2-Hydroxyglutaric Acid Diamide.—A solution of 7 g. of the barium salt of L-2-hydroxyglutaric acid in 40 ml. of water was passed through a short column of the cation exchanger Dowex-50 × 4 (50–100 mesh, H$^+$-form). The column was washed with water and the combined effluents evaporated to dryness *in vacuo* at 30°. The residual oil, 3.5 g., was kept in the desiccator overnight, dissolved in 20 ml. of ice-cold methanol and esterified with diazomethane to yield 4.1 g. of crude dimethyl 2-hydroxyglutarate. This material, 3.5 g., was dissolved in 20 ml. of dry methanol and the solution saturated with ammonia at 0°. After keeping for 24 hr. at room temperature 2.7 g. of the diamide was filtered off, m.p. 181–182° (lit.,[7] 182°) $[\alpha]^{22}_{589}$ −33°, (*l* 2; *c* 1.48 in water).

Anal. Calcd. for $C_5H_{10}O_3N_2$ (146.15): C, 41.09; H, 6.90; N, 19.17. Found: C, 41.03; H, 6.79; N, 18.79.

(+)-1,5-Diamino-2-hydroxypentane Dihydrochloride.—The L-2-hydroxyglutaric acid diamide, 0.5 g., was placed in a small filter paper thimble in the neck of a flask fitted with a reflux condenser. The flask contained a suspension of 1.0 g. of lithium aluminum hydride in 50 ml. of refluxing diglyme.[8] After 20 hr. the amide had been extracted into the boiling solution. After cooling excess lithium aluminum hydride was decomposed with 3 ml. of water followed by 3 ml. of 1 *N* sodium hydroxide. The precipitate was filtered off and washed with hot ethanol. After adjusting to pH 3 the solution was evaporated and the residue put onto a column of Dowex-50 × 4 (200–400 mesh; 54 × 1.2 cm. in 1 *N* hydrochloric acid). The column was eluted with 1 *N* hydrochloric acid (200 ml.) followed by 3 *N* hydrochloric acid which eluted the hydroxyamine after further 70–80 ml. effluent. The amine hydrochloride crystallized on evaporation of the hydrochloric acid *in vacuo* and was recrystallized twice from ethanol to give 0.08 g. of m.p. 166–167°, $[\alpha]^{28}_{589}$ +11.1°, (*l* 1; *c* 2 in water).

Anal. Calcd. for $C_5H_{16}ON_2Cl_2$ (191.1): C, 31.42; H, 8.44; N, 14.66. Found: C, 31.52; H, 8.47; N, 14.11.

(+)-1,5-Dibenzamido-2-hydroxypentane.—(+)-1,5-Diamino-2-hydroxypentane dihydrochloride, 0.09 g., were dissolved in 5 ml. of 1 *N* sodium hydroxide and 0.4 ml. of benzoyl chloride added in portions with stirring. After standing overnight in the refrigerator 0.08 g. of crystals were filtered off and recrystallized from ethyl acetate, m.p. 130–32°, $[\alpha]^{21}_{589}$ +23.6° (*l* 1; *c* 0.84 in pyridine).

Anal. Calcd. for $C_{12}H_{22}O_3N_2$ (326.4): C, 69.92; H, 6.77; N, 8.59. Found: C, 70.08; H, 6.96; N, 8.61.

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(7) C. Ravenna and R. Nuccorini, *Gazz. chim. ital.*, **58**, 861 (1928).

(8) Dried over calcium hydride and redistilled from lithium aluminum hydride.

The Chemistry of Ylids. VIII. Synthesis of Nitrones *via* Sulfur Ylids[1]

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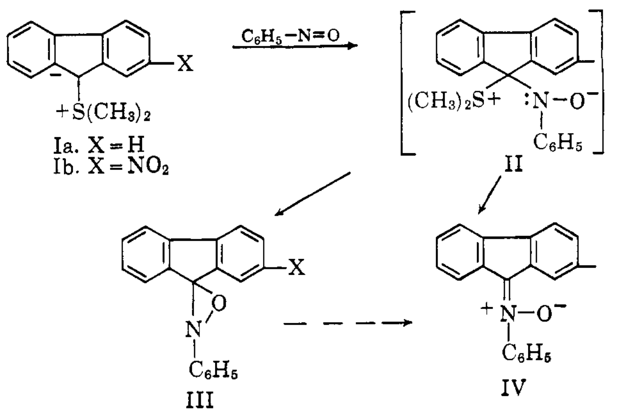
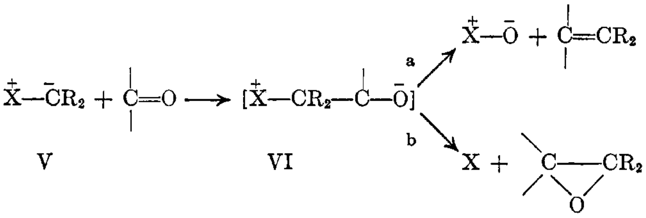
In our original report on the preparation and reactions of sulfur ylids[2] we noted briefly that 9-dimethylsulfoniumfluorenylide (Ia) reacted with nitrosobenzene to form what appeared to be N-phenylfluorenone ketoxime (IVa) rather than the expected oxazirane (IIIa). We wish to report further studies on this reaction.

It has been well established[3] that phosphorus- and arsenic-containing ylids (V. X = PR'$_3$, AsR'$_3$) react with carbonyl compounds by initial attack of the ylid carbanion on the carbonyl carbon to form an intermediate betaine (VI). The reaction goes to completion *via* a four-membered transition state resulting in the ultimate formation of an olefin and the appropriate phosphine oxide or arsine oxide (path a). It has been shown[4] that these same ylids will react with nitrosobenzene in an analogous fashion to form the expected N-phenylimines. For example, triphenylphosphoniumfluorenylide and nitrosobenzene afforded fluorenone anil in 84% yield.[4a]





Johnson and LaCount[2] have recently shown that sulfur ylids (V. X = SR'$_2$) also react with carbonyl compounds by attack of the ylid carbanion on the carbonyl carbon to form a similar betaine intermediate. However, the oxyanion portion of this betaine (VI. X = SR'$_2$) displaced the sulfide group forming an epoxide as the major product (path b). By analogy it was expected that sulfur ylids would react with nitrosobenzene to form oxaziranes (III), thereby providing another synthetic route to these unique compounds. Oxaziranes have been intensely studied since their original synthesis by Emmons.[5]

An exothermic reaction took place upon mixing the ylid (Ia) and nitrosobenzene, ultimately affording a quantitative yield of the *nitrone* (IVa). Microanalytical data and hydrolysis of the product to fluorenone were both consistent with either structure IIIa or IVa. That the product was, in fact, the nitrone (IVa) and not isomeric oxazirane (IIIa) was demonstrated by infrared absorption at 6.06 μ (C=N), 6.51 and 7.48 μ (N=O) and by the ultraviolet spectrum which showed the long wave length absorption (351 mμ) expected of a fluorenylidene system and not the simple fluorenyl spectrum expected for IIIa. The substance was also shown to react in a 1,3-addition reaction with diethyl fumarate to form an isoxazolidine.[6]

The generality of this reaction was demonstrated using 9-dimethylsulfonium-2-nitrofluorenylide (Ib) and dimethylsulfonium(diphenyl)methylide, both of which afforded the corresponding nitrones in good yield when

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(1) (a) We gratefully acknowledge the financial support of the National Science Foundation through Grant No. G-17345; (b) for the previous paper in this series see A. W. Johnson and V. J. Hruby, *J. Am. Chem. Soc.*, **84**, 3586 (1962).

(2) A. W. Johnson and R. B. LaCount, paper VI, *ibid.*, **83**, 417 (1961).

(3) G. Wittig, H. D. Weigmann, and M. Schlosser, *Chem. Ber.*, **94**, 676 (1961); A. W. Johnson and R. B. LaCount, *Tetrahedron*, **9**, 130 (1960).

(4) (a) A. W. Johnson, unpublished observations; (b) A. Schonberg and K. H. Brosowski, *Chem. Ber.*, **92**, 2602 (1959).

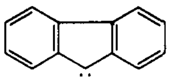
(5) W. D. Emmons, *J. Am. Chem. Soc.*, **79**, 5739 (1957).

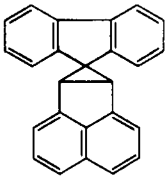
(6) G. R. Delpierre and M. Lamchen, *Proc. Chem. Soc.*, 386 (1960).

reacted with nitrosobenzene. Krohnke[7] had previously shown 9-(1-pyridinium)fluorenylide to react with *p*-nitroso-N,N-dimethylaniline to afford the corresponding nitrone and we have recently shown[2] that the same ylid will react with the unsubstituted nitrosobenzene to afford the nitrone (IVa).

Our curiosity as to the mechanism of the formation of nitrones from these sulfur ylids was aroused since, as mentioned above, we had expected to obtain the oxaziranes. Three explanations for this turn of events seemed feasible and were subsequently tested.

It was conceivable that the sulfur (and nitrogen) ylids were first decomposing to carbenes which then reacted with nitrosobenzene to form nitrones rather than oxaziranes. Franzen[8] has shown that nitrogen ylids can be decomposed to carbenes and several of the by-products from the reaction of the sulfur ylid (Ia) with carbonyl compounds were best accounted for by decomposition of Ia to the fluorenyl carbene (VII).[2] More recent work[1b] has demonstrated that other sulfur ylids can be decomposed under mild conditions to carbenes which can in turn be trapped with acenaphthylene. However, an attempt to trap the carbene by heating the sulfur ylid (Ia) with acenaphthylene gave none of the expected adduct (VIII). It was apparent, therefore, that under the conditions for nitrone formation, the ylid (Ia) was reacting as an ylid and not as a carbene.


VII


VIII

In an effort to determine how a carbene might react with nitrosobenzene we studied the reaction of 9-diazofluorene with the latter. An exothermic reaction took place resulting in the rapid evolution of nitrogen and the precipitation of a high yield of the nitrone (IVa). A similar reaction took place between diphenyldiazomethane and nitrosobenzene, again affording a nitrone. Schonberg and coworkers[9] have shown that diazofluorene will react with acenaphthylene under gentle heating to form the adduct (VIII), thereby demonstrating the facility with which diazofluorene is converted to a carbene. Thus, it initially appeared that the nitrone (IVa) was the product of a carbene reaction with nitrosobenzene. However, it is somewhat problematical whether it was a carbene (VII) or diazofluorene itself that was reacting with nitrosobenzene. Diazofluorene could well be reacting as an ylid, the nucleophilic C-9 of the fluorenyl portion attacking the nitrogen end of the nitroso group. The nitrone would then be the expected product by analogy with the sulfur ylid reactions. The spontaneity with which the reaction took place leads us to prefer the latter explanation and to conclude the nitrone (IVa) not to be the product of a carbene reaction with nitrosobenzene.

As an alternate explanation it appeared possible that the desired oxazirane (IIIa) was in fact the initial product of the ylid reaction but that it had isomerized to the nitrone (IVa) under the reaction conditions. Emmons[5] has shown that oxaziranes can be thermally isomerized to nitrones and Splitter and Calvin[10] noted that N-phenyloxaziranes were particularly labile, rearranging to anilides. As a result, several attempts were made to prepare the oxazirane (IIIa) and determine its stability.

The oxidation of fluorenone anil, a method for oxazirane synthesis developed by Emmons,[5] afforded not the expected IIIa but the isomeric nitrone (IVa). The fact that an oxidation did occur leads us to suspect that the oxazirane was initially formed but rapidly rearranged to the nitrone (IVa) under these conditions. Photolysis of the nitrone (IVa), a procedure by which Splitter and Calvin[10] isomerized nitrones to oxaziranes, gave only unchanged starting material. 9-Diazofluorene and nitrosobenzene would not react below 0°, both substances being recovered unchanged. Between 0 and 5° a red ethereal solution of the two reactants or a solid mixture in a capillary could be observed rapidly changing to yellow with simultaneous evolution of nitrogen and gradual precipitation of the nitrone. No intermediate product or color change could be observed in either case. Thus we were unable to prepare the oxazirane (IIIa). If the latter was an intermediate in the reaction between sulfur ylids and nitrosobenzene, it was obviously very short-lived.

As a third and rather remote explanation for the formation of IVa from the reaction of Ia with nitrosobenzene it was conceivable that in the intermediate betaine (II) the lone electron pair on nitrogen, rather than those on the oxyanion, actually displaced methyl sulfide. This was considered unlikely due to the relative nucleophilicity of the two groups. In addition, if such were the case one might expect to have obtained some nitrone from the reaction of a phosphorus ylid with nitrosobenzene since an analogous betaine intermediate was involved. Such was not the case.

We conclude that the reaction of sulfur and nitrogen ylids and of diazo compounds with nitrosobenzene is best explained by the initial formation of an unisolable oxazirane as a very short-lived intermediate which rapidly isomerized to a nitrone.

Experimental[11]

N-Phenylfluorenone Ketoxime (IVa). A. From the Ylid (Ia).—To a solution of 0.95 g. (8.9 mmoles) of nitrosobenzene in 40 ml. of dry ether was added 2.0 g. (8.9 mmoles) of 9-dimethylsulfoniumfluorenylide (Ia).[2] Nitrogen and heat were evolved and a yellow precipitate formed. After stirring for 3 hr. the yellow precipitate (2.3 g., 96%) was filtered and dried, m.p. 189–191°. Recrystallization from 95% ethanol gave fine yellow needles of IVa, m.p. 194.5–196.5°, $\lambda_{\max}^{\text{Nujol}}$ 6.06, 6.22, 6.51, 7.48, 13.00, 13.75 and 14.75 μ; $\lambda_{\max}^{\text{EtOH}}$ 236 mμ (log ϵ 4.5), 260 (4.4), and 351 (4.3).

Anal. Calcd. for $C_{19}H_{13}NO$: C, 84.10; H, 4.83; N, 5.16. Found: C, 84.40; H, 5.25; N, 5.01.

B. From 9-Diazofluorene[12]—A slurry of 1.92 g. (0.01 mole) of 9-diazofluorene and 1.07 g. (0.01 mole) of nitrosobenzene in 40 ml. of dry ether was stirred for 1 hr. During that time the red color vanished, nitrogen was evolved, and a yellow precipitate

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(7) F. Krohnke, *Chem. Ber.*, **83**, 253 (1950).

(8) V. Franzen, *ibid.*, **93**, 557 (1960); V. Franzen and G. Wittig, *Angew. Chem.*, **72**, 417 (1960).

(9) A. Schonberg, A. Mustafa, and N. Latif, *J. Am. Chem. Soc.*, **75**, 2267 (1953).

(10) J. S. Splitter and M. Calvin, *J. Org. Chem.*, **23**, 651 (1958).

(11) All melting points are uncorrected. Microanalyses were by A. Bernhardt, Mülheim, Germany. Infrared spectra were recorded as Nujol mulls on a Perkin–Elmer Infracord. Ultraviolet spectra were recorded on a B and L 505 Spectronic in 95% ethanol solutions.

(12) This reaction was originally reported by Staudinger and Miescher, *Helv. Chim. Acta*, **2**, 578 (1919).

formed. The latter was filtered and dried (2.38 g., 88%) then recrystallized from 95% ethanol as yellow needles, m.p. 194–196° (lit.,[12] m.p. 192–193°). It was shown to be identical to that prepared from A above by admixture melting point and comparison of infrared spectra.

C. From 9-(1-Pyridinium)fluorenylide.—Treatment of 1-(9-fluorenyl)pyridinium bromide with nitrosobenzene as described previously[2] gave yellow needles, m.p. 192–193°, identical to that prepared from A and B above.

Warming the nitrone (IVa) in ethanolic sulfuric acid for 1 hr. led to a disappearance of the yellow color. Quenching with water followed by extraction of the neutral and basic fragments with ether led to the recovery of the oily β-phenylhydroxylamine, λ_{max} 2.91 and 3.05 μ, and fluorenone, which crystallized from hexane as yellow needles, m.p. 81–83°, identical to an authentic sample.

A solution of 0.54 g. of the nitrone (IVa) and 0.34 g. of diethyl fumarate in 15 ml. of benzene was heated under reflux for 24 hr. Removal of the solvent followed by trituration with 95% ethanol gave 0.10 g. of unchanged nitrone, m.p. 194–196°. Dilution of the filtrate with water afforded 0.42 g. (58%) of crude 2-phenyl-3,3-diphenylene-4,5-dicarbethoxyisoxazolidine, m.p. 74–80°. Recrystallization from 80% ethanol gave colorless microcrystals, m.p. 76–78°, λ_{max} 5.65, 5.75, 13.25, 13.64, and 14.55μ.

Photolysis of the Nitrone (IVa).—A solution of 0.27 g. of the nitrone in 25 ml. of acetonitrile was irradiated in a quartz tube for 3 hr. using a Hanovia quartz lamp. No color change could be observed. Evaporation of the solvent and crystallization of the tan residue from 95% ethanol afforded unchanged nitrone, m.p. 193–194.5°.

Oxidation of Fluorenone Anil.—Ten milliliters of a solution of peracetic acid in methylene chloride prepared according to Emmons[5] directions, was added to a cold stirred solution of 1.25 g. of fluorenone anil[4,13] in 10 ml. of methylene chloride. After standing overnight at room temperature the solution was washed with water and dilute ammonia then dried. Removal of the solvent *in vacuo* left a brown solid which, upon trituration, afforded yellow crystals (0.90 g., 68%), m.p. 182–187°, which crystallized from 95% ethanol as fine yellow needles, m.p. 191–193°, identical to an authentic sample of the nitrone (IVa).

N-Phenylbenzophenone Ketoxime. A. From Diphenyldiazomethane.—To a red solution of 1.0 g. of diphenyldiazomethane[14] in 25 ml. of dry ether was added 0.55 g. of nitrosobenzene. Heat and nitrogen were evolved immediately and the nitrosobenzene slowly dissolved as a colorless precipitate began to form. After 15 min. the precipitate (0.96 g., 68%) was removed by filtration and dried. It crystallized from 60% ethanol as colorless fine plates, m.p. 223–225°, λ_{max} 6.10, 6.27, 6.65, 7.45, 12.79, and 14.50 μ; λ_{max}^{EtOH} 230 mμ (log ϵ 4.2) and 310 mμ (4.0).

Anal. Calcd. for $C_{19}H_{15}NO$: C, 83.49; H, 5.53; N, 5.13. Found: C, 83.56; H, 5.49; N, 5.35.

B. From Dimethylsulfonium(diphenyl)methylide.—Treating a slurry of dimethylbenzhydrylsulfonium bromide. in tetrahydrofuran with butyllithium resulted in a deep red solution of the sulfur ylid. Reaction of this solution with nitrosobenzene followed by quenching with water and extracting with ether gave the crude nitrone, m.p. 210–220°. Crystallization from 60% ethanol afforded colorless plates, m.p. 223–226°, identical to that prepared in A above.

Warming a solution of the nitrone (0.54 g.) in 20 ml. of 95% ethanol containing 6 ml. of 50% sulfuric acid for 1 hr. led to dissolution of the solid. The colorless solution was quenched with water then the neutral and basic components were separated and removed by ether extraction. The basic fraction (an oil) was identified as β-phenylhydroxylamine by its infrared spectrum. The neutral fraction was identified as benzophenone by its infrared spectrum and by conversion to its hydrazone, m.p. 97–100°, identical to an authentic sample.

N-Phenyl(2-nitro)fluorenone Ketoxime (IVb).—To a purple solution of 0.96 g. of dimethylsulfonium(2-nitro)fluorenylide (Ib) in 30 ml. of methylene chloride was added 0.30 g. of nitrosobenzene. The solution was heated under reflux for 1 hr. during which time the color changed to yellow. Evaporation of the solvent and trituration of the residue afforded 0.60 g. (76%) of crude nitrone (IVb), m.p. 217–220°. Crystallization from benzene afforded fine light orange needles, m.p. 224–225°, λ_{max} 6.60, 7.50, 13.00, 13.20, 13.75, and 14.43 μ.

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(13) G. Reddelien, *Chem. Ber.*, **43**, 2479 (1910).

(14) J. B. Miller, *J. Org. Chem.*, **24**, 560 (1959).

Some New Reactions of Methylsulfinyl and Methylsulfonyl Carbanion[1]

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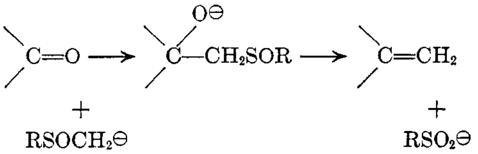
Received July 31, 1962

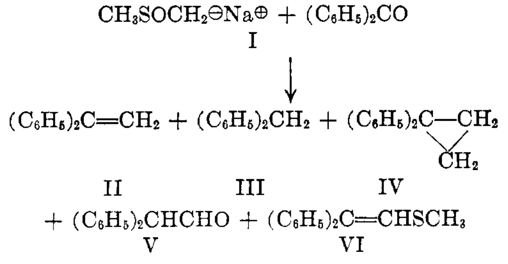
Recently we have described the generation and properties of the methylsulfinyl carbanion (I) and some applications of this extremely useful reagent in synthesis. In this and subsequent work, for example, solutions of the anion in dimethyl sulfoxide have been employed as the key feature of a very convenient and effective modification of the Wittig olefin synthesis.[2,3] It occurred to us that the reactivity of the methylsulfinyl carbanion and the extraordinary properties of dimethyl sulfoxide as a solvent might allow a Wittig type of olefin synthesis directly from the sulfinyl carbanion and certain carbonyl compounds:



(1)

Consequently an investigation was initiated of the reaction of such carbanions with benzophenone under conditions which are more drastic than those required to form the simple carbonyl addition product. The case of benzophenone seemed especially favorable since the carbonyl addition reaction is known to proceed in good yield[2] and is obviously not complicated by competing reactions such as enolate formation.[4]

In fact, the reaction of methylsulfinyl carbanion with benzophenone at 75–100° did afford distillable hydrocarbon products; a satisfactory conversion was obtained by rapid heating of the reactants from room temperature to 100° and maintenance at the higher temperature for several hours. Under these conditions a volatile product was obtained containing the hydro-



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[1] This work was supported by a grant (RG-6966) from the National Institutes of Health.

[2] E. J. Corey and M. Chaykovsky, *J. Am. Chem. Soc.*, **84**, 866 (1962).

[3] A solution of the methylsulfinyl carbanion in dimethyl sulfoxide is prepared by heating sodium hydride with excess dry sulfoxide under nitrogen at 75° and then standardized by aqueous titration of an aliquot with standard acid. An equivalent amount of this anion is then added to a solution of the phosphonium salt in dry dimethyl sulfoxide (under nitrogen). After a few minutes the carbonyl compound is added with stirring and the reaction is allowed to proceed at room temperature for thirty minutes (or longer with hindered carbonyl compounds). Dilution with water, extraction, and appropriate isolation procedures then afford the Wittig product in very satisfactory yields (often much superior to those obtained under the customary conditions in ether or tetrahydrofuran).

[4] During this investigation we learned of similar studies in the laboratory of Prof. C. Walling, Columbia University. Our results are published simultaneously through mutual agreement.