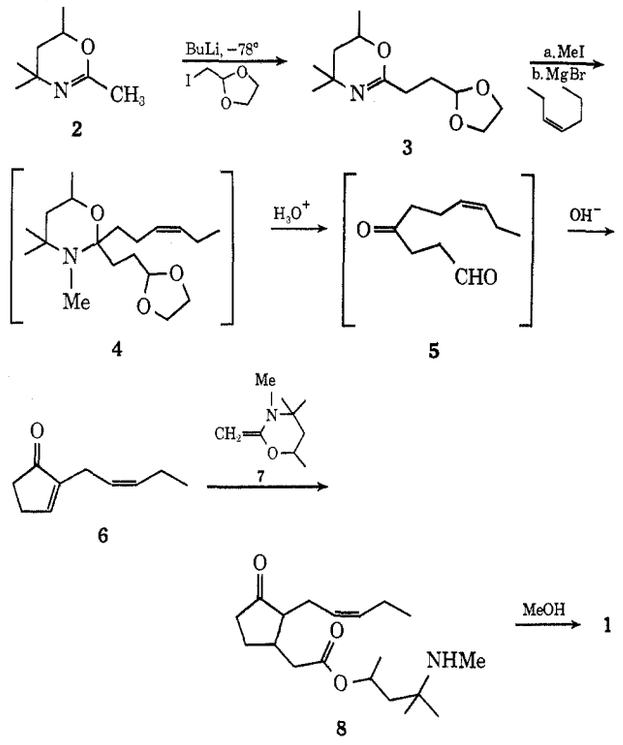
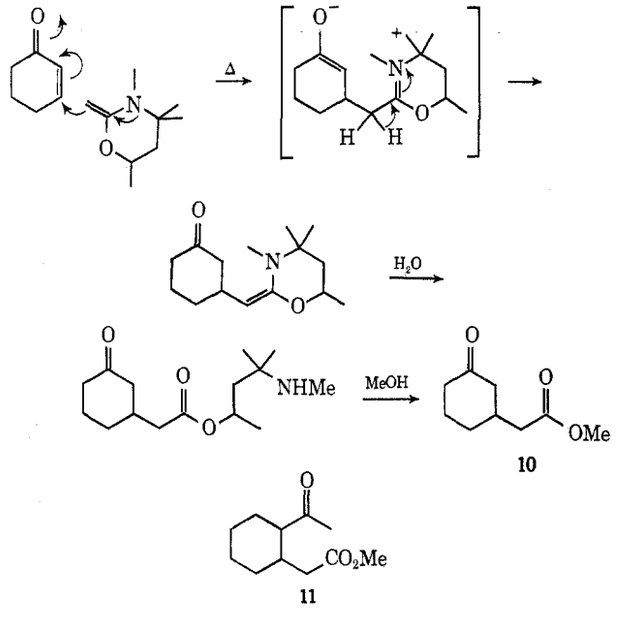
SCHEME I



(Scheme II). Thus, α,β-unsaturated carbonyl compounds are readily homologated to the acetic esters by

SCHEME II



treatment with **7** followed by hydrolysis and transesterification. In this manner, 2-cyclohexenone was converted to the keto ester (benzene, 80°, 3 hr) **10** in 55% yield and 2-acetylcyclohexene was transformed into the keto ester **11** (toluene, 110°, 3 hr) in 62% yield. Although these compounds could conceivably be prepared using sodio malonate, the absence of the hydrolysis–decarboxylation step in the present method is significant.

Addition of the ketene *N,O*-acetal **7** to the cyclopentenone **6** (3 hr, 135°) afforded the keto ester **8** after quenching in water. Transesterification using methanol and a catalytic amount of *p*-toluenesulfonic acid led to (±)-methyl jasmonate (**1**) (40% based on **6** recovered) whose properties were identical with those reported.[4]

Acknowledgment.—The authors are grateful to the National Institute of Health, National Science Foundation, and the Petroleum Research Fund Administered by the American Chemical Society for support of this work. Thanks are also due to the Lithium Corporation of America for their continued support.

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RECEIVED SEPTEMBER 20, 1972

The Photochemical Decomposition of Triphenyltriazafulvenes

Summary: Dehydrohalogenation of **1a**, **1b**, and **3** at −78° affords the triazafulvenes **2a**, **2b**, and **4**, photolysis of which affords a mixture of products; the intermediacy of the *exo*-methyleneazirine (triphenylazatriafulvene) **10** is strongly implicated.

Sir: An elegant approach to the synthesis of the theoretically interesting heterocyclic variant of cyclopropenone, azirinone, *via* decomposition at −30° of α-azidophenylketene gave only carbon monoxide and benzonitrile.[1] An analogous reaction an α-azidoallene or an isomeric triazafulvene might provide evidence for the presence of an equally interesting azatriafulvene. We now wish to report our observations on the photochemical decomposition of the triphenyltriazafulvenes, **2** and **4**.

The substituted 2-(1,3,4-triazolyl)diphenylcarbinol (**3**, X = OH) and 4-(1,2,3-triazolyl)diphenylcarbinols (**1a**, **1b**, X = OH)[2,3] were converted to the hydrochloride salts of the chlorides (**1a**, **1b**, **3**, X = Cl) by thionyl chloride in benzene at 30°. Dehydrohalogenation of these salts with triethylamine in THF at −78° gave intensely colored solutions of **2a** (λ_{max} 463 nm), **2b** (λ_{max} 454 nm), and **4** (λ_{max} 442 nm) which appeared to be quite stable for a long period of time at this temperature.[4] However, warming the THF solutions to 30° led to rapid dimerization to give the photochemically inert 4*H*,10*H*-ditriazo[1,2-*a*:1′,2′-*d*]-pyrazines, **5**, mp 278–280°, and **6**, mp 291–293°, characterized by their acid-catalyzed hydrolysis to **1a** (X = OH) and **3** (X = OH).[3,5] The fulvenes

(1) A. Hassner, R. J. Isbister, R. B. Greenwald, J. T. Klug, and E. C. Taylor, *Tetrahedron*, **25**, 1637 (1969).

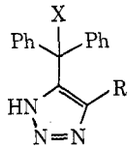
(2) These precursors resulted from the addition of excess phenyllithium to the corresponding carbomethoxytriazoles. Complete synthetic details and physical properties will appear in our full paper.

(3) All new compounds reported herein gave satisfactory elemental analyses and displayed structurally consistent ir, nmr, and mass spectra including an exact mass determination.

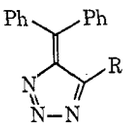
(4) A phenyl substituent at C-5 appears to be a requirement for stability in **2** based on the observation that when R = H the lifetime of this fulvene was <3 sec at −78°.

(5) Analogous (1,3) cycloadditions of 6,6-diphenyl-1,4-diazafulvene and 6,6-diphenyl-1,2,3,4-tetraazafulvene have been reported: W. Rohr, R. Swoboda, and H. A. Staab, *Ber.*, **101**, 3491 (1968); H. Behringer and M. Matner, *Tetrahedron Lett.*, 1663 (1966).

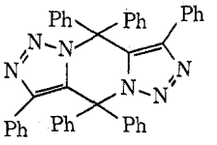
were further identified by their rapid reaction with methanol at −78° to give the ethers, **1a** (X = OCH_3), mp 101–102°, and **3** (X = OCH_3), mp 134–135°.



1



2
a, R = Ph
b, R = *p*-ClPh



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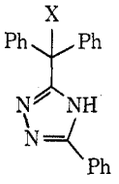
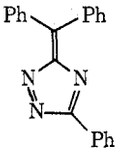


3



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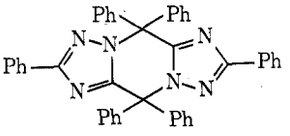


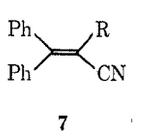
6

The irradiation[6] of either **2a** or **4** in THF–benzene (1:1) solution (0.025 *M*) at −78° for 4–5 hr led (>95% conversion) to a chromatographically separable mixture (see Table I) of benzonitrile,[7] diphenylacetylene,[7]

TABLE I
RATIOS OF PHOTOLYSIS PRODUCTS

Compd	PhCN	PhC≡CPh	7	8	9
2a	7	7	1	1	4
2b	13	13	2	1	1
4	6	6	1	1	1
14	10	10	—	1	2

2,3-diphenylquinoline (**8a**),[7,8] triphenylacrylonitrile (**7a**),[7,9] and a yellow crystalline dimer of $C_{21}H_{15}N$, mp 230–232°. *Anal.* Calcd for $C_{42}H_{30}N_2$: C, 89.65; H, 5.37; N, 4.98. Found: C, 89.55; H, 5.39; N, 4.99. This latter substance had ir absorbance at 1618 (C=N), 1598 (C=C), and 1577 (C=C) cm^{-1} and only aromatic proton resonances in the nmr spectrum while the structural symmetry present could be inferred from the mass spectrum (~70 eV) which displayed major ions at *m/e* 562 ($C_{42}H_{30}N_2^+$), 281 ($C_{21}H_{15}N^+$), and 204 ($C_{21}H_{15}N^+$–C_6H_5). The λ_{max} in EtOH occurred at 258 nm associated with the formation of a cation in concentrated sulfuric acid which had λ_{max} at 618 nm. This information, coupled with the observation that pyrolysis at 300° gives in >98% conversion only benzonitrile[7]



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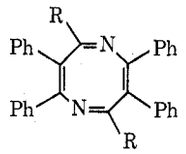
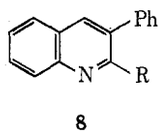


9
a, R = Ph
b, R = *p*-ClPh

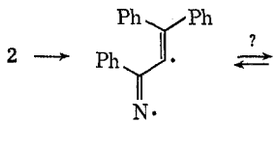


8

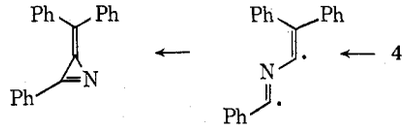
and hexaphenylpyridine,[7,10] provides a basis for a *tentative* structural assignment of hexaphenyl-1,5-diazocine (**9a**) to this dimer.[11]

The photolysis of **2b** under the previously described conditions afforded only diphenylacetylene, *p*-chlorobenzonitrile, 1-(*p*-chlorophenyl)-2,2-diphenylacrylonitrile,[7,12] mp 142–143°, 2-(*p*-chlorophenyl)-3-phenylquinoline,[7,13] mp 93–95°, and the diazocine[8] **9b**, mp 243–244°.

The two structurally diverse fulvenes **2** and **4** appear to undergo photochemically fragmentation by loss of nitrogen to common intermediates. This mechanistic symmetrization is best accommodated by the intervention of the triphenylazatriafulvene **10** which rearranges by a (1,2) phenyl shift to **7** and is an *especially* compelling intermediate in the conversion of **4** to **7**.[14] The appearance of **8** and **9** as photoproducts probably represent the ultimate result of further transformations of an intermediate triphenylazete (**13**) which arises from **11** or **12** by phenyl migration



11



10 12

7

and closure. The hypothesis that **8** and **9** are uniquely derived from **13** is supported by a reexamination[15] of the photochemistry of the triphenyl-*v*-triazine **14** which in benzene–THF (1:1) solution (0.025 *M*) upon irradiation[6] at 30° for 5 hr gave in addition to benzonitrile and diphenylacetylene both **8a** and **9a**. The $[{}_{\pi}2_s + {}_{\pi}4_s]$ dimerization[16] of **13** followed by electrolytic[17] opening would yield **9**. The path for conversion of **13** to **8** remains obscure; a *speculative*

(6) Photolyses were conducted using a 450-W Hanovia high-pressure mercury discharge lamp in a Pyrex probe.

(7) Identified by ir spectral comparison with an authentic sample and mixture melting point where applicable.

(8) W. Pfitzinger, *J. Prakt. Chem.*, **56**, 304 (1897).

(9) S. Wawzonek and E. M. Smolin, "Organic Syntheses," Collect. Vol. IV, Wiley, New York, N. Y., 1963, p 387.

(10) We wish to thank Dr. Merle Battiste for an authentic sample of this compound.

(11) The mass spectrum of **9a** resembles that of octaphenylcyclooctatetraene: R. C. Cookson, *et al.*, *J. Chem. Soc.*, 2052 (1965).

(12) G. H. Hitchings, P. B. Russell, and N. Whittaker, *ibid.*, 1019 (1956).

(13) K. Mukherjee, G. B. Behera, and M. K. Rout, *J. Inst. Chem., Calcutta*, **41**, 138 (1969).

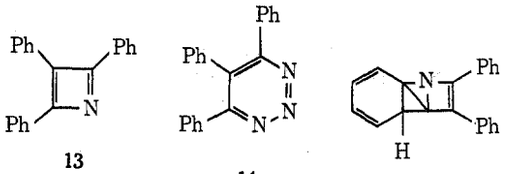
(14) Mechanistic interpretation of the photochemical conversion of β-styryl azide to phenylacetonitrile follows a parallel proposal: J. H. Boyer, W. E. Krueger, and G. J. Mikol, *J. Amer. Chem. Soc.*, **89**, 5504 (1967).

(15) Smolinsky and Chandross obtained **14** from the rearrangement of triphenylcyclopropenyl azide and report its photodecomposition to only diphenylacetylene and benzonitrile. A compound of constitution $C_{42}H_{30}N_2$ with spectral properties similar to **9a** was isolated by Smolinsky from this azide rearrangement reaction: E. A. Chandross and G. Smolinsky, *Tetrahedron Lett.*, 19 (1960). More recently Closs and Harrison reported that the photolysis of trimethyl-*v*-triazine gives 2-butyne and acetonitrile: G. L. Coss and A. M. Harrison, *J. Org. Chem.*, **37**, 1051 (1972).

(16) If the cycloaddition proceeds through a polar transition state, charge development is best accommodated by bond formation at the heteroatom sites. Of course, one other combination is possible to give ultimately a symmetrical diazocine.

(17) The ground-state conrotation required by orbital symmetry for the opening of **15** can avoid the strain of a developing trans bond by inversion at nitrogen: R. B. Woodward and R. Hoffman, "The Conservation of Orbital Symmetry," Verlag Chemie GmbH, Weinheim, West Germany, 1970, p 51.

proposal might invoke a [$_{\pi}2 + {}_{\pi}2$] intramolecular cyclization to **15** which by suitable hydrogen shift and bond reorganization is transformed into **8**.[18]



13 14 15

Acknowledgment.—We wish to thank the National Science Foundation (GP-27956) for support.

(18) An analogous sequence has been proposed for the transformation of tetraphenylcyclobutadiene to 1,2,3-triphenylnaphthalene: G. Büchi, C. W. Perry, and E. W. Robb, *J. Org. Chem.*, **27**, 4106 (1962). Other mechanistic proposals may, of course, be offered for this reaction.

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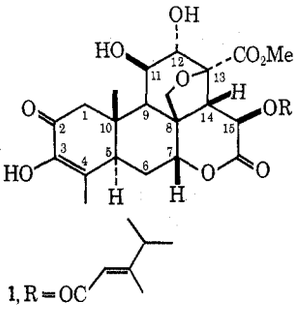
Bruceantin, a New Potent Antileukemic Simaroubolide from *Brucea antidysenterica*[1-3]

Summary: Bruceantin and bruceantarin, new antileukemic simaroubolides from *Brucea antidysenterica*, a plant used in Ethiopia in the treatment of cancer, are shown to have structures **1** and **2**, respectively.

Sir: *Brucea antidysenterica* Mill. is a simaroubaceous tree which is used in Ethiopia in the treatment of cancer.[4] In the course of a continuing search for tumor inhibitors from plant sources, we found that an alcoholic extract of *Brucea antidysenterica* Mill.[5] showed significant inhibitory activity *in vitro* against cells derived from human carcinoma of the nasopharynx (KB) and against two standard animal tumor systems.[6] We report herein the isolation and structural elucidation of a new potent antileukemic simaroubolide tumor inhibitor, bruceantin (**1**),[7] and the companion simaroubolide bruceantarin (**2**), from *Brucea antidysenterica*.

Fractionation of the alcohol extract, guided by assay against KB and P-388, revealed that the inhibitory activity was concentrated, successively, in the chloroform layer of a chloroform–water partition, the methanol layer of a 10% aqueous methanol–petroleum ether partition, the methanol layer of a 20% aqueous methanol–carbon tetrachloride partition and, finally, in the chloroform layer of a chloroform–40% aqueous methanol partition. Column chromatography of the final chloroform-soluble material on SilicAR CC7 yielded two KB cytotoxic fractions (A and B) on elution with 1% methanol in chloroform. Continued elution with 2% methanol in chloroform gave a third cytotoxic fraction (C). Careful rechromatography of fraction A on SilicAR CC7 with 20% ether in benzene gave bruceantin (**1**, 0.01%): $C_{28}H_{36}O_{11}$; $[\alpha]^{25}D$ −27.7° (*c* 3.0, pyridine); uv max (EtOH) 280 nm (ε 6450) and 221 (14,100), uv max (EtOH + NaOH) 328 nm (ε 4260) and 221 (15,500); ir (KBr) 2.90, 5.76, 6.05, 6.13, 8.70, and 9.45 μ; mass spectrum *m/e* 548.222 (M^+, calcd 548.225), 438, 420, 402, 297, 151, 111.0819 (calcd, $C_7H_{11}O$, 111.0809); nmr ($CDCl_3$) τ 8.88 [6 H, d, J = 6.5 Hz, $CH(CH_3)_2$], 8.56 (3 H, s, 10-CH_3), 8.11 (3 H, br s, 4-CH_3), 7.82 [3 H, s, $CH{=}C(CH_3)$], 7.29 (1 H, br m, OH), 6.47 (1 H, br s, OH), 6.24 (3 H, s, OCH_3), 4.39 [1 H, br s, $O_2CCH{=}C(CH_3)$], 3.87 (1 H, br s, OH), and 3.79 (1 H, d, $J_{15,14}$ = 13 Hz, 15-H).



1, R = OC
2, R = OCC_6H_5
3, R = $OCCH_3$
4, R = H
5, R = $OCCH_2CH(CH_3)CH(CH_3)_2$

Rechromatography of fraction B on SilicAR CC7 with 30% ether in benzene gave bruceantarin (**2**, 0.002%): $C_{28}H_{30}O_{11}$; mp 182–185°; $[\alpha]^{25}D$ −20.7° (*c* 0.6, pyridine); uv max (EtOH) 278 nm (ε 7000) and 231 (10,500), uv max (EtOH + NaOH) 330 nm (ε 4480) and 230 (9030); ir (KBr) 2.9, 5.78, 6.03, 6.08, 6.12, 7.88, 8.70, 9.0, 9.45, and 13.8 μ; mass spectrum *m/e* 542 (M^+), 437, 420, 402, 297, 151, 105, and 77; nmr ($CDCl_3$) τ 8.63 (3 H, s, 10-CH_3), 8.20 (3 H, br s, 4-CH_3), 6.56 (3 H, s, OCH_3), 3.58 (1 H, d, $J_{15,14}$ = 13 Hz, 15-H), 2.60 (3 H, m, B_2X portion of A_2B_2X, *m* and *p*-benzoate protons), and 2.07 (2 H, d of d, A_2 part of A_2B_2X system, J_{AB} = 7.5, J_{AX} = 1.5 Hz, *o*-benzoate protons).

Rechromatography of fraction C on SilicAR CC7 using 2:1 ether in benzene gave the known bruceine B (**3**, 0.002%), characterized by comparison of its melting point, $[\alpha]D$, and ir, nmr, uv, and mass spectra with those previously reported.[8]

Bruceantin (**1**) and bruceantarin (**2**) gave a positive ferric chloride test, and displayed in their uv spectra the large bathochromic shift with alkali characteristic of diosphenols. In addition, acetylation of bruceantin (**1**) gave a triacetate which displayed neither the uv absorption at 280 nm nor the associated bathochromic shift. The mass spectra of **1** and **2** displayed as primary fragmentations peaks corresponding to a

(1) Tumor Inhibitors. LXXXII. Part LXXXI is ref 2.

(2) S. M. Kupchan and G. Tsou, *J. Org. Chem.*, in press.

(3) Supported by grants from the National Cancer Institute (CA-11718) and American Cancer Society (T-275 and IC-57H), and a contract with the National Cancer Institute (NIH-NCI-C-71-2099).

(4) J. L. Hartwell, *Lloydia*, **34**, 221 (1971).

(5) Stem bark was collected in Ethiopia in June 1971. Leaves and the wood of stems from Ethiopia also yielded active extracts. We thank Dr. Robert E. Perdue, Jr., USDA, Beltsville, Md., for supplying the plant material.

(6) Activity was noted against P-388 leukemia in the mouse and Walker 256 intramuscular carcinosarcoma in the rat. Cytotoxicity and *in vivo* activity were assayed as in *Cancer Chemother. Rep.*, **25**, 1 (1962).

(7) Bruceantin showed significant antileukemic activity against P-388 lymphocytic leukemia over a 50–100-fold dosage range at the μg/kg level, and cytotoxicity (ED_{50}) against KB cell culture at 10^{-3} μg/ml. Bruceantarin showed only moderate activity against P-388, and the previously isolated[8] bruceine B showed only marginal activity against this system.

(8) J. Polonsky, Z. Baskevitch, A. Gaudemer, and B. C. Das, *Experientia*, **23**, 424 (1967).