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(14) The amount of incorporation in a standard 1-ml, 10-min incubation varied from 0.25 to 1.0%, depending on the specific enzyme preparation.
(15) The enzyme preparation itself apparently contains low levels of **2a**, as well as squalene. The stimulation of the reaction by added **2a** is restricted by the fact that squalene synthetase is inhibited by high substrate (and substrate analogue) concentrations.[3]
(16) GLC–mass spectrometry was performed on an AEI MS-12 equipped with a Biemann-Watson molecular separator and an Infotronics Model 2400 gas chromatograph fitted with 6 ft × 0.25 mm i.d. columns. The stationary phase was 2% Dexsil 300 on 80–100 Chromosorb GHP. Mass spectrum of **1b** at 50 eV ionization potential, *m/e* (% relative intensity): 396 (1.6), 327 (0.8), 285 (0.9), 259 (0.6), 205 (0.7), 204 (0.9), 203 (1.4), 191 (2.0), 189 (2.1), 177 (1.7), 163 (2.2), 149 (5.0), 137 (10.0), 123 (9.0), 121 (9.0), 109 (10.2), 107 (8.8), 95 (20.0), 81 (56.0), 69 (100). The peaks at 396 (M^+), 327 ($M^+ - 69$), 285 ($M^+ - 43 - 68$), and 259 ($M^+ - 68 - 69$), highly characteristic fragmentations of squalene and its analogs, occur here 14 mass units lower than the corresponding peaks in squalene itself.[25]
(17) Condensation of 3-desmethylfarnesyl bromide[9a] with the sodium salt of 2-mercapto-2-thiazoline (THF, −78°) gave 2-(3-desmethylfarnesylthio)-2-thiazoline (85% yield).[18,19] Reaction of this intermediate with BuLi and farnesyl bromide (−78°, THF), followed by Raney nickel desulfuration (EtOH, 0°), gave **1b** as a mixture of isomers.[18,19] The desired all-E isomer was isolated by chromatography on basic alumina.[19] The stereochemical assignment was established by the presence of an infrared band at 10.3 μ (trans disubstituted double bond)[26] and by the highly preferential formation of a thiourea clathrate.[27]
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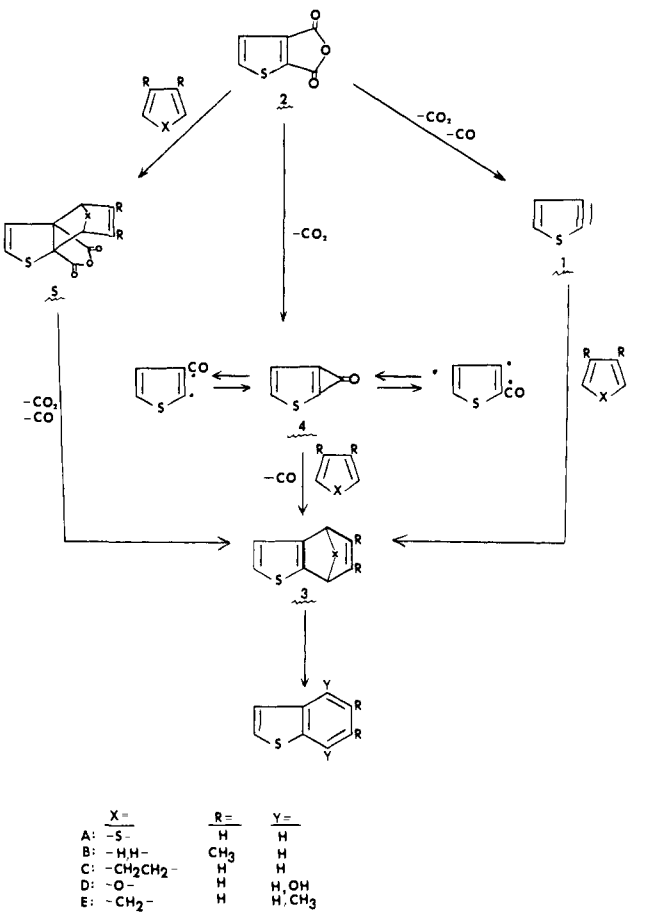
2,3-Thiophyne

Sir:

It is ironic that the existence of the very first type of aryne intermediate to be formulated,[1] the five-membered hetaryne, remains in doubt[2b,d] after 75 years. The many attempts to generate such species by methods successfully applied to the six-membered carbocyclic and heterocyclic analogues[2] either fail to give typical "aryne" products of cine-substitution and cycloaddition[2,3] or do so by demonstrated[4] nonaryne pathways. Although it has been claimed[2c] that this failure is due to "the prohibitive ring strain that would be associated with a dehydro bond in a five-membered heterocycle" the fact that cyclopentyne has been generated[5,6] suggests that this reason is insufficient. An additional factor is probably the ability of five-membered heterocycles to avoid aryne formation by undergoing unique reactions[4] unavailable to the electronically dissimilar[8] six-membered carbocyclic and heterocyclic analogues.



	X =	R =	Y =
A:	-S-	H	H
B:	-H,H-	CH_3	H
C:	$-CH_2CH_2-$	H	H
D:	-O-	H	H, OH
E:	$-CH_2-$	H	H, CH_3

A well-known method for generating arynes which might be expected to minimize this latter problem is the thermolytic elimination of CO and CO_2 from cyclic anhydrides.[9] Previous attempts to apply this method to five-membered hetarynes have led to either no reaction in the case of the anhydride of thiophene-3,4-dicarboxylic acid[3f] or a variety of nonaryne, oxygen-containing, condensation products from the anhydrides of the *N*-phenylpyrrole dicarboxylic acids.[3b] These results suggest that the probability of aryne formation would be optimized under high-temperature, vapor-phase conditions so that both CO and CO_2 are lost before any bimolecular reactions occur. The anticipated reactivity of the aryne[2c] and the probable instability of its dimerization products[10] under such conditions further dictates that a large excess of an aryne trapping agent be present. Accordingly, the flash vacuum thermolysis (FVT)[11] of the readily available[12] anhydride of thiophene-2,3-dicarboxylic acid (**2**) was carried out in the presence of several trapping agents as summarized in Table I.

The products from experiments A–E strongly suggest the intermediacy of an adduct **3** which aromatizes by desulfurization (A), dehydrogenation (B), a retro-Diels–Alder reaction (C), and carbon–oxygen (D) or carbon–carbon bond cleavage (E). Analogies for each of these processes in related systems are well known.[13] The cyclopentenothiopenes found in D are probably secondary reaction products of the thianaphthols analogous to the conversion of naphthols to indene.[14]

The most obvious origin of the adduct **3** would be a Diels–Alder reaction between the diene trap and the thiophyne **1.** Although such evidence ordinarily would be considered adequate to support claims for the generation of an aryne,[2] the known formation of thiophyne adducts via nonaryne mechanisms[4b] dictates that additional evidence or arguments be presented.

First of all, the only reports of the formation of "aryne ad-

Table I. FVT[a] of **2** with Trapping Agents

Expt	Trap	Products[b] (% yield)[c]
A	Thiophene	Thianaphthene (59); sulfur
B	2,3-Dimethyl-butadiene	5,6-Dimethylthianaphthene (13)
C	1,3-Cyclohexa-diene	Thianaphthene (14)
D	Furan	Thianaphthols[d] (1); cyclopentenothiophenes[d] (9)
E	Cyclopentadiene	4-(7) and 7-Methylthianaphthene (6)
F	Hydrogen	Thiophene (15); thianaphthene (32)

[a] Carried out by subliming **2** over a 4-cm coil of Nichrome wire at ca. 500° in a stream of the pure trapping agent at 1–5 mmHg. [b] Unless otherwise noted identified by spectral (ir, NMR, MS) comparison with authentic samples. [c] Based on **2** charged. [d] Spectral evidence only.

ducts" by nonaryne mechanisms occur with the single diene, tetracyclone; none of the dienes used in this study displays such reactivity.

Secondly, the possibility that the adduct **3** arises by loss of CO from a species derived from the diene and a thenoyl fragment **4** is considered unlikely, since no other products derived from this fragment were found in the reactions in Table I. Such products are obtained from the *N*-phenylpyrrole anhydrides[3b] and reactions of the thiophene anhydrides in the condensed phase.[12] Furthermore, with H_2 as a trap (expt F), thiophene (from **1** + H_2), thianaphthene (from **1** + thiophene), but no thiophene aldehydes (from **4** + H_2), whose stability under the reaction conditions was demonstrated, were found.

The possibility that the adduct **3** arises by loss of CO_2 and CO from a Diels–Alder adduct (**5**) of the diene and the maleic anhydride moiety of the thiophene anhydride **2** is considered unlikely, since such unprecedented dieneophilic reactivity reasonably should be paralleled with 2,3-dicyano- and 2,3-dicarbomethoxythiophene. Both of these compounds are recovered unchanged from FVT in the presence of thiophene, the most efficient trap utilized in this study. Furthermore, if *any* direct reaction between **2** and an electron-rich aromatic compound such as thiophene were occurring some Friedel–Crafts acylation also should be observed.[15] No such products were formed in spite of their demonstrated stability under the FVT conditions.

Finally, the possibility that the trapping agent in anyway induces the decomposition of the 2,3-anhydride **2,** as is observed with other five-membered hetaryne precursors,[4b] is eliminated by the extensive decomposition which **2** undergoes upon FVT with only N_2 as the carrier gas.[16]

Taken in toto the above results constitute the most convincing evidence to date for the generation of a five-membered hetaryne, thiophyne. Further studies on the properties of this and other arynes of this type are in progress.

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Synthesis of the Non-Tryptamine Moiety of the Aspidosperma-Type Indole Alkaloids via Cleavage of Cyclic α-Diketone Monothioketal. An Efficient Synthesis of (*dl*)-Quebrachamine and a Formal Synthesis of (*dl*)-Tabersonine

Sir:

Application of Marshall's ring cleavage method[1] on the ketoester **3** led easily to the dithianyl half ester **5** which was shown to be a suitable precursor for a construction of the non-tryptamine moiety of the Aspidosperma-type indole alkaloids.[2]

Readily available 4-ethoxycarbonylcyclohexanone ethyleneketal (**1**)[3] was converted into the ketoester **3,** bp 78–80° (1 mmHg), in 90% yield through two steps ((1) LDA[4]–EtBr (2) 1 N H_2SO_4). According to Woodward's method,[5] **3** was treated with pyrrolidine followed by propane-1,3-dithiol di-*p*-toluenesulfonate[5,6] to yield the α-diketone monothioketal **4,** mp 76–78°, in 65% yield from **3.**

By following Marshall's procedure, **4** was treated with sodium hydride in the presence of 3 molar equiv of water to give the oily dithianyl half ester **5**;[7] NMR ($CDCl_3$) (δ) 3.96 (1 H, t, J = 7.0 Hz, $_H\!\times\!\overset{S}{S}\!-$).

A standard DCC procedure on **5** with tryptamine afforded the oily dithianyl amide **6,** NMR ($CDCl_3$) (δ) 3.87 (1 H, t, J = 6.5 Hz, $_H\!\times\!\overset{S}{S}\!-$), in 60% yield from **4.** Hydrolysis (MeI, aqueous CH_3CN, reflux)[8] of the dithianyl amide **6** led to the stereoisomeric lactams **8** and **9** in 83% total yield instead of the formylamide **7.** The products may have resulted via **7** by the catalytic effect of hydriodic acid generated during the reaction.[8] The ratio of α-ethyl isomer **8** (mp 247–249°; ir (Nujol) 3180, 1728, 1620 cm^{-1}; NMR ($CDCl_3$) (δ) 0.91 (3 H, t, J = 7.0 Hz), 1.23 (3 H, t, J = 7.5 Hz), 4.11 (2 H, q, J = 7.5 Hz)) to β-ethyl isomer **9** (mp 172–173°; ir (Nujol) 3370, 1728, 1630 cm^{-1}; NMR ($CDCl_3$) (δ) 0.83 (3 H, t, J = 7.8 Hz), 1.33 (3 H, t, J = 7.0 Hz), 4.29 (2 H, q, J = 7.0 Hz)) was about 1 to 6, but this was not a serious problem for this synthetic purpose, since one of the asymmetric centers was lost in a later stage.[9] Reduction of the α-ethyl isomer **8** to the corresponding amino alcohol **10,** (mp 232.5–235°; ir (Nujol) 3260 cm^{-1}; NMR ($CDCl_3$ + Me_2SO-d_6) (δ) 0.90 (3 H, t, J = 7.0 Hz)) was accomplished in 95% yield, by $LiAlH_4$ in boiling tetrahydrofuran. Similar treatment on the β-ethyl isomer **9** afforded the corre-