Tetrahedron Letters No. 44, pp 3847 - 3850, 1974. Pergamon Press. Printed in Great Britain.

DIELS-ALDER REACTIONS OF AZODIPHOSPHONIC ACID, TETRAPHENYL ESTER

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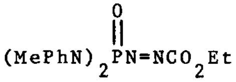
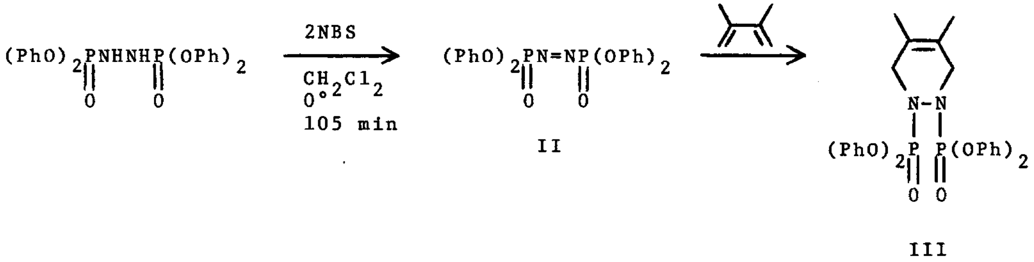
(Received in USA 7 August 1974; received in UK for publication 24 September 1974)

Recent publication of the first reported Diels-Alder reaction with an azophosphonoyl system, compound I[1], leads me to report results with azodiphosphonic acid, tetraphenyl ester II. The known azo compound II is prepared from the hydrazide by oxidation with two equivalents of N-bromosuccinimide[2]. It may be isolated as an unstable blue solid, but it is most conveniently used as a deep-blue methylene chloride solution at 0°. The blue color of the solution is not completely discharged on standing 18 hours at 0°. At room temperature a solution of II will completely decompose in several hours. Decomposition of II at temperatures higher than 25° was not examined. Under conditions reported here and in the literature[2], the azo compound II while being unstable offers no hazard.



$\mathrm{(MePhN)_2}\overset{\mathrm{O}}{\overset{\|}{\mathrm{P}}}\mathrm{N{=}NCO_2Et}$

I



A solution of II prepared by oxidizing 4.96 g (.01 mole) of the hydrazide in 100 ml of methylene chloride at 0° was first washed with $Na_2S_2O_5$ solution, then with water, and finally was dried over Na_2SO_4 at 0°. To this solution was added 2.45 g (.03 mole) of 2,3-dimethylbutadiene. After 20 minutes the blue color of II was totally discharged. The reaction mixture was concentrated under vacuum, and the oily residue was purified by chromatography on silica gel (Woelm, Grade I). Elution with 9:1 benzene-ethyl acetate gave 4.1 g (72.5% yield) of the cycloadduct III, m.p. 91-3° (ether). NMR: δ (rel. to TMS in $CDCl_3$) = 1.54 (s, 6H), 3.92 (br.t., 4H), and 7.1-7.5 (m, 20H). Further elution of the column with 1:1 benzene-ethyl acetate gave 0.65 g (13% yield) of recovered hydrazide. The recovered hydrazide arose primarily from incomplete reaction during the oxidation step.

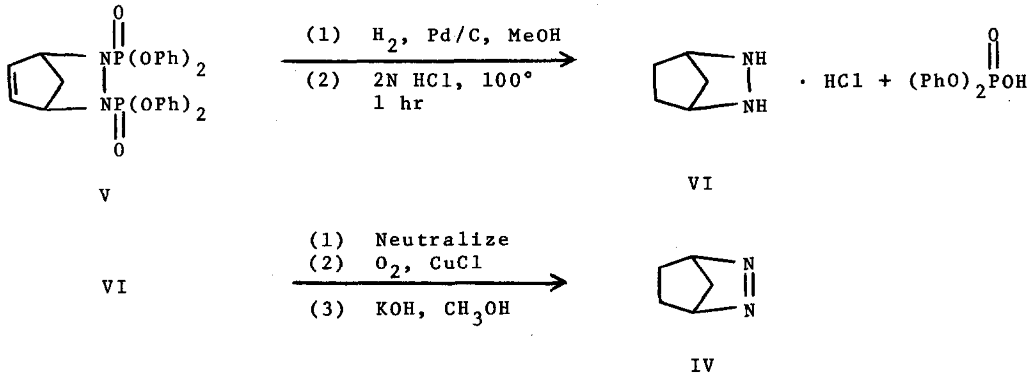
Compound II can also be used efficiently as a dienophile with a range of other known dienes (see table). The rate of reaction of II with these dienes generally follows the order expected from the reaction of the dienes with diethyl azodicarboxylate[3]. However, II appears to be more reactive than diethyl azodicarboxylate[3] and is markedly more reactive than the previously reported azophosphonoyl system I[1]. The low yield of cycloadduct from reaction with 1,3-cyclohexadiene parallels results from the same reaction of azodicarboxylates. The thermal instability of II does limit its synthetic utility; the rather unreactive diene, tetraphenylcyclopentadienone, gives no adduct with II and only decomposition products of II are found.

Reaction of II with Dienes at 0°

Diene	Time of Reaction (min)	Yield of Adduct[a] (%)
Cyclopentadiene	<1	68
2,3-Dimethylbutadiene	20	73
1-Methylbutadiene	20	69
1,3-Cyclohexadiene	180	10
1-Phenylbutadiene	720	51
Tetraphenylcyclopentadienone	--	0

[a] Satisfactory analyses were obtained for all products.

Among the interesting uses of azodicarboxylate Diels-Alder reactions has been the preparation of bicyclic azo compounds such as IV[4]. However, in this reaction sequence refluxing 20% alcoholic KOH is required to remove the alkoxycarbonyl groups, and this hydrolysis procedure limits the types of other functional groups which can be in the molecule. Recently, the use of dibenzyl azodicarboxylate followed by hydrogenolysis of the benzyloxycarbonyl groups has been reported as a method to circumvent this difficulty[5]. The diphosphonoyl adduct V offers the opportunity to use acid hydrolysis to prepare IV:



Hydrogenation of V was followed by reflux of the crude hydrogenation product for one hour in 2N HCl to give VI plus diphenyl phosphate. After extraction of the phosphate with ether, the aqueous solution was neutralized and oxidized by air and cuprous chloride[6] to give the cuprous chloride complex of IV in 91% yield. Treatment of the complex with KOH in methanol gave the known 2,3-diazabicyclo-[2,2,1]-2-heptene in 30% yield, m.p. 90-95° (Lit.[6] m.p. 99-99.5°). No attempts were made to optimize the conditions of these reactions or to attempt other oxidation procedures.

The scope of cycloaddition reactions of various azophosphonoyl systems and further reactions of the adducts themselves are currently under investigation.

Acknowledgment. The author expresses his thanks to Mr. Paul Unger and his associates for spectral measurements, to Mr. George Maciak and his associates for microanalyses, and to Dr. E. C. Taylor and Dr. J. E. Baldwin for helpful discussions during this research.

References

1) R. J. Cremlyn, M. J. Frearson, and D. R. Milnes, J. Chem. Soc., Chem. Communications, 1974, 319.

2) H. Bock and G. Rudolf, Chem. Ber., 94, 1457 (1961).

3) B. T. Gillis, "Azo Compounds as Dienophiles," 1,4-Cycloaddition Reactions, Ed. J. Hamer (Academic Press) (1967).

4) O. Diels, J. H. Blom, and W. Koll, Ann., 443, 242 (1925).

5) M. L. Heyman and J. P. Snyder, Tetrahedron Letters, 1973, 2859.

6) S. G. Cohen, R. Zand, and C. Steel, J. Am. Chem. Soc., 83, 2895 (1961).