The Reaction of 4-Phenyl-1,2,4-triazoline-3,5-dione with Conjugated Dienes[1-3]

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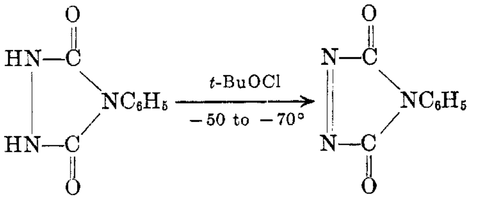
The *cis*-azo dienophile, 4-phenyl-1,2,4-triazoline-3,5-dione (II), has been prepared by a convenient laboratory method utilizing lead tetraacetate as an oxidant. The dione II was allowed to react *in situ* with a number of dienes. The reported high reactivity of this compound has been confirmed and a strong preference has been noted for Diels–Alder type of addition over other modes of reaction, even where these are favored when using *trans*-azo dienophiles.

Since the discovery of the Diels–Alder reaction,[4] electron-poor azo compounds such as ethyl azodicarboxylate have been known to be highly effective dienophiles. More recently, Baranger and Levisalles[5] have shown that this reactivity is also exhibited by cyclic diacyl diimides and similar azo compounds and a number of these have been prepared.[6,7] Cookson, Gilani, and Stevens[8] established 4-phenyl-1,2,4-triazoline-3,5-dione (II) as a dienophile by *in situ* reaction with butadiene, cyclopentadiene, cycloheptatriene, and bicycloheptadiene. They had prepared the dienophile by *t*-butylhypochlorite oxidation of 4-phenylurazole (I) at −50 to −70°.

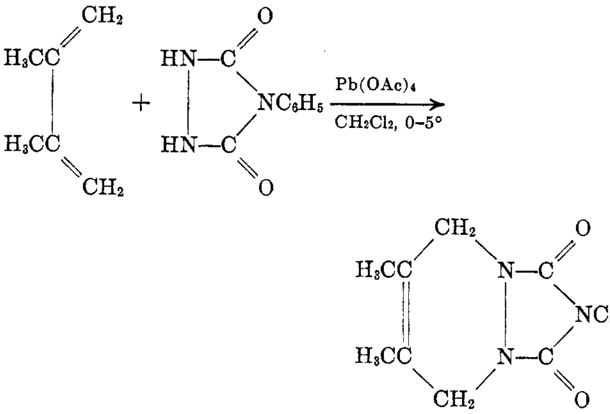


I II

This investigation was undertaken in order to compare the reactivity of the *cis*-azo dienophile II with *trans*-azo dienophiles, such as ethyl azodicarboxylate which has been observed to undergo alternate modes of reaction[9-12] when used with less reactive or hindered dienes.

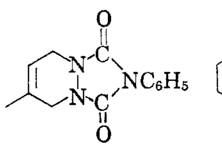
The method of Clement[6] was adapted to the synthesis of II. This involved the use of lead tetraacetate at 0–5° in the solvent methylene chloride for the oxidation of I. This method proved to be quite satisfactory for a large number of dienes, and the inconvenience of extremely low temperatures and the use of *t*-butylhypochlorite was avoided. The presence of II could easily be noted by its carmine red color which was found to be retained up to 0.5 hr or longer in the solvent methylene chloride.

Thus, when a slurry of I in methylene chloride was stirred and cooled in an ice–water bath and a cold solution of lead tetraacetate in methylene chloride was added in the *absence* of any diene, an intense red color was produced. In the *presence* of 2,3-dimethyl-1,3-butadiene no red color appeared owing to the extremely rapid addition. The reaction, upon work-up, furnished a good yield of the Diels–Alder adduct III.



III

Treatment of other dienes with II also resulted in exclusively Diels–Alder addition. The results are summarized in Table I.



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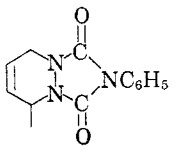

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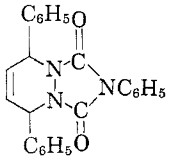

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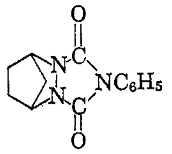

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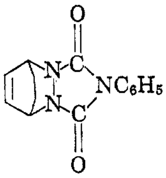
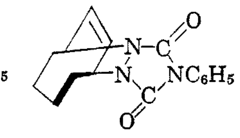
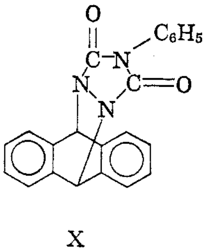


VIII



IX



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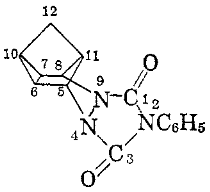

XI

A reaction which deserves special comment was the reaction of II with cyclopentadiene. The resultant adduct was reported by Cookson, *et al.*,[8] but no mention was made of the melting point or points. The possibility of formation of *exo* and *endo* isomers exists. Both isomers may be formed, *a priori*, or one isomer

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[1] This investigation was supported by Grant GP-1589 from the National Science Foundation, under the title "Azo Dienophiles."

[2] Presented in part at the 151st National Meeting of the American Chemical Society, Pittsburgh, Pa., March 1966, Abstract, No. K-074.

[3] Abstracted from the Ph.D. Dissertation of J. D. Hagarty, Duquesne University, 1966.

[4] O. Diels, J. H. Blom, and W. Knoll, *Ann.*, **443**, 242 (1925).

[5] P. Baranger and J. Levisalles, *Bull. Soc. Chim. France*, 704 (1957).

[6] R. A. Clement, *J. Org. Chem.*, **27**, 1115 (1962).

[7] T. J. Kealy, *J. Am. Chem. Soc.*, **84**, 966 (1962).

[8] R. C. Cookson, S. S. H. Gilani, and I. D. R. Stevens, *Tetrahedron Letters*, **14**, 615 (1962).

[9] B. T. Gillis and P. E. Beck, *J. Org. Chem.*, **27**, 1947 (1962).

[10] B. Franzus and J. H. Surridge, *ibid.*, **27**, 1951 (1962).

[11] B. T. Gillis and P. E. Beck, *ibid.*, **28**, 3177 (1963).

[12] R. Huisgen and H. Pohl, *Ber.*, **93**, 527 (1960).

TABLE I

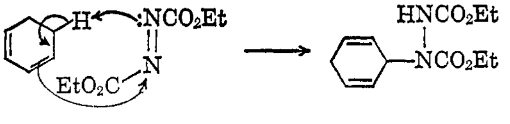
Diene	Adduct	Mp, °C	Yield, %	Anal,[a] %		
				C	H	N
2,3-Dimethyl-1,3-butadiene	III[b]	174–175.5	62	65.21	5.86	16.29
Isoprene	IV[c]	110–112	81	64.03	5.56	17.37
Piperylene	V[d]	135–138	50	64.36	5.50	17.37
1,4-Diphenyl-1,3-butadiene	VI[e]	160–161	70	75.45	5.14	11.23
Cyclopentadiene	VII[f]	133–134 141.5–144	58	63.10	4.65	18.21
1,3-Cyclohexadiene	VIII[g]	172–174	73	66.09	5.30	16.61
1,3-Cyclooctadiene	IX[h]	207–208	15	68.03	6.22	14.99
Anthracene	X[i]	226–227	46	74.64	4.34	12.00
Bicycloheptadiene	XI[j]	171–172.5	27	67.57	5.02	15.90

[a] All analytical data are within 0.3% of the calculated values. [b] Systematic name 5,8-dihydro-6,7-dimethyl-2-phenyl-*s*-triazolo[1,2-*a*]pyridazine-1,3(2H)-dione. [c] Systematic name 5,8-dihydro-6-methyl-2-phenyl-*s*-triazolo[1,2-*a*]pyridazine-1,3(2H)-dione. [d] Systematic name 5,8-dihydro-5-methyl-2-phenyl-*s*-triazolo[1,2-*a*]pyridazine-1,3(2H)-dione. [e] Systematic name 5,8-dihydro-2,5,8-triphenyl-*s*-triazolo[1,2-*a*]pyridazine-1,3(2H)-dione. [f] Systematic name 5,8-dihydro-5,8-methano-2-phenyl-*s*-triazolo[1,2-*a*]pyridazine-1,3(2H)-dione. [g] Systematic name 5,8-dihydro-5,8-ethano-2-phenyl-*s*-triazolo[1,2-*a*]pyridazine-1,3(2H)-dione. [h] Systematic name 5,10-ethano-5,6,7,8,9,10-hexahydro-2-phenyl-*s*-triazolo[1,2-*a*][1,2]diazocine-1,3(2H)-dione. [i] Systematic name 5,10-*o*-benzeno-5,10-dihydro-2-phenyl-*s*-triazolo[1,2-*b*]phthalazine-1,3(2H)-dione. [j] Systematic name 10,5,8-ethylylidene-2-phenyl-5,6,7,8-tetrahydro-*s*-triazolo-[1,2-*a*]cyclopropa[*d*]pyridazine-1,3(2H)-dione.

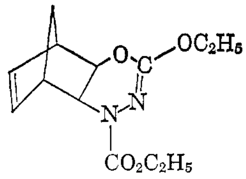
might be converted to the other without bond breaking, although inversion of both nitrogen atoms would be necessary. This inversion is not possible for its carbon analog, *i.e.*, the N-phenylmaleimide adduct of cyclopentadiene. In the case of VII, it might be expected that the conversion of *endo* to *exo* would have a higher barrier to inversion than the 19 kcal/mole reported for 1,2-dicarbomethoxy-3,6-diphenyl-1,2,3,6-tetrahydropyridazine.[13]

When adduct VII was recrystallized from methanol with only gentle warming and a melting point taken it was observed that two forms were present. The lower melting form, mp 131–133°, was present in a lesser amount than the higher melting form. When the melt was allowed to solidify and remelted, only the higher melting form was present. Concentration of the filtrate from the first recrystallization without heating resulted in recovery of more of the lower melting form, which exhibited the greater solubility. When these crystals were melted and allowed to solidify, the new melting point was 142–144°. The nmr spectra of the two forms were identical, however, even at −35°. Elemental analysis showed that solvent was not included in the lower melting crystal structure. Thus, no inversion or equilibration between the *exo* and *endo* forms occurs in solution, and the different melting points are due to polymorphism of one isomer, presumably the *endo* isomer.

In the reaction of 1,3-cyclohexadiene with II, the *only* product isolated was the 1,4 Diels–Alder addition product (VIII) in good yield and it has the same configuration as the cyclopentadiene adduct by comparison of the nmr spectra of VII and VIII. In contrast, when 1,3-cyclohexadiene is allowed to react with ethyl azodicarboxylate, a *trans*-azo dienophile, only a small amount of the Diels–Alder type of addition occurs. Instead, the main product arises from the following abstraction–addition mechanism.[9,10]



Using bicyclo[2.2.1]heptadiene, the homoconjugate Diels–Alder addition product (XI) was formed in 27% yield and was the only product isolated. The adduct, *per se*, was reported by Cookson, *et al.*,[8] and the correctness of his assignment is borne out by the nmr spectra reported in detail below. This type of addition has been observed several times previously for bicycloheptadiene,[14] although Tufariello, *et al.*,[15] found that ethyl azodicarboxylate also gave compound XIII. Ullman[14b] as well as Cookson and co-workers,[14e] used nmr very successfully in determining the structure of the products of the reaction of bicyclo[2.2.1]-heptadiene and maleic anhydride.



XIII

The structure of the adduct XI from bicyclo[2.2.1]-heptadiene and II was readily determined by means of the infrared and nmr spectra. The infrared spectrum of XI showed no N—H absorptions, but an intense C=O peak at 5.85 and a less intense peak at 5.65 μ, along with various phenyl absorptions. The nmr spectrum showed a broad singlet at 2.52 (1 H), a somewhat broadened doublet at 4.54 (2 H), a broad singlet 1.82 (2 H), and a multiplet at 1.65 ppm (3 H). The peak due to the five phenyl protons occurred at 7.53 ppm. This nmr spectrum compares very favorably with that of the homoconjugate addition adduct of bicycloheptadiene with ethyl azodicarboxylate reported by Cristol, *et al.*,[14a] and confirmed by Moriarty.[14f]

The reaction of 2,5-dimethyl-2,4-hexadiene with II resulted in no Diels–Alder adduct. A low yield of a compound was obtained which showed an N-H band and two carbonyl bands of unequal intensity in the infrared spectrum. The nmr spectrum of the product showed sharp singlets at 1.48 (6 H), 1.68 (6 H), and

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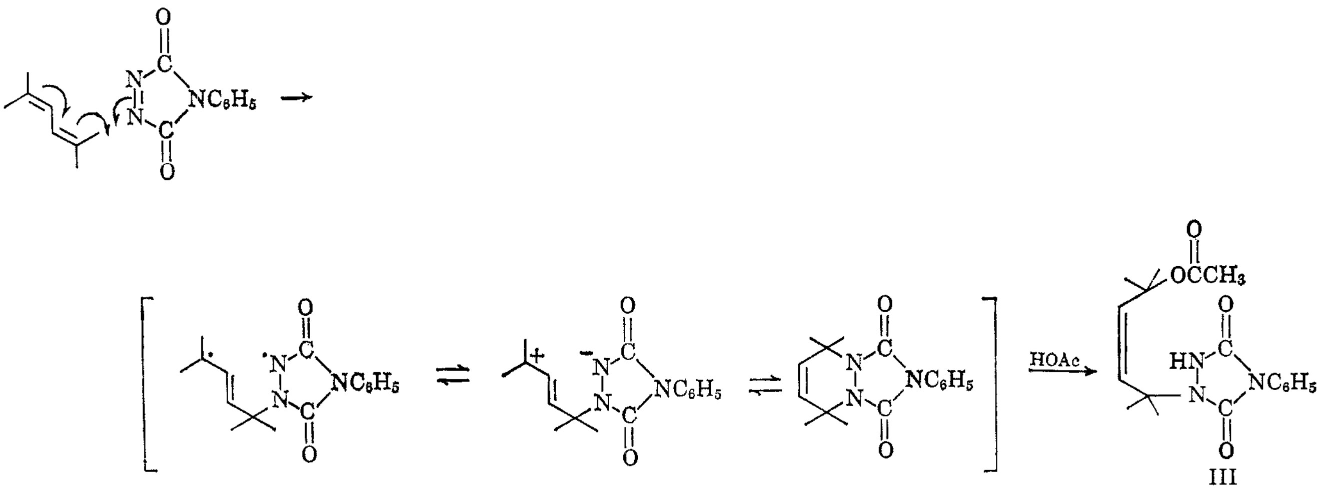
(13) J. C. Breliere and J. M. Lehn, *Chem. Commun.*, 426 (1965).

(14) (a) S. T. Cristol, E. L. Allred, and D. L. Wetzel, *J. Org. Chem.*, **27**, 4058 (1962); (b) E. F. Ullman, *Chem. Ind.* (London), 1173 (1958); (c) H. K. Hall, Jr., *J. Org. Chem.*, **25**, 42 (1960); (d) A. T. Blomquist and Y. C. Meinwald, *J. Am. Chem. Soc.*, **81**, 667 (1959); (e) R. C. Cookson, J. Dance, and J. Hudec, *J. Chem. Soc.*, 5416 (1964); (f) R. M. Moriarty, *J. Org. Chem.*, **28**, 2385 (1963).

(15) J. J. Tufariello, T. F. Mich, and P. S. Miller, *Tetrahedron Letters*, 2293 (1966).

SCHEME I



2.02 ppm (3 H). There were also two peaks in the vinyl region at 5.77 (1 H) and 5.86 (1 H), and one in the phenyl region at 7.44 ppm (5 H). The compound analyzed correctly for $C_{18}H_{23}N_3O_4$. These results are consistent with the structure XII which could arise as shown in Scheme I.

In general, this method of lead tetraacetate oxidation of I and the *in situ* reaction of II with a wide variety of dienes was quite satisfactory. Only the most unreactive dienes such as hexachlorocyclopentadiene and hexachlorobutadiene failed to react under the conditions employed. The chief limitation of this dienophile is that the mixture cannot be heated to force reaction without the decomposition of II. Another important observation was the strong almost complete preference for undergoing the Diels–Alder-type addition even when other reactions are possible. This may be attributed to the two favorable factors of *cis* configuration and electron deficiency which are exhibited by 4-phenyl-1,2,4-triazoline-3,5-dione (II).

Experimental Section[16]

Ethyl Carbazate.—A mixture of 200 g (1.8 moles) of diethyl carbonate and 88 g (1.8 moles) of 85% hydrazine hydrate was shaken for 20 min, after which time the mixture became one phase. After standing overnight the mixture was vacuum distilled through a 12-in. Vigreux column and a large fraction, bp 86–90° (10 mm), was collected. A total of 96.5 g (52%) of ethyl carbazate, mp 44–45.5°, was obtained.

Addition of Ethyl Carbazate to Phenyl Isocyanate and Cyclization.—The method of Zinner and Deucker[17] was used for the synthesis of 4-phenylurazole (I). From 64 g (0.62 mole) of ethyl carbazate and 67.2 g (0.57 mole) of phenyl isocyanate in benzene was obtained 128 g (89%) of the urea derivative, mp 154°.

Treatment of 77.5 g (0.35 mole) of the urea derivative with 200 ml of hot 4 *N* potassium hydroxide and subsequent careful neutralization resulted in 55.5 g (90.2%) of 4-phenylurazole (I), mp 206–207°.[17]

General Procedure for Reaction of 4-Phenyl-1,2,4-triazoline-3,5-dione (II) with Dienes.[18]—This procedure was used for reaction of 2,3-dimethyl-1,3-butadiene (n^{25}_{D} 1.4325, lit.[19] n^{20}_{D} 1.4377), isoprene (n^{25}_{D} 1.4260, lit.[19] $n^{18.3}_{D}$ 1.4221), piperylene (n^{25}_{D} 1.4302, lit.[19] $n^{16.5}_{D}$ 1.4402), 1,4-diphenyl-1,3-butadiene (mp 148°, lit.[20] mp 151°), cyclopentadiene (n^{25}_{D} 1.4030, lit.[19] n^{20}_{D} 1.4039), 1,3-cyclohexadiene (n^{25}_{D} 1.4730, lit.[19] n^{20}_{D} 1.4744), 1,3-cyclooctadiene (n^{25}_{D} 1.4912, lit.[21] n^{25}_{D} 1.4901), and anthracene (mp 214–215°, lit.[19] mp 217°) with II.

A slurry was prepared by mixing 4.0 g (0.023 mole) of 4-phenylurazole (I) with 100 ml of methylene chloride. This mixture was stirred and cooled in an ice–water bath to 0–5°. A moderate excess of freshly distilled (or recrystallized) diene was added. (Large excesses of diene cause difficulty in the isolation of the product.) A cold solution of 13.4 g (0.026 mole) of recrystallized lead tetraacetate dissolved in 100 ml of methylene chloride was added dropwise with continued stirring. A sticky, white precipitate usually formed which slowly dissolved. Stirring was continued for 1 or 2 hr after the addition was complete. The methylene chloride was removed by means of an aspirator with only gentle warming. The resulting white solid was washed successively with 75-ml portions of water, 0.1 *N* nitric acid, and 0.1 *N* sodium hydroxide, then was filtered and dried. The product was purified by dissolving in hot methanol, decolorizing with activated charcoal, and recrystallizing.

All of the resultant adducts showed intense C=O absorption at 5.8–5.9 and a sharp but lower intensity band at 5.6–5.7 μ, along with various phenyl absorptions and an absence of N—H bands in their infrared spectra. For data on the adducts, see Table I.

Reaction of Bicyclo[2.2.1]heptadiene with II.—In a flask equipped with magnetic stirrer and cooled in an ice–water bath was placed 4.0 g (0.023 mole) of 4-phenylurazole, 3.0 g of bicyclo[2.2.1]heptadiene (n^{25}_{D} 1.4706, lit.[22] n^{20}_{D} 1.4699), and 100 ml of methylene chloride. A cold solution of 13.5 g of lead tetraacetate in 100 ml of methylene chloride was added very slowly as the red color faded. The color was completely absent 20 min after addition was complete. The solvent was removed with an aspirator while the mixture was kept below room temperature. The remaining solid was washed twice with cold water. Two recrystallizations from methanol yielded 2.5 g (17%) of XI, as white needles, mp 171–172.5°.[23]

Reaction of 2,5-Dimethyl-2,4-hexadiene with II.—To 4.0 g (0.023 mole) of 4-phenylurazole (I) and 3.8 g (0.035 mole) of

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[16] Boiling points and melting points are uncorrected. Microanalyses were performed by Dr. Alfred Bernhardt, Mülheim, Germany. Infrared spectra were taken with a Perkin-Elmer Model 137 double-beam spectrophotometer. The nmr spectra were taken with a Varian A-60 using either carbon tetrachloride or deuteriochloroform as solvent and tetramethylsilane as an internal standard.

[17] G. Zinner and W. Deucker, *Arch. Pharm.*, **294**, 370 (1961).

[18] The 2,3-dimethyl-1,3-butadiene was a gift from Houdry Process Corp., Philadelphia, Pa. Isoprene, 1,4-diphenyl-1,3-butadiene, and anthracene were purchased from Eastman Kodak Co. Nopadiene, 1,3-cyclohexadiene, 1,3-cyclooctadiene, and cyclooctatetraene were purchased from Aldrich Chemical Co. Piperylene was obtained from Enjay Chemical Co. The 2,5-dimethyl-2,4-hexadiene was obtained from Matheson Coleman and Bell. Cyclopentadiene was obtained by distillation of dicyclopentadiene, which was obtained from Union Carbide Corp. Hexachlorocyclopentadiene was a gift from Hooker Chemical Co., and hexachlorobutadiene was a gift from Diamond Alkali Co.

[19] "Handbook of Chemistry and Physics," 45th ed, Chemical Rubber Publishing Co., Cleveland, Ohio, 1963.

[20] W. Wadsworth, Jr., and W. Emmons, *J. Am. Chem. Soc.*, **83**, 1733 (1961).

[21] A. Cope, M. Kinter, and R. Teller, *ibid.*, **76**, 2757 (1954).

[22] L. Schmerling, J. Luvisi, and R. Welch, *ibid.*, **78**, 2819 (1956).

[23] Reference 8 reported mp 173–174°.

2,5-dimethyl-2,4-hexadiene (n^{25}D 1.4743, lit.[24] n^{23}D 1.4752) in 100 ml of methylene chloride was added dropwise a solution of 13.5 g (0.026 mole) of lead tetraacetate in methylene chloride. The mixture was stirred and cooled to 0–5° in an ice–water bath during the addition. No red color appeared indicating rapid addition was occurring. Stirring as continued for 30 min. The mixture was filtered to remove a small amount of suspended solid and quickly washed twice with 75-ml portions of cold water. Drying was accomplished by swirling for 2 min over anhydrous sodium sulfate. The solvent was removed and the remaining solid was recrystallized twice from ether with the aid of a Dry Ice–acetone bath to give 1.4 g (18%) of white, crystalline XII, mp 107–108°. The infrared spectrum of XII contained an N-H band at 3.1 C═O bands at 5.75 and 5.85, and a C—O band at 8.0 μ. The nmr showed singlets at 1.48, 1.66, 2.02, 5.77, and 5.86 (6:6:3:1:1) and a multiplet at 7.44 ppm (5 H).

Anal. Calcd for $C_{18}H_{23}N_3O_4$: C, 62.58; H, 6.71; N, 12.17. Found: C, 62.44; H, 7.05; N, 12.04.

Attempted Reaction of Other Dienes with II.—The reaction of nopadiene (n^{25}D 1.5020, lit.[25] n^{25}D 1.5044) with II by the same procedure resulted in an oil that reverted to starting materials upon purification attempts. The infrared spectrum showed no N—H bands but C═O bands at 5.65 and 5.85 μ were present. The nmr contained complex multiplets in the C—H region, an olefinic peak at 5.5, and a phenyl peak at 7.45 ppm.

When an attempt was made to treat cyclooctatetraene (n^{25}D 1.5360, lit.[25] n^{20}D 1.5290), hexachlorobutadiene (n^{25}D 1.5530, lit.[26] n^{20}D 1.5542), and hexachlorocyclopentadiene (n^{25}D 1.5602, lit.[27] n^{25}D 1.5629) with II, no adduct formed. Rather, when the lead tetraacetate solution was added to a slurry of 4-phenylurazole in methylene chloride and in the presence of these compounds, the red color of II persisted. Continued treatment or warming ultimately resulted in the complete decomposition of the dienophile.

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[24] E. Braude and J. Coles, *J. Chem. Soc.*, 1425 (1952).

[25] W. Reppe, *Ann.*, **560**, 1 (1948).

[26] L. Kogan, N. Burmakin, and N. Chernyak, *Izv. Vysshikh Ucheb Zavedenii, Khim. i Khim. Tekhnol.*, 126 (1958).

[27] J. Krynitsky and R. Bost, *J. Am. Chem. Soc.*, **69**, 1919 (1947).

The Reaction of Triphenylphosphine with Peroxycyclohexadienones[1]

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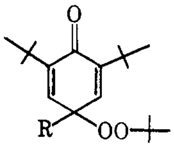
Triphenylphosphine reacts with 4-*t*-butylperoxy-4-methyl-2,6-di-*t*-butyl-2,5-cyclohexadien-1-one (**1a**) in *n*-heptane or chlorobenzene solution at 100° to form 2,6-di-*t*-butyl-*p*-cresol (**2**), 2,6-di-*t*-butyl-4-neopentylphenol (**3**), isobutene, and triphenylphosphine oxide, together with lesser amounts of 2,6-di-*t*-butyl-*p*-benzoquinone (**4**), 2,4,6-tri-*t*-butyl-4-methyl-2,5-cyclohexadien-1-one (**5**), and isobutane. A homolytic mechanism is proposed for this reaction and supported by further experiments. Reaction of 4-*t*-butylperoxy-2,4,6-tri-*t*-butyl-2,5-cyclohexadien-1-one (**1b**) with triphenylphosphine in *n*-heptane at 100° gives 2,4,6-tri-*t*-butylphenol (**11**), quinone **4**, 2,6-di-*t*-butyl-4-*t*-butoxyphenol (**12**), isobutene, triphenylphosphine oxide, and a trace of isobutane. This reaction also appears to occur largely *via* a homolytic mechanism, but incursion of a competing process which does not involve free radicals is indicated.

Mixtures of hindered phenols with compounds containing phosphorus or sulfur are widely used as inhibitors of hydrocarbon autoxidation.[4] Many inhibitor systems of this type owe their special effectiveness to the phenomenon of synergism; *i.e.*, their inhibitory power is greater than would be expected if the effects of the individual components were simply additive. An attractive rationalization for many of the observed synergistic effects is that the components function in different ways which are mutually reinforcing.[4a–c] Thus, the phenolic compound (primary stabilizer) can act as a trap for peroxy radicals, while the compound of phosphorus or sulfur (costabilizer) may function as a decomposer of the hydroperoxides which are responsible for chain initiation.[4a–c] However, in many cases it is quite clear that other reactions involving the inhibitors are likely to occur, and, in general, the complexity of these systems has precluded their description in terms of complete reaction mechanisms. One possible complicating factor, which to our knowledge has received attention in only one previous study,[4c] is that certain costabilizers may react with the peroxycyclohexadienones formed *in situ* from peroxy radicals and hindered phenols. Since reactions of peroxycyclohexadienones with phosphorus-containing costabilizers had not previously been investigated, we therefore thought it would be of interest to examine the interaction of two representative peroxides of this type (**1a** and **1b**) with triphenylphosphine. Although this phosphine is not particularly useful as a costabilizer itself, it was felt that its action upon peroxycyclohexadienones should parallel that of certain other compounds of trivalent phosphorus (*e.g.*, phosphites) which are more commonly used in multicomponent inhibitor systems. However, it should be remarked at the outset that this parallelism was not expected to be completely general, since reaction modes of phosphines and phosphites with certain oxygenated species were known to be strongly dependent upon structural and environmental factors.[5]



1a, R = Me
b, R = *t*-Bu

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[1] Part IV of a series on oxidation inhibitors. Part III: W. H. Starnes, Jr., *J. Org. Chem.*, **31**, 3164 (1966).

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[3] American Embassy, Bonn/Bad Godesberg, Germany.

[4] See, *inter alia*, (a) K. U. Ingold, *Chem. Rev.*, **61**, 563 (1961), and references therein; (b) "Aging and Stabilization of Polymers," M. B. Neiman, Ed., Consultants Bureau, New York, N. Y., 1965, pp 29–33, 114–118, and references therein; (c) N. P. Neureiter and D. E. Bown, *Ind. Eng. Chem., Prod. Res. Develop.*, **1**, 236 (1962); (d) L. Friedman, U. S. Patent 3,039,993 (1962).

[5] (a) W. G. Bentrude, *Tetrahedron Letters*, 3543 (1965); (b) S. A. Buckler, *J. Am. Chem. Soc.*, **84**, 3093 (1962); (c) C. Walling and M. S. Pearson, *ibid.*, **86**, 2262 (1964).