isolated. This product, on refluxing in ethanol with a trace of *p*-toluenesulfonic acid, was converted into an isomer m.p. 124–124·5°. Both isomers showed very similar IR spectra with strong CO and SO_2 absorption bands.

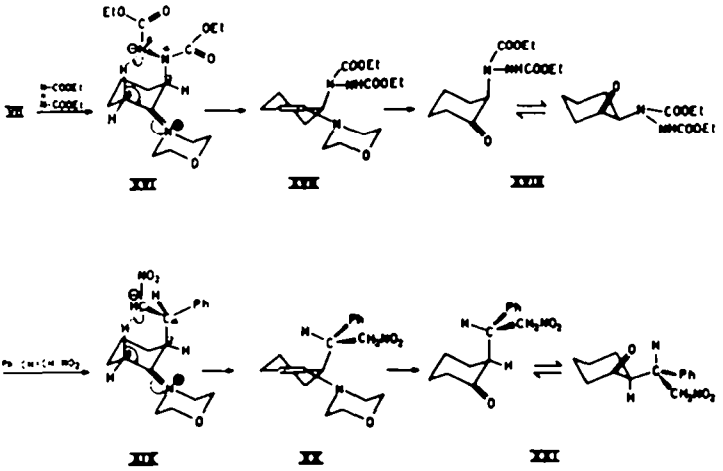
[8] Further studies in progress indicate that the rearrangement of IX to X consists in a reversion of IX into the starting enamine and phenyl vinyl sulfone, which then recombine to generate again the mixture of IX and X. Since the compound X, as well as the other less substituted enamines including XIV, is stable under these conditions and is not converted to the more substituted isomer, we can postulate that the two isomers IX and X do not arise from equilibration.

DISCUSSION

The above results and those previously reported on the reaction of the enamines with ethyl azodicarboxylate[5] and β-nitrostyrene,[1] demonstrate that the same enamine behaves differently with different electrophilic reagents. In fact in these reactions either the less substituted or the more substituted enamine is found to be the main product. If the mechanism in Chart 1 is correct and the enamines III and IV are generated from the same dipolar intermediate II, we think the reaction depends on the particular structure and conformation in which II is arranged in the different cases. From inspection of scale models, of the several possible conformers, that we can postulate for II, the most stable appears to be that with the cyclohexane ring in a chair conformation with the substituent in 2 position axially oriented. This preferred conformation was demonstrated, for instance, for the immonium salts obtained in the C-alkylation of cyclohexanones enamines with alkyl halogenides.[9]

Moreover, it is also in agreement with the stereochemical considerations concerning allylic and pseudo-allylic systems with an hexocyclic double bond, where the same type of interaction, termed $A^{(1,3)}$ strain, is operating.[10]

CHART 4



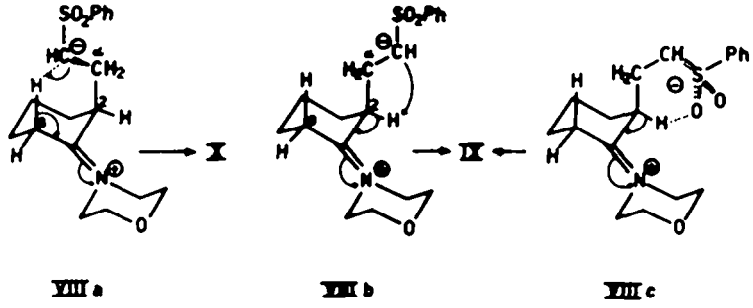
On the basis of these considerations, we postulated[5] the conformation XVI, as the most probable, for the dipolar intermediate of the reaction of cyclohexanone enamines with ethyl azodicarboxylate. From the molecular models it can be seen that in this structure the rotation around the axial C_2—N_α bond is strongly restricted, because the bulky COOEt group attached to the N_α atom sterically interferes with the cyclohexane ring. Therefore, in the most stable rotomer such a group is arranged in the less hindered *anti* conformation with respect to the same ring. A direct consequence is that the negatively charged N_β atom lies very near to the axial hydrogen atom at the 6 position. An intramolecular transfer of this hydrogen to the N_β atom, through a six-membered cyclic transition state, then accounts for the formation of the enamine XVII[5] (Chart 4).

[9] S. Karady, M. Lenfant and R. E. Wolff, *Bull. Soc. Chim. Fr.* 2472 (1965).
[10] F. Johnson and S. K. Malhotra, *J. Amer. Chem. Soc.* **87**, 5492 (1965).

Analogous considerations can be made for the intermediate XIX of the reaction with β-nitrostyrene, because of the steric hindrance due to the phenyl group (Chart 4). In fact, also in this case the less substituted enamine was obtained[1] and, on the basis of such a stereochemistry, the *erythro* configuration XXI was assigned to the hydrolysis product.[11]

In the intermediate VIII (Chart 2) of the reaction with phenyl vinyl sulfone, as bulky groups are lacking at C_α atom, the free rotation around the axial C_2—C_α bond is possible. Then both rotomers with $-\overset{\ominus}{C}H-SO_2Ph$ group in the *syn* (VIIIa) and *anti* conformation (VIIIb), with respect to the cyclohexane ring, are possible. From VIIIa the less substituted alkylated enamine X is formed as already described, whereas VIIIb would lead to the more substituted isomer IX. Even in the latter case the transfer of the equatorial hydrogen from nuclear C_2 to the negatively charged carbon atom must take place in an intramolecular pathway. In fact, if an intermolecular process occurred, the axial hydrogen at C_6 atom would be available for such a transfer and consequently the enamine X instead of IX would be formed. On this assumption, the more substituted enamine IX would be formed from VIIIb through a four-membered cyclic transition state (Chart 5).

CHART 5



VIII a VIII b VIII c

This mechanism is likely if the negatively charged carbon atom, as well as that of the α-sulfonyl carbanions,[12] is sp^3 rather than sp^3–p hybridized. In this case, as the orbital occupied by the lone pair is very strongly directed, the approach to the equatorial hydrogen is facilitated.

On the other hand, the participation of the sulfonyl group to the intramolecular hydrogen transfer, as in VIIIc (Chart 5), cannot be ruled out.[13] Such a mechanism

[11] The *erythro* configuration for the *p*-bromophenyl derivative has been very recently demonstrated by X-ray crystal structure determination (results to be published).

[12] For the question of pyramidal *vs* planar α-sulfonyl carbanions see: [a] D. J. Cram, *Fundamentals of Carbanions Chemistry*. Academic Press, New York and London (1965); [b] H. Hogeveen, F. Montanari and F. Taddei, *J. Chem. Soc.* 965 (1964); [c] H. Hogeveen, G. Maccagnani, F. Montanari and F. Taddei, *Ibid.* 4101 (1964); [d] E. J. Corey and T. H. Lowry, *Tetrahedron Letters* 793, 803 (1965).

[13] As regards the ability of sulfonyl oxygen atoms to form hydrogen bonds with proton-donors see: [a] P. Biscarini, G. Galloni and S. Ghersetti, *Spectrochim. Acta* **20**, 267 (1964); [b] G. Galloni and S. Ghersetti, *Boll. sci. fac. chim. ind. Bologna, Italy* **21**, 1 (1963).

however is more likely in the case of NO_2, CO, etc. groups rather than the SO_2 group, on account of the different manner of charge delocalization in the corresponding α-carbanions.[13a]

The formation of the more substituted enamine as major product in the case of 1-N-morpholino-cyclohexene and, under conditions in which rearrangement does not occur, of 1-N-piperidino-cyclohexene can be explained in terms of relative conformational stability of the rotomers VIII. The fact that the *anti* rotomer, VIIIb or VIIIc, is less overcrowded and then more favoured than the *syn* VIIIa, can account for these results. But the different behaviour of the pyrrolidine derivative indicates that other factors are also involved in the reaction. This problem is being investigated.

EXPERIMENTAL

All the m.ps were uncorrected. The IR spectra were recorded in KBr pellets (NaCl region) with Perkin–Elmer Model 13 double beam Infrared Spectrophotometer and the NMR spectra were recorded with Varian DP-60 NMR Spectrometer at 56·4 Mc, with TMS as internal standard, using CCl_4 soln unless otherwise noted.

Reaction of 1-N-*morpholino-cyclohexene with phenyl vinyl sulfone*

(a) 1-N-*Morpholino-2-(β-phenylsulfonylethyl)cyclohex-1-ene* (IX). Compound VII (5 g, 30 mmoles) was added to a soln of phenyl vinyl sulfone[14] (5 g, 30 mmoles) in dry ether (40 ml), or benzene or cyclohexane. The mixture was allowed to stand at room temp for 48 hr (or refluxed for 4 hr). After partial removal of the solvent (and addition of ether when benzene or cyclohexane were used) IX (4·3 g) was filtered off, washed with a few ml dry ether and recrystallized from ligroin as white needles, m.p. 101–102°. (Found: C, 64·31; H, 7·43; N, 4·49. $C_{18}H_{25}NO_3S$ requires: C, 64·45; H, 7·51; N, 4·17%.) NMR spectrum: 7·45 τ (—CH_2—N—); 6·78 τ (—CH_2—SO_2—); 6·45 τ (—CH_2—O—); 2·36 τ (C_6H_5—).

By addition of 10% HCl (30 ml) to the reaction mixture, after removal of the solvent, the *hydrochloride* XIIIa was obtained after standing at room temp for 24 hr. XIIIa was filtered off, washed with ether and recrystallized from a large amount of benzene as white needles, m.p. 158–160°. (Found: C, 57·90; H, 7·21; N, 3·83. $C_{18}H_{26}ClNO_3S$ requires: C, 58·13; H, 7·04; N, 3·76%.) XIIIa suspended in cold water and cautiously neutralized with NH_4OH gave IX in 92% yield.

(b) *Reaction of* XIIIa *with lithium aluminium hydride.* The hydrochloride XIIIa (3 g, 9 mmoles) was suspended in dry ether (200 ml) under vigorous stirring. A suspension of LAH (0·2 g, 50 mmoles) in dry ether (50 ml) was added all at once. The stirring was carried on at room temp for 3 hr. The solid was filtered off and the ethereal soln, on evaporation under red. press, afforded IX (1·4 g, 52% yield), m.p. and mixed m.p. 101–102°. The solid which contained some LAH was extracted with a large amount of hot benzene. The unchanged XIIIa (1·5 g, 48% yield) was recovered from the concentrate benzene soln.

(c) *Attempted reaction of* IX *with ethyl azodicarboxylate.* To a soln of IX (2 g, 6 mmoles) in dry benzene (15 ml) ethyl azodicarboxylate (1 g, 6 mmoles) was added. The red soln was allowed to stand at room temp for 168 hr. The solvent was evaporated under red. press and the residue was refluxed for 2 hr with AcOH (6 ml), AcONa (2 g) and H_2O (6 ml). The mixture was cooled, made alkaline with NH_4OH, extracted with benzene and chromatographed on Al_2O_3 (Merck, acc. to Brockmann). By elution with benzene and benzene–acetone (9:1) XI (1·48 g, 93% yield) and ethyl hydrazodicarboxylate (0·7 g) were recovered.

(d) *Ratio of the isomeric enamines in the reaction mixture.* Phenyl vinyl sulfone (4 g, 24 mmoles) was dissolved in dry benzene (15 ml). VII (4 g, 24 mmoles) was added and the soln was refluxed for 4 hr. After cooling, excess ethyl azodicarboxylate (5 g, 30 mmoles) was added. The soln was kept at room temp for 72 hr, the solvent was removed and the oily residue refluxed for 2 hr with AcONa (5 g), AcOH (15 ml) and H_2O (15 ml). After cooling, the mixture was made alkaline with NH_4OH, extracted with benzene and chromatographed on alumina. It was eluted with benzene, benzene–acetone (9:1) and acetone. Every fraction was tested by TLC. The conclusive results of the separation

[14] H. Boehme and H. Bentler, *Chem. Ber.* **89**, 1464 (1956).

were: XI: 16·3 mmoles (68%); XII: 5·63 mmoles (23%); phenyl β-morpholinoethyl sulfone[15]: 2·35 mmoles; *trans*-2,6-bis(N,N'-dicarbethoxyhydrazino)cyclohexanone[5]: 1·34 mmoles; ethyl hydrazodicarboxylate: 3·97 mmoles. The reported percentages were calculated with respect to the starting enamine.

2-(β-Phenylsulfonylethyl)cyclohexanone (XI)

(a) Compound IX (1·8 g) was refluxed for 2 hr with a mixture of AcOH (6 ml), AcONa (2 g) and H_2O (6 ml). After cooling, the soln was made alkaline with NH_4OH and the ppt after standing overnight in refrigerator, was filtered off (1·3 g, 93% yield) and recrystallized from ligroin as white needles, m.p. 71–72°. (Found: C, 63·07; H, 6·88; S, 12·23. $C_{14}H_{18}O_3S$ requires: C, 63·13; H, 6·81; S, 12·03%.) IR spectrum: 1700 cm^{-1} (CO); 1310 and 1350 cm^{-1} (SO_2). XI gave a *p-nitrophenyl hydrazone*, m.p. 139–140°. (Found: N, 10·56. $C_{20}N_{23}N_3O_4S$ requires: N, 10·46%.)

(b) A mixture of 1-N-morpholino-cyclohexene (3·35 g) and phenyl β-chloroethyl sulfone[16] (2·04 g) in dry dioxan (8 ml) was refluxed for 12 hr. The solid formed by cooling was filtered off and washed with ether. To the combined filtrates 10% HCl (10 ml) was added and the resulting soln was refluxed for 5 hr. The soln was then concentrated until cloudy, diluted with water and extracted with ether. The solid obtained by removal of the solvent was recrystallized from ligroin as white needles, m.p. and mixed m.p. 71–72°.

Thermal conversion of IX *into* X

Compound IX (1 g, 3 mmoles) was dissolved in dry benzene (10 ml), refluxed for 24 hr and then ethyl azodicarboxylate (0·5 g, 3 mmoles) was added. The soln was allowed to stand at room temp for 72 hr, the solvent was evaporated and the residue treated with AcOH, AcONa and H_2O as described for the preparation of XI. After extraction with benzene and chromatographic separation on alumina, XII (0·5 g, 38% yield) was isolated. Use of protic solvents, as for instance EtOH, or addition of catalytic amounts of TsOH, during the heating of IX, did not affect the results of conversion.

Reaction of 1-N-*piperidino-cyclohexene with phenyl vinyl sulfone*

(a) 1-N-*Piperidino-2-(β-phenylsulfonylethyl)cyclohex-6-ene* (XIV). A mixture of phenyl vinyl sulfone (5 g, 30 mmoles) and 1-N-piperidino-cyclohexene (5 g, 30 mmoles) in dry benzene (15 ml) was refluxed for 4 hr. After removal of the solvent under red. press, dry ether was added. By standing in refrigerator for 1–2 hr, XIV was obtained as a solid (4 g). The product was filtered and washed with a few ml dry ether yielding white crystals, m.p. 89–90°. (Found: C, 67·81; H, 8·34; N, 4·07. $C_{19}H_{27}NO_2S$ requires: C, 68·44; H, 8·16; N, 4·20%.)

XIV was found to be extremely unstable and even after short storage it changed into the ketone XI. Freshly prepared, it reacted with ethyl azodicarboxylate to give XII, as reported.

(b) *Ratio of isomeric enamines in the reaction mixture.* A soln of 1-N-piperidino-cyclohexene (4 g, 24 mmoles) and phenyl vinyl sulfone (4 g, 24 mmoles) in dry benzene (15 ml) was refluxed for 4 hr. After cooling, ethyl azodicarboxylate (5 g, 30 mmoles) was added and the mixture was worked up as described for the reaction of 1-N-morpholino-cyclohexene. The results of the chromatographic separation (with respect to the starting enamine) were: XI: 4·28 mmoles (18%); XII: 15·5 mmoles (65%); ethyl hydrazodicarboxylate: 7·61 mmoles.

The same reaction was carried out at room temp for 48 hr using the same amounts of reagents; after addition of ethyl azodicarboxylate, the mixture was worked up as described. The results were: XI: 15·3 mmoles (65%); XII: 5 mmoles (21%); ethyl hydrazodicarboxylate: 11·36 mmoles.

2-(β-Phenylsulfonylethyl)-6-(N,N'-dicarbethoxyhydrazino)cyclohexanone (XII)

Compound XIV (1 g, 3 mmoles) was dissolved in dry benzene (10 ml), ethyl azodicarboxylate (0·52 g, 3 mmoles) was added and the soln was kept at room temp for 72 hr. The solvent was removed under red. press and 10% HCl (10 ml) was added. After standing at room temp for 48 hr, XII as a

[15] Ju-Shih Tsung and Ju-Yiin Chi, *Hua Hsüeh Hsüeh Pao* **26**, 31 (1960); *Chem. Abstr.* **56**, II, 17635 (1961).

[16] G. Farina, F. Montanari and A. Negrini, *Gazz. Chim. Ital.* **89**, 1548 (1959).

solid was obtained (1·2 g, 90% yield) as white crystals, m.p. 138–140° (XIIa). (Found: C, 54·64; H, 6·33; N, 6·24. $C_{20}H_{28}N_2O_7S$ requires: C, 54·52; H, 6·40; N, 6·38%.) IR spectrum: 3310 cm^{-1} (NH). NMR spectrum (chf): 3·31 τ (—N*H*—); 5·25 τ (>C*H*—N—NH—); 5·83 τ (—C*H*$_2$—CH$_2$); 6·93 τ (—C*H*$_2$—SO$_2$—); 8·77 τ (—CH$_2$—C*H*$_2$). XIIa gave a *p-nitrophenylhydrazone* which after several recrystallizations had m.p. 177–178°. (Found: C, 54·48; H, 5·75; N, 12·29. $C_{26}H_{32}N_6O_8S$ requires: C, 54·24; H, 5·77; N, 12·17%.)

When the hydrolysis was carried out by heating with AcONa and dil AcOH, the isomeric XIIb, m.p. 105–107° was obtained. The same compound was formed also on refluxing XIIa in dil AcOH. (Found: C, 54·19; H, 6·68; N, 6·50%.) IR spectrum: 3280 cm^{-1} (NH). NMR spectrum (chf): 2·27 τ (C$_6$*H*$_5$—); 3·31 τ (—N*H*—); 5·19 τ (>C*H*—N—NH—); 5·81 τ (—C*H*$_2$—CH$_2$); 6·82 τ (—C*H*$_2$—SO$_2$—); 8·75 τ (—CH$_2$—C*H*$_2$). The *p*-nitrophenylhydrazone of XIIb was found to be identical to that of XIIa.

Reaction of 1-N-*pyrrolidino-cyclohexene with phenyl vinyl sulfone*

1-N-Pyrrolidino-cyclohexene (3·6 g, 24 mmoles) and phenyl vinyl sulfone (4 g, 24 mmoles) in dry benzene (15 ml) were refluxed for 4 hr. After cooling, ethyl azodicarboxylate (5 g, 30 mmoles) was added and the mixture was worked up as described in the previous sections. The ratio of isomeric enamines followed from the results of the chromatographic separation (with respect to the starting enamine): XI: 1·96 mmoles (8%); XII: 19·3 mmoles (81%); ethyl hydrazodicarboxylate: 3·78 mmoles.

The same reaction, carried out at room temp for 48 hr, afforded: XI: 3·38 mmoles (13%); XII: 17·68 mmoles (67%); ethyl hydrazodicarboxylate: 5 mmoles.

2,6-*Bis-(β-phenylsulfonylethyl)cyclohexanone* (XV)

1-N-Pyrrolidino-cyclohexene (4·5 g, 30 mmoles) and phenyl vinyl sulfone (5 g, 30 mmoles) in dry benzene (40 ml) were refluxed for 4 hr. Phenyl vinyl sulfone (5 g, 30 mmoles) was added and the soln was refluxed for further 4 hr. The solvent was removed, 10% HCl (40 ml) was added, the mixture was kept at room temp for 48 hr and then extracted with benzene. After evaporating the solvent, the residue was treated with cold EtOH (10–15 ml) and XV (3·5 g) was obtained as a solid which recrystallized from EtOH, as white crystals, m.p. 108–110°. (Found: C, 60·52; H, 6·46. $C_{22}H_{26}O_5S_2$ requires: C, 60·80; H, 6·03%.) IR spectrum: 1700 cm^{-1} (CO); 1310 and 1154 cm^{-1} (SO_2). *p-nitrophenylhydrazone* m.p. 170–171°. (Found: N, 7·53. $C_{28}H_{31}N_5O_6S_2$ requires: N, 7·37%.) From ethanolic liquors a mixture of mono- and bis-derivative was obtained.

By treating the compound m.p. 108–110° with EtONa in EtOH on a steam bath for 1 hr and allowing to stand at room temp overnight, or refluxing for 30 hr in EtOH with catalytic amounts of TsOH, an isomeric product, m.p. 124–124·5° was recovered. (Found: C, 60·98; H, 5·97%.) IR spectrum: 1708 cm^{-1} (CO); 1300 and 1152 cm^{-1} (SO_2).

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