Nitrile Oxides. XI. Dimerization of a Sterically Hindered Nitrile Oxide. Dimesitylfurazan Oxide[1]

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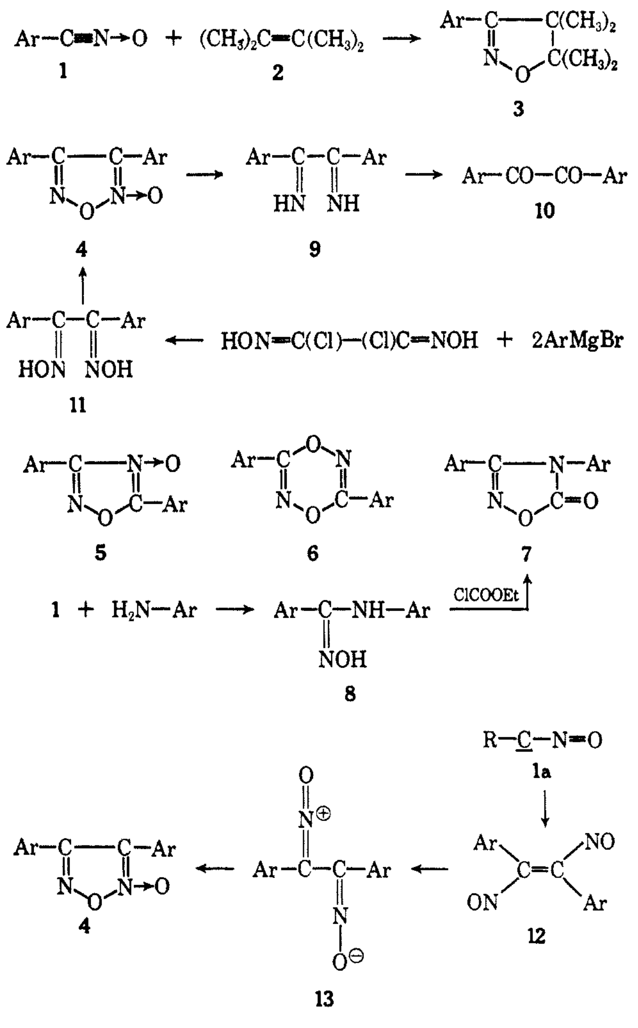
Contrary to earlier reports, mesitonitrile oxide (**1**), under very specific conditions, may form a dimer for which the structure of dimesitylfurazan oxide (**4**) was ascertained by mass spectrum, chemical degradation, and an independent synthesis. Sterical considerations require the dimerization of **1** to **4** to proceed *via* a nitrosocarbene intermediate.

It was reported in earlier communications that aromatic nitrile oxides sterically hindered by substituents of appropriate size in *ortho,ortho* position will not undergo the spontaneous dimerization to furazan oxides (furoxans, 1,2,5-oxadiazole 1-oxides), generally characteristic of nitrile oxides.[1,2] At temperatures above 100°, these nitrile oxides rearranged neatly to the corresponding isocyanates.

The remarkable stability of mesitonitrile oxide (**1**), for instance, was demonstrated by the successful 1,3-dipolar cycloaddition to 2,3-dimethylbutene-2 (**2**), an extremely unreactive olefin. Heretofore, tetrasubstituted ethylenes were generally considered inert toward nitrile oxides.[3] During the reaction of **1** with **2** which required refluxing for 21 hr in an excess of the hydrocarbon, besides a 18% yield of 4,4,5,5-tetramethyl-3-mesityl-4,5-dihydroisoxazole (**3**) and a major amount of mesityl isocyanate, 12% of a dimer of **1**, melting at 130°, was obtained. The same dimer was formed in approximately the same yield when **1** was refluxed for 24–48 hr with a petroleum fraction, free of olefins, boiling at ~65°. The main product under these conditions was mesityl isocyanate. The formation of the dimer is restricted to a rather narrow temperature range; at 50° **1** remained mostly unchanged over comparable reaction times, while at temperatures above 75°, the rearrangement to the isocyanate predominates. If **1** was heated quickly to reflux in an inert higher boiling solvent, such as ligroin (bp 100–110°) or toluene, an almost quantitative conversion to mesityl isocyanate was observed.[2b]

For reasons of analogy, it seemed obvious to assume that the dimer had the structure of a dimesitylfurazan oxide (**4**), were it not for extreme steric hindrance involved in the direct head to head combination of two molecules of **1** to **4**. Further doubt on the furazan oxide structure was cast by the impossibility of deoxygenating the dimer to the corresponding furazan (1,2,5-oxadiazole) by means of trivalent phosphorus compounds, a reaction generally applicable to all furazan oxides investigated so far.[4]

Therefore, the less sterically hindered structures **5**, **6**, or **7** had to be considered too. Structures **5** and **6** would both result from a head to tail dimerization of **1**, while **7** would require 1,3-dipolar cycloaddition of **1** to mesityl isocyanate, shown to be present in the reaction mixture. Formula **7** was ruled out by an independent synthesis. Mesitonitrile oxide (**1**) added mesidine to form mesito-N-mesitylamidoxime (**8**).[5] Compound **8** reacted with ethyl chloroformate under ring closure directly to **7**. The synthetic product was different from the dimer. The infrared spectrum of the dimer is complex (as is that of known diarylfurazan oxides[6]), all major bands are compatible with structure **4**. Since nothing is known about the spectral differences between the furazan oxides and the ring systems **5** and **6**, no valid conclusions can be drawn.



Ar = 2,4,6-trimethylphenyl

The mass spectrum shows, in addition to the parent peak (322), major peaks at 306, 262, 161, and 145. The first one, corresponding to loss of one oxygen, is indica-

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[1] Previous communication: C. Grundmann and R. Richter, *J. Org. Chem.*, **33**, 476 (1968).

[2] (a) C. Grundmann and J. M. Dean, *Angew. Chem.*, **76**, 682 (1964); (b) C. Grundmann and J. M. Dean, *J. Org. Chem.*, **30**, 2809 (1965); (c) C. Grundmann, *Fortschr. Chem. Forsch.*, **7**, 62 (1966).

[3] R. Huisgen, *Angew. Chem.*, **75**, 604 (1963).

[4] C. Grundmann, *Chem. Ber.*, **97**, 575 (1964).

[5] C. Grundmann and H.-D. Frommeld, *J. Org. Chem.*, **31**, 157 (1965).

[6] (a) N. E. Boyer, G. M. Czerniak, H. S. Gutkowsky, and H. R. Synder, *J. Amer. Chem. Soc.*, **77**, 4238 (1955); (b) J. H. Boyer, U. Toggweiler, and G. A. Stoner, *ibid.*, **79**, 1748 (1957).

tive of a heterocyclic N-oxide,[7] thus ruling out structure **6**. The peak at 262 corresponds to loss of the fragment N_2O_2 (60) which is only compatible with the furoxan structure **4** for the dimer, while the peaks at 161 and 145 corresponding to mesitonitrile oxide and mesitonitrile are of no diagnostic value. Under the same conditions, diphenylfurazan oxide shows a strictly analogous pattern with strong peaks at P-16 and P-60.

Reduction of the dimer with zinc and acetic acid did not produce the mesitildioxime (**11**), as expected from analogous experience with other diarylfurazan oxides,[8] but a base $C_{20}H_{24}N_2$, which turned out to be mesitildiimine (**9**). Contrary to the other known ketimines, the compound is surprisingly stable to hydrolysis, but treatment with boiling 2 *N* sulfuric acid converted it neatly into mesityl diketone (**10**) (mesitil), identical with a specimen prepared according to the literature.[9]

Finally, the structure of the dimer was proved by an independent synthesis. Mesitylmagnesium bromide reacted with dichloroglyoxime to mesitildioxime (**11**), a compound which cannot be obtained by oximation of **10**.[10] Dehydrogenation of **11** with sodium hypobromite gave dimesitylfurazan oxide (**4**) identical with the dimer of I.

Although furazan oxide formation from nitrile oxides is probably the longest known reaction of this class of compounds, it is still the least understood mechanistically. 1,3-Dipolar cycloaddition is ruled out, since it violates the principle of maximum gain in σ bonding invariably found valid in all of the many other types of such cycloadditions. Furthermore, 1,3-dipolar cycloaddition, being firmly established as a concerted (four-center, "no mechanism") addition[11] is virtually impossible for steric reasons in the case of mesitonitrile oxide. We are, therefore, inclined to assume that the formation of the furazan oxide might occur—at least in this case—in a multistep reaction by the dimerization of the nitrile oxide to 1,2-dinitrosoethylene **12**, involving the mesomeric structure **1a** with carbene character as first suggested by Huisgen. The transient intermediate **12** rearranges then *via* the dipolar structure **13** to the furazan oxide **4**.

Studies of Stuart–Briegleb models which are supposed to represent a close approximation to the actual spatial requirements or organic molecules indicate that even in the case of the sterically hindered mesitonitrile oxide such a route would still be possible,[12] although the intermediate **12** could only exist in the *trans* configuration. Nevertheless, **4** is a very rigid structure with both aromatic rings twisted severely out of plane with the furazan ring. Even in diphenylfurazan oxide both aromatic rings, although they may rotate freely, cannot be brought simultaneously in one plane with the heterocyclic ring. One would, therefore, expect little difference in the ultraviolet spectra of both compounds; the observed data, however, are in the right direction, showing a hypsochromic shift of the first band of **4** as compared with diphenylfurazan oxide.

In conclusion, the formation of dimesitylfurazan oxide from mesitonitrile oxide might be the first experimental evidence for Huisgen's mechanism, since no other pathway suggested so far for this dimerization could overcome the steric restrictions of this case.

Experimental Section[13]

Reaction of Mesitonitrile Oxide with 2,3-Dimethylbutene-2.—Mesitonitrile oxide (2.0 g) and 2,3-dimethylbutene-2 (4 ml) were heated for 12 hr to 64°, then refluxed (71°) for an additional 9 hr. The reaction mixture, diluted with 200 ml of cyclohexane, was chromatographed through a column of basic aluminum oxide (Woelm). The filtrate and the cyclohexane washings contained only mesityl isocyanate identified as reported earlier.[2b] Benzene extracted from the column a fraction (345 mg) which yielded after recrystallization from methanol 240 mg (12%) of dimesitylfurazan oxide (**4**), mp 129–130°. Further extraction with benzene–ether (50:1) gave a fraction (550 mg, 18%) of 4,4,5,5-tetramethyl-3-mesityl-4,5-dihydroisoxazole (**3**), mp 71°, after recrystallization from petroleum ether (bp 35–45°).

Anal. Calcd for $C_{16}H_{22}NO$: C, 78.32; H, 9.45; N, 5.71; mol wt, 245. Found: C, 78.17; H, 9.50; N, 5.64; mol wt, 240 (osmometric, acetone).

Dimesitylfurazan Oxide from Mesitonitrile Oxide.—Mesitonitrile oxide (1.61 g) and 30 ml of ligroin,[14] bp 60–65° (the minimum amount to afford a homogeneous reaction mixture at the boiling point), were refluxed for 48 hr with exclusion of moisture. The reaction mixture was filtered from small amounts of insolubles, if necessary, then the solvent removed by distillation and the residue subjected to vacuum sublimation in a cold finger apparatus, cooled with Dry Ice and acetone. At 0.01 mm and 40–65° bath temperature, all mesityl isocyanate collected at the condenser within 2–3 hr. The residue was dissolved in methanol (5 ml) and kept overnight at $-10°$, whereby 320 mg (20%) of dimesitylfurazan oxide (**4**) separated. After two recrystallization from methanol colorless shiny leaflets were obtained, mp 133°.

Anal. Calcd for $C_{20}H_{22}N_2O_2$: C, 74.51; H, 6.88; N, 8.69; mol wt, 322. Found: C, 74.67; H, 7.05; N, 8.61; mol wt, 314, 321 (osmometric, acetone or chloroform).

The ultraviolet spectrum of **4** (in ethanol) showed bands at λ_{max} 273 mμ (° 11,000) and diphenyfuroxan (inethanol) showed bands at λ_{max} 283 mμ (ϵ 5700).[6b]

The mass spectra of **4** and diphenylfurazan oxide were determined with the Associated Electrical Industries double focusing mass spectrograph MS 9, 8000 V, 70 eV, temp <250°.

Mesito-N-mesitylamidoxime (8).—Mesitonitrile oxide (0.5 g) and mesidine (0.5 g) were refluxed in methanol (20 ml) for 5 min. Upon gradual dilution with H_2O, the amidoxime crystallized. One recrystallization from methanol yielded 550 mg of pure **8**, mp 202–203° dec.

Anal. Calcd for $C_{19}H_{24}N_2O$: C, 76.99; H, 8.16; N, 9.45. Found: C, 77.25; H, 8.30; N, 9.22.

3,4-Dimesityl-4,5-dihydro-1,2,4-oxadiazolone-5 (7).—Compound **8** (190 mg) and ethyl chloroformate (0.7 ml) were refluxed for 3 hr in chloroform (20 ml). After evaporation of the solvent the residue crystallized on addition of methanol and scratching, 140 mg of **7**, mp 155–156°, were obtained after one recrystallization from methanol.

Anal. Calcd for $C_{20}H_{22}N_2O_2$: N, 8.69. Found: N, 8.75.

Mesitildiimine (9).—Dimesitylfurazan oxide (771 mg) was dissolved on the steam bath in acetic acid (40 ml) and H_2O (8 ml), 8 g of zinc granules (50 mesh) added, the reaction mixture stirred for 4.5 hr at 80–90°, filtered hot, and the undissolved metal washed with 12 ml of acetic acid water (5:1). After addition of 50 ml of H_2O, 24 mg of neutral by-products separated overnight at 0° and were removed by filtration. The filtrate

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[7] A. Chatterjee, P. L. Majunder, and A. B. Ray, *Tetrahedron Lett.*, 159 (1965); T. A. Bryce and J. R. Maxwell, *Chem. Commun.*, 206 (1965).

[8] J. V. R. Kaufman and J. P. Picard, *Chem. Rev.*, **59**, 429 (1959).

[9] R. C. Fuson and T. Corse, *J. Amer. Chem. Soc.*, **60**, 2066 (1938).

[10] E. P. Kohler and R. Baltzly, *ibid.*, **54**, 4015 (1932).

[11] R. Huisgen, *Angew. Chem.*, **75**, 742 (1963).

[12] It must be noted, however, that completely valid conclusions cannot be drawn from these studies, since the appropriate building blocks for some of the structures under consideration do not yet exist, *e.g.*, for $-C\equiv N\rightarrow O$ or $\equiv N\rightarrow O$ in a five-membered ring. But the above considerations are still valid for mesitonitrile which can be built and is certainly less crowded as **1** as far as the C atom involved is concerned. Dimesityl-1,2,5-oxadiazole can be constructed, and it is easily seen on the model that the additional oxygen at N^2 present in **4**, adds little if anything to the steric requirements.

[13] Melting points were determined with the Fisher–Johns melting point apparatus and are uncorrected. Microanalyses were by Galbraith Laboratories, Knoxville, Tenn.

[14] Commercially available Skellysolve B was redistilled and the fraction boiling within the above given limits was used.

was evaporated at the water pump to dryness from a 60° water bath and the residue distilled again to dryness twice after adding each time 25 ml of H_2O in order to complete the removal of acetic acid. The residue dissolved mostly at room temperature in 50 ml of 2 N hydrochloric acid. Again, insoluble neutral products were filtered, and the filtrate was oversaturated with concentrated ammonia, whereupon a crystalline precipitate of **9** (542 mg, 76%) was obtained. After repeated recrystallizations from ligroin slightly yellowish compact prisms, mp 182–183°, were obtained.

Anal. Calcd for $C_{20}H_{24}N_2$: C, 82.14; H, 8.27; N, 9.58; mol wt, 292. Found: C, 81.95; H, 8.25; N, 9.38; mol wt, 291 (osmometric, acetone).

Mesitildiimine was also obtained in 66% yield from mesitildioxime (**11**) by the same procedure. The reduction of dimesitylfurazan oxide with sodium and ethanol gave **9** in 59% yield. Compound **4** was not affected by tin(II) chloride in boiling methanol or by heating with an excess of tri-*n*-butylphosphine for 3 hr to 140°.

Heating **9** (148 mg) with acetic anhydride (4 ml) for 4 hr to 100° yielded on cooling N,N′-diacetylmesitilidiimine (148 mg, 78%). After recrystallization from methanol, pale yellow needles, mp 264°, were obtained.

Anal. Calcd for $C_{24}H_{28}N_2O_2$: C, 76.56; H, 7.50; N, 7.44; mol wt, 376. Found: C, 76.27; H, 7.67; N, 7.26; mol wt, 379 (osmometric, chloroform).

N,N′-Dibenzoylmesitildiimine was obtained in 36% yield by benzoylation of **9** with benzoyl chloride and pyridine in the usual manner. After crystallization from ether, it melted at 247°.

Anal. Calcd for $C_{34}H_{32}N_2O_2$: C, 81.57; H, 6.44. Found: C, 81.74; H, 6.59.

Hydrolysis of Mesitildiimine.—Mesitildiimine (0.3 g) was heated on the steam bath for 3 hr with 30 ml of 2 N sulfuric acid whereby a yellow solid precipitated gradually from the solution. After cooling, the formed product was filtered and washed with water (0.25 g, 85%). One recrystallization yielded pure mesitil (**10**), mp 122°, identical with an authentic specimen.[9] Compound **10** was further characterized by oxidation with sodium peroxide to mesitoic acid according to the procedure given in the literature.[10]

Mesitildioxime (11).—A solution of mesitylmagnesium bromide was prepared from bromomesitylene (80 g), ethylene bromide (40 g), and magnesium turnings (17.5 g) in tetrahydrofuran (100 ml). To avoid precipitation of the Grignard compound 150 ml of tetrahydrofuran was added on completion of the reaction. With ice cooling, a solution of dichloroglyoxime (16 g) in tetrahydrofuran (150 ml) was then added dropwise within 2 hr. After the reaction mixture was left overnight at 25°, 300 ml of the solvent were removed by distillation and the residue was decomposed with ice and saturated ammonium chloride solution. The precipitated **11** was filtered off and was washed thoroughly with dilute hydrochloric acid and H_2O. The dioxime has a strong tendency to adsorb inorganic salts. The crude **11** (22 g, 70%) was recrystallized from dioxane or, preferably, acetic acid, mp 310° dec. A dioxime of structure **11** can occur in several stereoisomers; it has not been ascertained whether this material was uniform in this respect.

Anal. Calcd for $C_{20}H_{24}N_2O_2$: C, 74.04; H, 7.46; N, 8.64. Found: C, 73.96; H, 7.60; N, 8.42.

Dimesitylfurazan Oxide from Mesitildioxime.—Mesitildioxime (3.2 g) was dissolved in warm pyridine (100 ml) and 1 N sodium hydroxide (100 ml). Water (50 ml) was added, and the solution, which must remain clear, cooled quickly to 5°. Within 30 min, a cold solution of 1.6 g of bromine in 100 ml of 2 N sodium hydroxide was added with stirring. After 2 hr, the precipitate was filtered and washed with water. The dimesitylfurazan oxide (**4**) thus obtained (2.4 g, 75%, mp 130°) was almost pure. One recrystallization from ethanol yielded a product, mp 132°, which did not depress the melting point of a specimen prepared from mesitonitrile oxide. The infrared spectra of both samples were strictly superimposable.

Registry No.—**3,** 16031-57-5; **4,** 16031-58-6; **7,** 16031-59-7; **8,** 16031-60-0; **9,** 16031-61-1; **10,** 4746-81-0; **11,** 16031-62-2; N,N′-diacetylmesityldiimine 16031-64-4; N,N′-dibenzoylmesityldiimine, 16031-63-3.

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A Study of the Interaction of 1,3-Diaxial Sulfur Atoms

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A series of ethylene thioketals was prepared by the reaction of 1,3-cyclohexanediones and phloroglucinol with ethanedithiol. The uv spectra and physical properties of these compounds are discussed.

In the reaction between 5,5-dimethyl-1,3-cyclohexanedione and ethanedithiol the bisthioketal, 13,13-dimethyl-1,4,8,11-tetrathiadispiro[4.1.4.3]tetradecane, was isolated. It was noted that compound **4** possessed ultraviolet absorption at 246 mμ which was similar to values reported for acyclic mercaptols. The absorption for cyclic thioketals can be ascribed to resonance interactions as proposed by Fehnel and Carmack.[2]

The distance between the 1,3-diaxial sulfur atoms in **4** is relatively close to that between sulfur atoms in the thioketal ring. This suggested the possibility of the occurrence of 1,3-diaxial sulfur interactions as well as the interactions present within the thioketal ring.

A series of mono-, di-, and triethylene thioketals was synthesized and the ultraviolet spectra studied to determine if 1,3-diaxial and 1,3,5-triaxial sulfur orbital interactions do exist. The observed maxima and extinction coefficients are given in Table I.

The results indicate that there is no marked interaction between 1,3-diaxial sulfur atoms since the long wavelength absorption at 246 mμ remains constant for the series of thioketals studied. The additive effect in the molar extinction coefficients are approximately the values which would be expected with multiple chromophores. However, a proportionately larger increase in the molar extinction coefficient was observed on the introduction of a second thioketal grouping β to the first in the parent compound 1,4-dithiaspiro[4.5]decane (**1**). A simple additive effect would give an extinction coefficient of ~630 but the observed values were 748, 729, and 728, respectively, for **2**,

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(1) Taken in part from the dissertation presented by J. L. Diebold, 1964, to the Graduate School of the University of Kansas in partial fulfillment of the requirements for the Ph.D. Degree.

(2) E. A. Fehnel and M. Carmack, *J. Amer. Chem. Soc.*, **71**, 84 (1959).