Studies of Benzoylsulfene. V.[1] The Reaction of Benzoylsulfene with Enamines

Otohiko TSUGE, Sumio IWANAMI, and Shigeru HAGIO[2]
Research Institute of Industrial Science, Kyushu University, Hakozaki, Fukuoka
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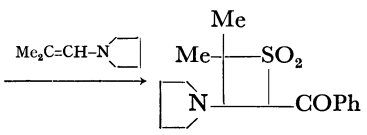
The reaction of benzoylmethanesulfonyl chloride with enamines derived from cyclohexanone in the presence of triethylamine has been studied. The chloride reacted with 1-(1-morpholino)- and 1-(1-piperidino)cyclohexene in the presence of triethylamine, affording the corresponding acyclic sulfones. On the other hand, the reaction of the chloride with 1-(1-pyrrolidinyl)cyclohexene gave 2-benzoylmethanesulfonylcyclohexanone and 2,3-dibenzoyl-2,3,4,5,6,7-hexahydrothianaphthene 1,1-dioxide. The latter compound, whose structure corresponded to the compound derived from the 2:1 adduct of benzoylsulfene and the enamine with the elimination of sulfur dioxide and pyrrolidine, reacted with hydrazine hydrate to give 1,4-diphenyl-5*a*,6,7,8,9,9*a*-hexahydrothianaphtheno[2,3-*d*]-pyridazine, which was then transformed into 3,4,6-triphenylpyridazine.

In general, sulfenes ($RCH{=}SO_2$) generated *in situ* from aliphatic sulfonyl chlorides and triethylamine (NEt_3) react with enamines derived from aldehydes and cyclic ketones to give four-membered cyclic sulfones. Examples are the additions of methanesulfonyl chloride to 2-methyl-1-pyrrolidinyl-1-propene[3] and 1-(1-morpholino)cyclohexene[4] in the presence of NEt_3, which gave the corresponding thiethane 1,1-dioxides.

However, the study concerning the reaction of benzoylmethanesulfonyl chloride (I) with an enamine in the presence of NEt_3 has not been extended beyond that of Opitz,[5] who reported that the reaction of benzoylsulfene ($PhCOCH{=}SO_2$), generated from I and NEt_3, with 2-methyl-1-pyrrolidinyl-1-propene gave the four-membered cyclic sulfone, whose structure corresponded to the (2+2) cycloadduct of benzoylsulfene to the enamine.

$$\underset{\text{I}}{PhCOCH_2SO_2Cl} \xrightarrow[NEt_3]{-HCl} [PhCOCH{=}SO_2]$$



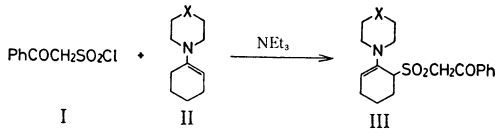
In previous papers, the reactions of I with anils[6] and carbodiimides[7] in the presence of NEt_3 were investigated and it was found that the corresponding (4+2) and/or (2+2) cycloadducts of benzoylsulfene to the C=N bond were formed. These facts indicate that benzoylsulfene is more reactive than usual sulfenes ($RCH{=}SO_2$) and that, in the cycloaddition reaction benzoylsulfene behaves as a 1,2- or 1,4-dipole.

We plan to develop the cycloaddition reactions of benzoylsulfene with various compounds. In the present paper we wish to report on the reaction of benzoylsulfene with enamines derived from cyclohexanone, which unexpectedly led to the formation of acyclic sulfones and an abnormal product.

Results and Discussion

The reaction of benzoylmethanesulfonyl chloride (I) with equimolar amounts of 1-(1-morpholino)cyclohexene (IIa) and NEt_3 in dioxane at room temperature for 1.5 hr gave a crystalline compound, IIIa, mp 135°C (decomp.), in a 61% yield, besides triethylammonium chloride in a quantitative yield. The results of elemental analysis and the molecular weight (M^+ *m/e* 349) of IIIa were consistent with the expected 1:1 adduct of benzoylsulfene and IIa. The IR spectrum of IIIa exhibited characteristic bands ascribed to the $\nu_{C=O}$ and $\nu_{C=C}$ at 1685 and 1640 cm^{-1} respectively. On the other hand, the NMR spectrum in deuteriochloroform ($CDCl_3$) showed signals at τ 5.5 (1H, $\geqslant C\underline{H}$, multiplet), 5.13 and 4.63 (each 1H, $-SO_2-C\underline{H}_2-COPh$, doublet, J= 15 Hz), and 4.56 (1H, $=C\underline{H}-$, triplet, J=3.7 Hz), besides signals of cyclohexenyl- and morpholino-methylene protons and of phenyl protons.

On the basis of these spectral data and the following chemical transformations, it seems reasonable to conclude that IIIa is 6-benzoylmethanesulfonyl-1-(1-morpholino)cyclohexene.



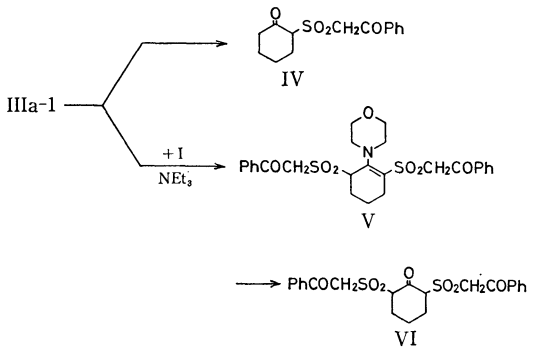
I II III

a: X=O, b: X=CH_2

The hydrolysis of IIIa with dilute hydrochloric acid gave 2-benzoylmethanesulfonylcyclohexanone (IV), mp 103°C (decomp.), in an almost quantitative yield; its structure was confirmed by the spectral studies as well as by the elemental analysis. Furthermore, IIIa reacted with I in the presence of NEt_3 to afford 1,3-di(benzoylmethanesulfonyl)-2-(1-morpholino)cyclohexene (V), mp 152.5—153°C (decomp.), which was subsequently hydrolyzed to 2,6-di(benzoylmethanesulfonyl)-cyclohexanone (VI), mp 141—142°C, in a 37% yield. The structures of V and VI were established on the basis of the spectral studies and of the elemental analyses.

1) Part IV in this series: O. Tsuge and S. Iwanami, This Bulletin, **44**, 2750 (1971).
2) Present address: Sanyo Kasei Co., Ltd., Kyoto-shi.
3) G. Opitz and H. Adolph, *Angew. Chem.*, **74**, 77 (1962).
4) G. Stork and I. Borowitz, *J. Amer. Chem. Soc.*, **84**, 313 (1962).
5) G. Opitz, *Angew. Chem.*, **79**, 162 (1967).
6) O. Tsuge and S. Iwanami, This Bulletin, **43**, 3543 (1970).
7) O. Tsuge and S. Iwanami, *Nippon Kagaku Zasshi*, **92**, 448 (1971).

The mass spectrum of IIIa was also in harmony with the proposed structure.



A similar reaction of I with 1-(1-piperidino)cyclohexene (IIb) in the presence of NEt_3 gave 6-benzoylmethanesulfonyl-1-(1-piperidino)cyclohexene (IIIb), mp 151°C (decomp.), in a 61% yield.

On the other hand, I reacted with 1-(1-pyrrolidinyl)-cyclohexene (IIc) under similar conditions to give IV and a novel product, VII, mp 183°C (decomp.), in 11 and 22% yields respectively.

The compound VII was assumed, as a result of the spectral studies and the elemental analysis as well as the chemical transformations, to be 2,3,4,5,6,7-hexahydro-2,3-dibenzoylthianaphthene 1,1-dioxide. The molecular formula ($C_{22}H_{20}O_4S$) of VII was in agreement with that of the compound derived from a 2:1 adduct of benzoylsulfene and IIc upon the elimination of sulfur dioxide and pyrrolidine. It is obvious that VII contains two benzoyl groups in the molecule, because the hydrolysis of VII with methanolic sodium hydroxide afforded two moles of benzoic acid per mole of VII, and the IR spectrum of VII showed characteristic bands at 1670 ($\nu_{C=O}$), 1300 and 1130 cm^{-1} (ν_{SO_2}). In the mass spectrum, the parent ion peak (M^+) appeared at *m/e* 380, together with major peaks at *m/e* 316 (M^+-SO_2), 211 (316^+-PhCO), 106 (211^+-PhCO) and 105 ($PhCO^+$).

The NMR spectrum of VII is illustrated in Fig. 1. As is shown in Fig. 1, two methine protons appeared at τ 4.48 (1H, doublet with J=5.5 Hz) and 4.20 (1H, multiplet, changed to a doublet with J=5.5 Hz when irradiated at τ 7.6 (2H, quasi-equatorial protons at the 4- and 7-positions)) respectively.

Furthermore, VII reacted with hydrazine hydrate to give 1,4-diphenyl-5*a*,6,7,8,9,9*a*-hexahydrothianaphtheno[2,3-*d*]pyridazine (VIII), mp 198°C (decomp.), in a quantitative yield. The structure of VIII was confirmed by the spectral studies and elemental analysis as well as by the chemical transformation. The NMR spectrum of VIII in $CDCl_3$ showed a multiplet (2H, two methine protons) at τ 6.35; this fact seems to exclude the possibility of an alternate structure, VIII', for VIII.

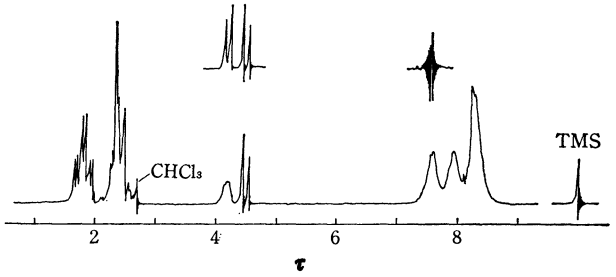
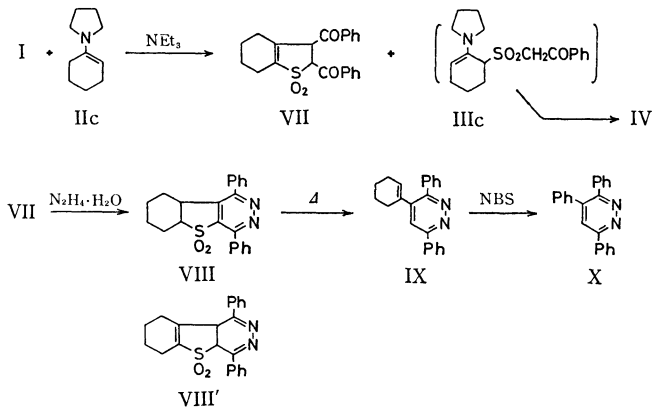


Fig. 1. NMR spectrum of VII in $CDCl_3$.



The thermal decomposition of VIII at 210°C gave 4-(1-cyclohexenyl)-3,6-diphenylpyridazine (IX), mp 160°C, whose structure was established by the spectral studies and by the transformation to 3,4,6-triphenylpyridazine (X) in a 33% yield. The treatment of IX with *N*-bromosuccinimide in carbon tetrachloride afforded X, mp 176°C (lit,[8] mp 176—177.5°C), which was identical with an authentic sample prepared by the reported method.[8]

Incidentally, the formation of IV in the reaction of I with IIc may be illustrated by the hydrolysis of the initially-formed 6-benzoylmethanesulfonyl-1-(1-pyrrolydinyl)cyclohexene (IIIc).

It is known that, in the reaction of sulfonyl chlorides with enamines in the presence of NEt_3, the formation of acyclic sulfones is favored by increasing the substitution at the α-carbon of the sulfonyl chloride and also of the enamine.[9] Recently, Looker[10] found that the additions of methanesulfonyl and arenesulfonyl chlorides to 1,3-diphenyl-2-(1-pyrrolidinyl)propene in the presence of NEt_3 gave the corresponding acyclic sulfones, and suggested that the acyclic sulfones were formed by the ring opening of the initially-formed cyclic sulfones.

The reaction of methanesulfonyl chloride with IIa gave the four-membered cyclic sulfones, as was mentioned at the beginning of this paper, while phenylmethanesulfonyl chloride reacted with IIc to afford, on hydrolysis, 2-phenylmethanesulfonylcyclohexanone, which was assumed to be derived from 1-phenylmethanesulfonyl-2-(1-pyrrolidinyl)cyclohexene.[10]

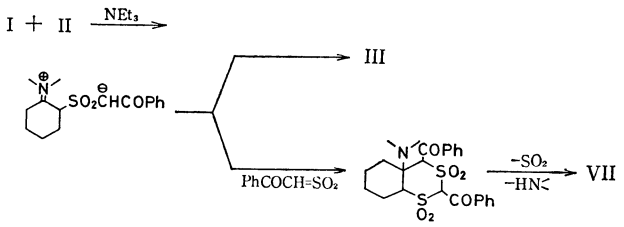
It is, then, of interest to form acyclic sulfones III and/or the hexahydrothianaphthene VII *via* the reaction of benzoylsulfene with II.

Although the exact course of the reaction of benzoylsulfene with II is not clear, the formation of the betaine intermediate by a two-step sequence (the formation of a betaine intermediate, followed by proton transfer)

8) R. A. Carboni and R. V. Lindsey, Jr., *J. Amer. Chem. Soc.*, **81**, 4342 (1959).

9) A. G. Cook, "Enamines: Synthesis, Structure, and Reactions," Marcel Dekker, New York and London (1969), p. 115.

10) J. J. Looker, *J. Org. Chem.*, **31**, 2973 (1966).



seems more reasonable than that through the ring opening of a cyclic sulfone. On the other hand, the formation of VII may be explained if the further addition of benzoylsulfene to the betaine intermediate and the subsequent elimination of both sulfur dioxide and pyrrolidine are assumed.

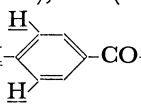
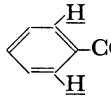
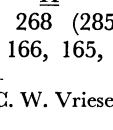
Experimental

All the melting points are uncorrected. The IR spectra were measured in KBr disks, while the NMR spectra were recorded on a 60 MHz Hitachi R-20 NMR spectrometer, using TMS as the internal reference. The mass spectra were obtained on a Hitachi RMS-4 mass spectrometer, using a direct inlet and an ionization energy of 70 eV.

Materials. Benzoylmethanesulfonyl chloride (I), mp 88°C (lit,[11] mp 87.5—88.2°C), was prepared according to the method of Truce and Vriesen.[11] 1-(1-Morpholino)- (IIa), bp 105—107°C/10 mmHg (lit,[12] bp 113—114°C/12 mmHg), 1-(1-piperidino)- (IIb), bp 107—109°C/13 mmHg (lit,[13] bp 108.5/12 mmHg) and 1-(1-pyrrolidinyl)cyclohexene (IIc), bp 87—88°C/3 mmHg (lit,[13] bp 110—111°C/12 mmHg) were prepared from cyclohexanone and the corresponding amines.

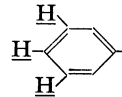
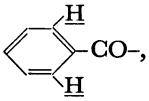
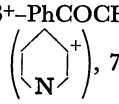
Reaction of I with IIa in the Presence of NEt_3. To a solution of 1.7 g (0.01 mol) of IIa and 1.0 g (0.01 mol) of NEt_3 in 10 m*l* of dioxane, a solution of 2.2 g (0.01 mol) of I in 40 m*l* of dioxane was added, drop by drop, at room temperature over a period of 30 min while the mixture was being stirred. After the reaction mixture had been stirred at the same temperature for 1 hr, triethylammonium chloride precipitated in a quantitative yield was removed by filtration. The filtrate was evaporated *in vacuo* to leave a residue, which was crystallized on trituration with methanol. Recrystallization from methanol gave 6-benzoylmethanesulfonyl-1-(1-morpholino)cyclohexene (IIIa) mp 135°C (decomp.), as colorless prisms. Yield, 2.2 g (61%).

Found: C, 61.90; H, 6.73; N, 3.97%. Calcd for $C_{18}H_{23}O_4NS$: C, 61.88; H, 6.64; N, 4.01%.

NMR ($CDCl_3$): τ 6.7—8.4 (10H, C<u>H</u>$_2$ in cyclohexenyl ring and -C<u>H</u>$_2$-N-C<u>H</u>$_2$-, multiplet), 6.38 (4H, -C<u>H</u>$_2$-O-C<u>H</u>$_2$-, triplet), 5.5 (1H, >C<u>H</u>, multiplet), 5.13, 4.63 (each 1H, -SO_2-C<u>H</u>$_2$-COPh, doublet, J=15 Hz), 4.56 (1H, =C<u>H</u>-, triplet, J=3.7 Hz), 2.3—2.55 (3H,  , multiplet), 1.8—2.1 (2H,  , multiplet). Mass: *m/e* 349 (M^+), 285 (M^+-SO_2), 268 (285$^+$-OH), 180 (285$^+$-PhCO), 167 (285$^+$-PhCOCH), 166, 165, 164, 163, 120 ($PhCOCH_3^+$), 105 ($PhCO^+$), 86  , 77 (Ph^+).

A similar reaction of I with IIb in the presence of NEt_3 gave 6-benzoylmethanesulfonyl-1-(1-piperidino)cyclohexene (IIIb), mp 151°C (decomp.), as colorless prisms in a 61% yield.

Found: C, 65.68; H, 7.50; N, 4.00%. Calcd for $C_{19}H_{25}O_3NS$: C, 65.69; H, 7.25; N, 4.03%.

IR: cm^{-1} 1685 ($\nu_{C=O}$), 1640 ($\nu_{C=C}$), 1300, 1115 (ν_{SO_2}). NMR ($CDCl_3$): τ 6.1—8.9 (16H, C<u>H</u>$_2$ in rings, multiplet), 5.5 (1H, >C<u>H</u>, multiplet), 4.8—5.3 (2H, -SO_2-C<u>H</u>$_2$-COPh, multiplet), 4.6 (1H, =C<u>H</u>-, broad triplet), 2.3—2.6 (3H,  , multiplet), 1.8—2.0 (2H,  , multiplet). Mass: *m/e* 347 (M^+), 283 (M^+-SO_2), 178 (283$^+$-PhCO), 165 (283$^+$-PhCOCH), 164, 163, 120 ($PhCOCH_3^+$), 105 ($PhCO^+$), 84  , 77 (Ph^+).

Hydrolysis of IIIa. After a suspension of 100 mg of IIIa in 6 m*l* of 1 N aqueous hydrochloric acid had been stirred at room temperature for 1 hr, the crystals were collected by filtration, washed with water, and then dried; yield, 75 mg (93%). Recrystallization from methanol gave 2-benzoylmethanesulfonylcyclohexanone (IV), mp 103°C (decomp.), as colorless prisms.

Found: C, 59.95; H, 5.82%. Calcd for $C_{14}H_{16}O_4S$: C, 59.99; H, 5.75%. IR: cm^{-1} 1710, 1680 ($\nu_{C=O}$). NMR ($CDCl_3$): τ 7.2—8.4 (8H, CH_2 in cyclohexanone ring, multiplet), 5.55 (1H, >C<u>H</u>, double doublet, J=6 and 8 Hz), 1.9—2.6 (5H, phenyl protons, multiplet). Mass: *m/e* 280 (M^+), 216 (M^+-SO_2), 215, 188 (216$^+$-CO), 161 (M^+-PhCOC<u>H</u>$_2$), 120 ($PhCOCH_3^+$), 105 ($PhCO^+$), 77 (Ph^+).

Similarly, 100 mg of IIIb were hydrolyzed with hydrochloric acid to afford 74 mg (92%) of IV.

Reaction of IIIa with I in the Presence of NEt_3. To a stirred solution of 2.2 g of IIIa and 0.6 g of NEt_3 in 20 m*l* of dioxane, a solution of 1.4 g of I in 30 m*l* of dioxane was added, drop by drop, at room temperature over a period of 30 min. After the reaction mixture had been stirred at the same temperature for 30 min, triethylammonium chloride (0.85 g, 96%) was removed by filtration. The filtrate was evaporated *in vacuo* to leave a residue, from which IIIa (1.1 g, 48%) was separated when it was treated with 10 m*l* of methanol. The methanol filtrate was allowed to stand overnight to afford 1.1 g (37%) of 1,3-di(benzoylmethanesulfonyl)-2-(1-morpholino)cyclohexene (V), which, on recrystallization from methanol, gave colorless prisms, mp 152.5—153°C (decomp.).

Found: C, 58.93; H, 5.76; N, 2.93%. Calcd for $C_{26}H_{29}O_7NS_2$: C, 58.75; H, 5.50; N, 2.63%. IR: cm^{-1} 1680 ($\nu_{C=O}$), 1610 ($\nu_{C=C}$), 1300, 1120 (ν_{SO_2}). NMR ($CDCl_3$): τ 6.0—8.5 (14H, C<u>H</u>$_2$ in cyclohexenyl and morpholino ring, multiplet), 5.18, 5.32 (each 1H, -SO_2-C<u>H</u>$_2$-COPh, doublet, J=17.5 Hz), 4.70, 5.11 (each 1H, -SO_2-C<u>H</u>$_2$-COPh, doublet, J=14.5 Hz), 5.10 (1H, >C<u>H</u>, multiplet), 1.8—2.6 (10H, phenyl protons, multiplet). Mass: *m/e* 349 (M^+-PhCOCH=SO_2).

Hydrolysis of V. A suspension of 0.3 g of V in 15 m*l* of methanol was refluxed with 0.5 m*l* of concentrated hydrochloric acid for 3 hr. The reaction mixture was then evaporated *in vacuo* to leave crystals, which, on recrystallization from a benzene-petroleum benzine (bp 45—60°C) mixture, gave 0.23 g (95%) of 2,6-di(benzoylmethanesulfonyl)cyclohexanone (VI), mp 141—142°C, as colorless prisms.

Found: C, 56.99; H, 4.54%. Calcd for $C_{22}H_{22}O_7S_2$: C,

11) W. E. Truce and C. W. Vriesen, *J. Amer. Chem. Soc.*, **75**. 2525 (1953).

12) R. Dulon, E. Elikik, and A. Veillard, *Bull. Soc. Chim. Fr.* **1960**, 967.

13) G. Opitz and E. Tempel, *Ann. Chem.*, **699**, 74 (1966).

57.14; H, 4.80%. IR: cm^{-1} 1712 ($\nu_{C=O}$), 1680 ($\nu_{C=O}$), 1310, 1125 (ν_{SO_2}). NMR ($CDCl_3$): τ 7.0—8.2 (6H, $C\underline{H}_2$ in cyclohexanone ring, multiplet), 5.3 (2H, $>C\underline{H}$, multiplet), 5.05 (4H, $-SO_2-C\underline{H}_2-COPh$, singlet), 1.9—2.7 (10H, phenyl protons, multiplet).

Reaction of I with IIc in the Presence of NEt_3. The reaction of 2.2 g of I with 1.5 g of IIc in the presence of 1.0 g of NEt_3 in dioxane was carried out in a manner similar to that used in the reaction of IIa, and then triethylammonium chloride was removed by filtration. The filtrate was evaporated *in vacuo* to leave a residue, which was crystallized on trituration with methanol. Filtration and recrystallization from methanol gave 0.37 g (22%) of 2,3-dibenzoyl-2,3,4,5,6,7-hexahydrothianaphthene 1,1-dioxide (VII), mp 183°C (decomp.), as colorless needles.

Found: C, 69.47; H, 5.36%. Calcd for $C_{22}H_{20}O_4S$: C, 69.46; H, 5.30%.

The compound IV was obtained from the filtrate; yield, 0.3 g (11%).

Hydrolysis of VII. A solution of 0.4 g of VII in 30 m*l* of methanol was stirred with 1 m*l* of 1 N aqueous sodium hydroxide at room temperature for 12 hr. The reaction mixture was evaporated *in vacuo*, and then a residue was extracted with benzene and water. The water extract was neutralized with hydrochloric acid, giving 0.21 g of benzoic acid, while from the benzene-extract an unidentified substance was obtained in a trace amount.

1,4-Diphenyl-5a,6,7,8,9,9a-hexahydrothianaphtheno[2,3-d]pyridazine (VIII). After a solution of 0.11 g of VII in 30 m*l* of methanol had been stirred with three drops of 80% hydrazine hydrate at room temperature for 3 hr, filtration afforded yellow crystals. Recrystallization from methanol gave 90 mg (83%) of VIII, mp 198°C (decomp.), as yellow needles.

Found: C, 69.95; H, 5.42; N, 7.38%. Calcd for $C_{22}H_{20}O_2N_2S$: C, 70.20; H, 5.36; N, 7.44%. IR: cm^{-1} 1312, 1135 (ν_{SO_2}). Mass: *m/e* 376 (M^+), 312 (M^+-SO_2).

Thermal Decomposition of VIII. After the thermal decomposition of 350 mg of VIII had been carried out at 210°C for 10 min, the product was extracted with hot ligroin (bp 60—85°C). The ligroin-extract was evaporated *in vacuo* to leave a residue, which, on recrystallization from benzene, gave 4-(1-cyclohexenyl)-3,6-diphenylpyridazine (IX), mp 160°C, as yellow prisms. Yield, 96 mg (33%).

Found: C, 84.40; H, 6.29; N, 8.71%. Calcd for $C_{22}H_{20}N_2$: C, 84.58; H, 6.45; N, 8.97%. NMR ($CDCl_3$): τ 7.5—8.7 (8H, $C\underline{H}_2$, multiplet), 4.0 (1H, $=C\underline{H}-$, multiplet), 1.6—2.8 (11H, phenyl protons, multiplet). Mass: *m/e* 312 (M^+), 308 (M^+-2H_2), 283 (M^+-N_2-H).

3,4,6-Triphenylpyridazine (X). A mixture of 200 mg of IX and 200 mg of *N*-bromosuccinimide in 100 m*l* of carbon tetrachloride was refluxed with a trace amount of benzoyl peroxide for 20 hr. After the reaction mixture had been concentrated *in vacuo*, the precipitated crystals were washed with a dilute aqueous sodium hydrogensulfide solution and then water. The insoluble substance was chromatographed on silica gel, using chloroform as the eluent, to afford 30 mg (15%) of crystals. Recrystallization from ethanol gave colorless prisms of X, mp 176°C (lit,[8] mp 176—177.5°C), which was identical with an authentic sample prepared by the reported method.[8]