Novel Phototransformations of Bridgehead-Dimethyl-Substituted Dibenzobarrelene. Structure of the Photoproducts[1]

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Single-crystal X-ray diffraction studies have revealed that the phototransformation products of 11,12-dibenzoyl-9,10-dihydro-9,10-dimethyl-9,10-ethenoanthracene (1) are correctly represented as 1,5-dibenzoyl-4,8-dimethyl-2,3:6,7-dibenzocyclooctatetraene (9), the dibenzopentalene derivative 13, and the hexacyclic peroxycarbinol 17 and not the earlier reported structures 1,4-dibenzoyl-5,8-dimethyl-2,3:6,7-dibenzocyclooctatetraene (3), the benzonaphthalene derivative 6, and the carbinol 5, respectively. Both singlet-state-mediated "tri-π-methane" rearrangement and the triplet-state-mediated "di-π-methane" rearrangement of 1 could give rise to a 1,4-diradical intermediate 8, which could then lead to the cyclooctatetraene 9 by a Grob-type fragmentation or undergo a 1,2-rearrangement to the dibenzopentalene 13. The hexacyclic peroxycarbinol 17 could arise through the oxygen quenching of the diradical intermediate 14, derived from 12, followed by extensive rearrangements.

In an earlier publication,[3] we had reported the results of our studies on the phototransformations of a few dibenzobarrelenes containing 1,2-dibenzoylalkene moieties, including that of a bridgehead-dimethyl-substituted dibenzobarrelene such as 11,12-dibenzoyl-9,10-dihydro-9,10-dimethyl-9,10-ethenoanthracene (1). It has been observed that the irradiation of 1 gives rise to a mixture of products, depending on the reaction conditions. Thus, the irradiation of 1 in methanol gave a mixture of two products, identified as 1,4-dibenzoyl-5,8-dimethyl-2,3:6,7-dibenzocyclooctatetraene (3) and 2,3-dibenzoyl-2,3-dihydro-1,4-dimethyl-2,3-benzonaphthalene (6), whereas irradiation of 1 in benzene gave a mixture of 3, 6, and a carbinol derivative of 5 (Scheme I). On the basis of well-established mechanistic pathways for the phototransformations of benzo and naphthobarrelene derivatives,[4] it had been suggested that the dibenzocyclooctatetraene 3 and the benzonaphthalene 6 arise through a singlet-state-mediated intramolecular cycloaddition, leading to the polycyclic cage intermediate 2, followed by its thermal reorganization. The carbinol derivative 5, on the other hand, had been assumed to arise from the dibenzosemibullvalene 4 formed through the triplet-state-mediated "di-π-methane" rearrangement of 1. Just recently, Pokkuluri, Scheffer, and Trotter,[5] in a notable contribution to the photorearrangement of dibenzobarrelenes, have shown that certain bridgehead-substituted dibenzobarrelenes could undergo photorearrangement through a "tri-π-methane" route, leading to 1,4-diradical intermediates, which could subsequently lead to cyclooctatetraene derivatives with C_2 symmetry and dibenzopentalene derivatives. This prompted us to reexamine the structures of the photoproducts formed from the dimethyldibenzobarrelene 1 through X-ray crystallographic analysis.[6] The results of these studies show that all the photoproducts from 1 are correctly identified as 1,5-dibenzoyl-4,8-dimethyl-2,3:6,7-dibenzocyclooctatetraene (9), the dibenzopentalene derivative 13, and the hexacyclic peroxycarbinol 17[7] and not the earlier reported structures 3, 6, and 5, respectively, for these compounds (Scheme II).

X-Ray Crystallographic Analysis of the Photoproducts from 1. Single-crystal X-ray structure determination of the photoproducts (9, 13, and 17) shows discrete molecular units at general positions. The compounds 9, 13, and 17 crystallize in the space groups $P2_1/c$, $P2_1/n$, and $P1$, respectively. None of the three structures show any kind of molecular disorder. The projection view of the three molecules, along with solvent molecules in the lattice, wherever present are shown in Figures 1–3, respectively. Pertinent structural parameters are listed in Table I of the supplementary material.

Compound 9 has a central eight-membered ring to which two six-membered aromatic rings are fused. The core eight-membered ring has a "tub shape" with a planar base consisting of carbon atoms C_7, C_8, C_{15}, and C_{16}. The fused six-membered aromatic rings make a dihedral angle of 81.4° with each other.

Compound 13 has a tetracyclic, 6,5,5,6-member fused-ring core, which is rather planar (mean deviation from the least-squares plane = 0.2 Å). The two halves, 6,5- and 5,6-membered fused rings make an angle of 2.8°. This molecule crystallizes with 0.5 molecule of benzene per molecule of 13 in the lattice. All the phenyl rings are planar within acceptable deviation.

The crystal lattice of 17 contains a molecule of CH_3OH, from which it was crystallized. One of the five-membered rings contains the peroxy linkage with O–O distance being

(1) Contribution No. NDRL-3315 from the Notre Dame Radiation Laboratory and No. RRLT-PRU-11 from the Regional Rsearch Laboratory, Trivandrum.

(2) (a) Regional Research Laboratory, Trivandrum. (b) Jawaharlal Nehru Centre for Advanced Scientific Research. (c) University of Missouri—St. Louis. (d) University of Notre Dame.

(3) Kumar, C. V.; Murty, B. A. R. C.; Lahiri, S.; Chakachery, E.; Scaiano, J. C.; George, M. V. *J. Org. Chem.* **1984**, *49*, 4923–4929.

(4) For some pertinent references, see: (a) Zimmerman, H. E.; Givens, R. S.; Pagni, R. M. *J. Am. Chem. Soc.* **1968**, *90*, 6096–6108. (b) Zimmerman, H. E.; Bender, C. O. *J. Am. Chem. Soc.* **1970**, *92*, 4366–4376. (c) Bender, C. O.; Shugarman, S. S. *J. Chem. Soc., Chem. Commun.* **1974**, 934–935. (d) Bender, C. O.; Brooks, D. W. *Can. J. Chem.* **1975**, *53*, 1684–1689. (e) Zimmerman, H. E. In *Rearrangements in Ground and Excited States*; de Mayo, P.; Ed.; Academic: New York, 1980; Vol. 3, Chapter 16, pp 131–166.

(5) Pokkuluri, P. R.; Scheffer, J. R.; Trotter, J. *J. Am. Chem. Soc.* **1990**, *112*, 3676–3677.

(6) We thank Professor J. R. Scheffer for providing us with a preprint of his publication (ref 5) and suggesting we reexamine the structure of the photoproducts from dibenzobarrelene derivatives by diffraction studies.

(7) The analytical data reported for 17 in the earlier publication (ref 3) appear to be incorrect. Recent attempts to determine the molecular weight of 17 through high-resolution mass spectrometry were unsuccessful since it was undergoing facile fragmentation and the M^+ peak could not be detected.

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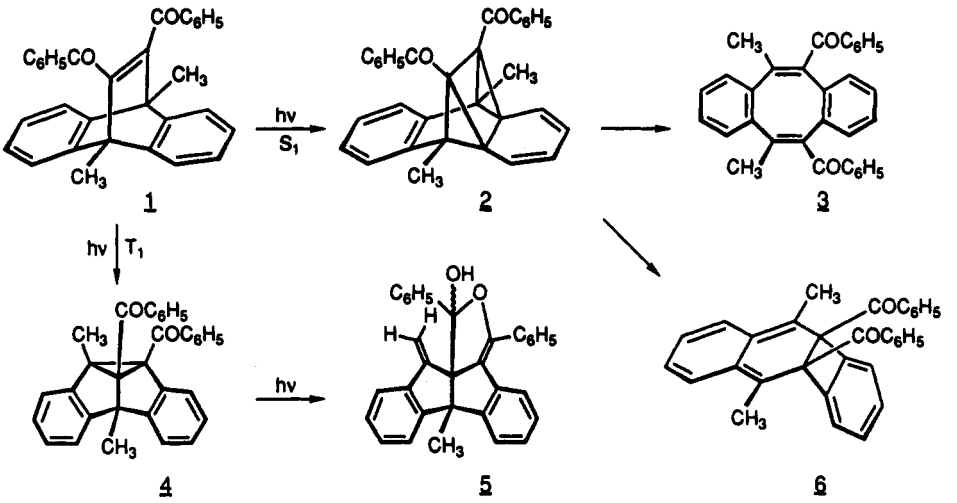
Scheme I



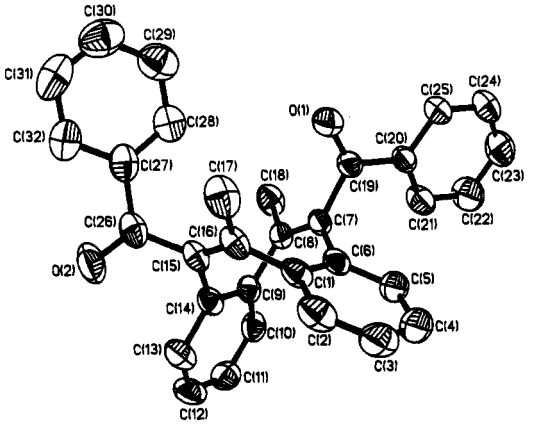


Figure 1. The projection view drawing of the structure of *9*. The thermal ellipsoids are drawn at 50% probability.

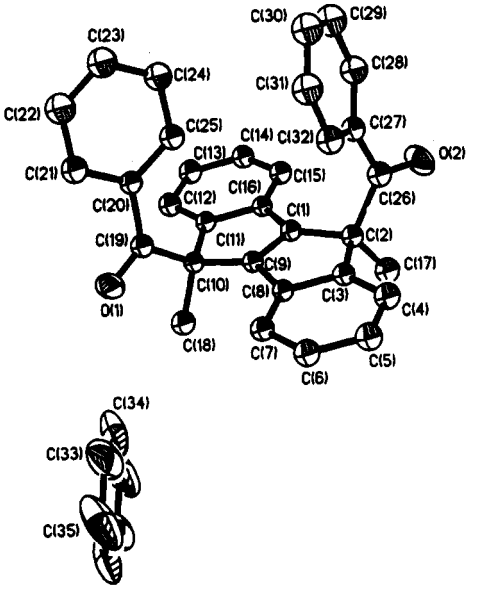


Figure 2. The projection view drawing of the structure of *13*. The thermal ellipsoids are drawn at 25% probability.

1.478 (4) Å, which is comparable with the average peroxide distance of 1.464 (9) Å.[8] The two "wings" of the fused ring core, each half containing a six- and five-membered ring,

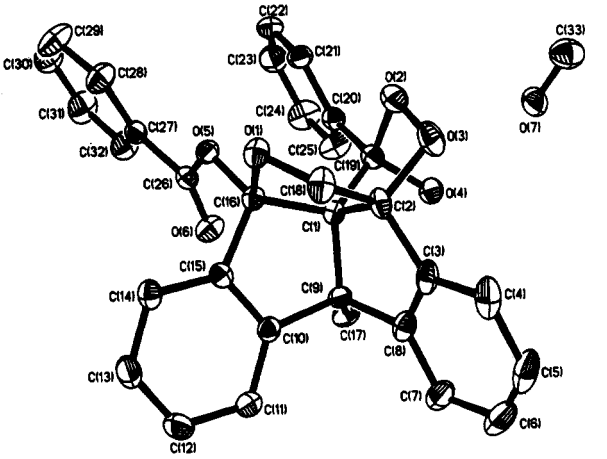


Figure 3. The projection view drawing of the structure of *17*. The thermal ellipsoids are drawn at 50% probability.

make an angle of 75.8° (dihedral angle). All the bond lengths and angles are as expected for the molecular arrangement in **17**.

No unusual nonbond interactions were found in all three cases (**9**, **13**, and **17**).

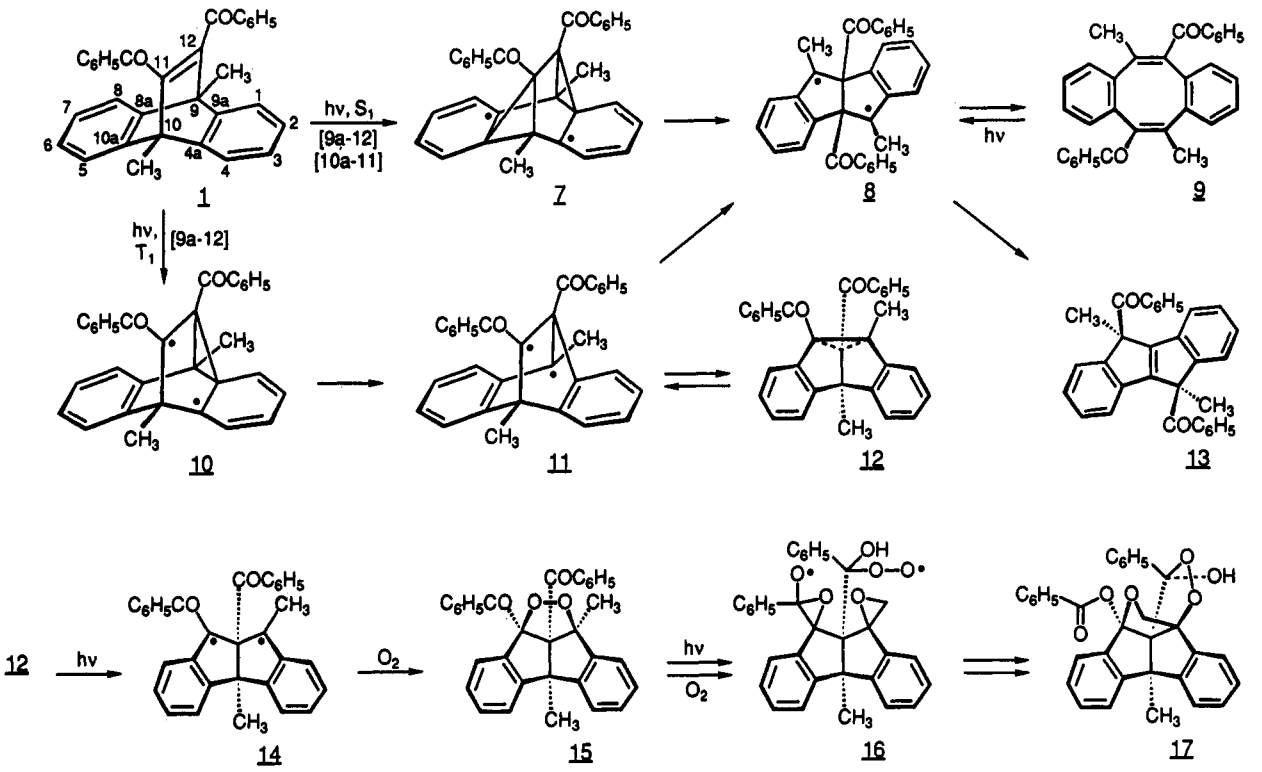
Discussion

Probable pathways for the formation of **9**, **13**, and **17** from **1** are shown in Scheme II. The formation of the cyclooctatetraene **9**, with C_2 symmetry, for example, could be through a singlet-state-mediated tri-π-methane rearrangement, involving [9a–12] and [10a–11] bond interactions, and leading to the diradical intermediate **7**, which can subsequently give the benzylic, 1,4-diradical intermediate **8**. A similar tri-π-methane rearrangement had been invoked earlier in the photorearrangement of dimethyl 9,10-dimethyl-9,10-dihydro-9,10-ethenoanthracene-11,12-dicarboxylate, postulating the intermediacy of a bisbenzylic biradical, analogous to **8**.[5] A Grob-type of fragmentation of **8** will result in **9**, whereas the rearrangement of **8**, involving benzoyl group migrations, would lead to the dibenzopentalene derivative **13**. Although examples of 1,2-rearrangements of diradicals in photochemistry are not numerous,[5,9] it would be reasonable

(8) Allen, F. W.; Kennard, O.; Watson, D. J.; Brammer, L.; Orpen, A. G. *J. Chem. Soc., Ferkin Trans. 2* **1987**, S1.

(9) For some recent references on 1,2-rearrangements of photochemically generated 1,3-diradicals, see: (a) Zimmerman, H. E.; Pratt, A. C. *J. Am. Chem. Soc.* **1970**, *92*, 6259–6267. (b) Zimmerman, H. E.; Kamat, A. P. *J. Am. Chem. Soc.* **1988**, *110*, 900–911.

Scheme II



to assume that the presence of the carbonyl moiety in the migrating groups (benzoyl groups) in 8 would facilitate the rearrangement to 13.

The formation of the hexacyclic peroxycarbinol 17 from 1 is somewhat intriguing. It appears that the triplet-state-mediated di-π-methane rearrangement of 1, involving an initial [9a–12] bond interaction (one of the four possible degenerate interactions[5]) would result in the diradical 10, which could rearrange to the 1,3-diradical intermediate 11, which is the precursor of the dibenzosemibullvalene 12. The fact that none of 12 is isolated from the photolysis of 1 would suggest that 12, even if formed, would be unstable due to the steric crowding of the substituents present in the cyclopropane ring and hence would revert back to the precursor diradical 11 or undergo further photocleavage leading to a new diradical 14. In the presence of adventitious oxygen present in the system, the diradical 14 would be quenched to give the cyclic peroxide 15. It may be mentioned in this connection that Scheffer et al. have recently isolated a peroxide, analogous to 15, from the photorearrangement of dimethyl 9,10-dichloro-9,10-dihydro-9,10-ethenoanthracene-11,12-dicarboxylate and confirmed its structure through X-ray crystallographic analysis.[10] Subsequent transformation of 14, involving cleavage of the peroxy linkage and hydrogen atom abstraction from the methyl group, followed by reaction with oxygen and subsequent rearrangements would lead to the diradical intermediate 16. Further rearrangements of 16 through multistep pathways would ultimately give rise to the hexacyclic peroxycarbinol 17. Although oxygen quenching of several 1,3-diradical intermediates are reported in the literature,[11] the trapping of 14 by oxygen to give ultimately 17 is one of the few examples of oxygen trapping of the diradical intermediates involved in the photorearrangement of dibenzobarrelenes.

It is pertinent to point out that the irradiation of 1 in the complete absence of oxygen does not give any 17; only a mixture of 9 and 13 is formed under these conditions. Thus, the irradiation of 1 in benzene for 1 h, under argon bubbling, gave rise to mostly 9 (79%), along with a small amount (10%) of 13. The fact that the triplet yield of 1 is fairly high ($\phi_T = 0.7$)[3] and that the cyclooctatetraene 9 is the major product of irradiation of 1 under oxygen-free conditions would suggest that there is a triplet-state-mediated pathway also available for the formation of 9. It is quite likely that the diradical intermediate 11, formed through the triplet-state-mediated pathway, may be undergoing further transformation to 8, which could then lead to 9, as shown in Scheme II.

It has been reported earlier[3] that the cyclooctatetraene 9 (earlier representation 3), on irradiation, is converted to 13 (earlier representation 5). This would suggest that 9 perhaps is initially converted to the diradical 8, which would then rearrange to 13.

Experimental Section

X-ray Structure Determination of 9, 13, and 17. Colorless crystals of 9, 13, and 17 with appropriate dimension were subjected to X-ray crystallographic analysis using a Siemens R3 automated four-circle diffractometer. Summary of crystal data and intensity collection parameters are presented in Table I of the supplementary material. Data reduction and structure solution were achieved by SHELXTL-PLUS structure solution software package.[12] All calculations were performed on a VAX station II GPX computer using SHELXTL-PLUS software.

Irradiation of 1 in the Absence of Oxygen. A solution of 1 (440 mg, 1 mmol) in benzene (200 mL) was irradiated for 1 h (RPR, 3500 Å) under argon bubbling and worked up by removal of the solvent under vacuum and chromatographing the residue over silica gel. Elution with a mixture (1:5) of chloroform and

(10) Private communication from Professor J. R. Scheffer (letter dated October 15, 1990).

(11) For a recent review on the quenching of diradicals by oxygen, see: Adam, W.; Grabowski, S.; Wilson, R. M. *Acc. Chem. Res.* **1990**, *23*, 165–172.

(12) Sheldrick, G. M. Siemens Analytical X-Ray Division, Madison, Wisconsin, 1989.

petroleum ether gave 45 mg of 13, mp 151-152 °C (mixture mp), after recrystallization from cyclohexane. Further elution of the column with a mixture (1:4) of chloroform and petroleum ether gave 350 mg (79%) of 9, mp 211-212 °C (mixture mp), after recrystallization from cyclohexane.

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Supplementary Material Available: Summary of crystal data and intensity collection parameters, a complete list of atomic coordinates, anisotropic displacement coefficients, H atom coordinates and isotropic displacement coefficients, and bond distances and bond angles for 9, 13 and 17 (19 pages). Ordering information is given on any current masthead page.

Development of an Asymmetric Approach to the 3,8-Diazabicyclo[3.2.1]octane Moiety of Quinocarcin via Intermolecular 1,3-Dipolar Cycloadditions of Photochemically Generated Azomethine Ylides

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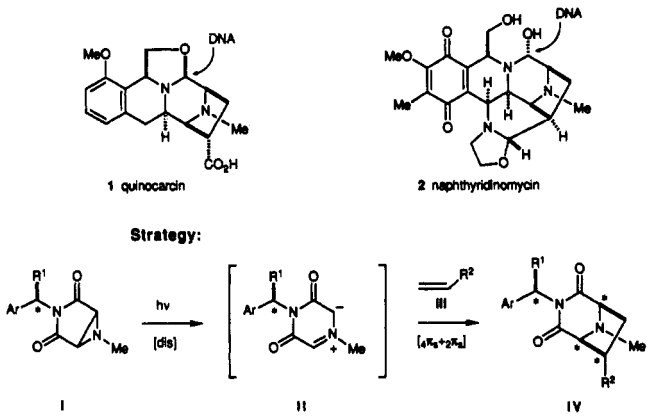
Exploratory work culminating in an enantioselective approach to the DNA-reactive alkaloid quinocarcin (1) is detailed. The key step involves auxiliary-controlled dipolar cycloaddition between photochemically generated azomethine ylides such as 11 and Oppolzer's chiral acryloyl sultam (-)-32 to assemble the 6-exo-substituted 3,8-diazabicyclo[3.2.1]octane core of 1. The synthetic sequence begins with condensation of the benzylamines 3 and maleic anhydride to give the N-alkylated maleimides 6. Triazoline formation (MeN_3) followed by photolytic ($\lambda > 3000$ Å) extrusion of nitrogen leads to the corresponding aziridines 10. Upon irradiation at 2537 Å, these aziridines undergo electrocyclic ring-opening to give azomethine ylides 11, which can be trapped with (-)-32 to give the 6-exo-substituted cycloadduct 33 (diastereoselectivity, ds >25:1). These results stand in sharp contrast to cycloadditions of 11 with (achiral and chiral) acrylate ester dipolarophiles as well as acrylonitrile, which proceed with no appreciable facial selectivity. The expected *re*-face selectivity of (-)-32 was confirmed in one case by X-ray crystallographic analysis of endo-adduct 35a. Removal (and recovery) of the chiral sultam auxiliary can be effected by titanium(IV)-mediated alcoholysis to give ester derivatives of the cycloadducts.

Introduction

Quinocarcin (1) and naphthyridinomycin (2) are potential antitumor antibiotics isolated from *Streptomyces* broths.[1,2] Both of these compounds have been shown to inhibit DNA (and in some systems RNA) synthesis,[3] and the citrate salt of 1 exhibits good activity against a variety of tumor systems.[4] The inhibition of DNA synthesis by 2 appears to occur at the template level via the irreversible and selective binding of these drugs to dG-dC base pairs. Computational studies on quinocarcin support nucleophilic attack of the 2-amino group of guanine onto an imminium species derived from the hemiaminal at C(7).[5] Since the critical DNA-drug interaction (as well as any preceeding recognition step) necessarily involves the combination of chiral molecules, it stands to reason that one of the two possible antipodal forms of the drug (presumably the naturally occurring one) would be more active and/or selective.[6] These considerations provide impetus for the development of asymmetric syntheses of these bioactive molecules and analogues thereof (Scheme I).[7,8]

An attractive strategy for the asymmetric synthesis of 1 and 2 focuses on construction of the 3,8-diazabicyclo-[3.2.1]octane skeleton IV embodied in both targets via the stereocontrolled 1,3-dipolar cycloaddition of an azomethine

Scheme I



ylide II and an olefinic dipolarophile III.[9] If sufficient diastereofacial/topological control could be maintained

† Address inquiries concerning the X-ray structure determination to this author at the Department of Chemistry, The University of Akron, Akron, OH 44325.

(1) Quinocarcin: Tomita, F.; Takahashi, K.; Shimizu, K. *J. Antibiot.* **1983**, *36*, 463. Takahashi, K.; Tomita, F. *Ibid.* **1983**; *36*, 468. Hirayama, N.; Shirahata, K. *J. Chem. Soc., Perkin Trans. 2* **1983**, 1705.

(2) Naphthyridinomycin: Kluepfel, D.; Baker, H. A.; Piattoni, G.; Sehgal, S. N.; Sidorowicz, A.; Singh, K.; Vezina, C. *J. Antibiot.* **1975**, *28*, 497. Sygusch, J.; Brisse, F.; Hanessian, S.; Kluepfel, D. *Tetrahedron Lett.* **1974**, 4021. Eratta, *Ibid.* **1975**, 170. Cyanocycline A: Zmijewski, M. J., Jr.; Goebel, M. *J. Antibiot.* **1982**, *35*, 524. Hayashi, T.; Noto, T.; Nawata, Y.; Okazaki, H.; Sawada, M.; Ando, K. *Ibid.* **1982**, *35*, 771. SF-1739 HP/naphthocyanidine: Itoh, J.; Omoto, S.; Kodama, Y.; Hisamatsu, T.; Niida, T.; Ogawa, Y. *Ibid.* **1982**, *35*, 642.

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