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.

Acknowledgment. This research was generously supported by the Robert A. Welch Foundation and the T.C.U. Research Foundation.

References and Notes

(1) R. Stoermer and B. Kahlert, *Ber.*, **35,** 1633 (1902).
(2) (a) R. W. Hoffman, "Dehydrobenzene and Cycloalkynes", Academic Press, New York, N.Y., 1967; (b) p 293; (c) p 290; (d) T. Kauffmann and R. Wertheim, *Angew. Chem., Int. Ed. Engl.*, **10,** 20 (1971).
(3) (a) S. Gronowitz and B. Holm, *Acta Chem. Scand.*, **23,** 2207 (1969); (b) M. P. Cava and L. Bravo, *Tetrahedron Lett.*, 4631 (1970); (c) D. A. deBie, H. C. van der Plas, and G. Geurtsen, *Rec. Travl. Chim. Pays-Bas*, **90,** 594 (1971); (d) M. P. David and J. E. McOmie, *Tetrahedron Lett.*, 1361 (1973); (e) M. G. Reinecke and R. H. Walter, *J. Chem. Soc., Chem. Commun.*, 1044 (1974); (f) B. F. Arynes, S. W. Longworth, and J. E. W. McOmie, *Tetrahedron*, **31,** 1775 (1975).
(4) (a) M. G. Reinecke and H. W. Adickes, *J. Am. Chem. Soc.*, **90,** 511 (1968); (b) G. Wittig and M. Rings, *Justus Liebigs Ann. Chem.*, **719** 127 (1968).
(5) L. K. Montgomery, F. Scardiglia, and J. D. Roberts, *J. Am. Chem. Soc.*, **87,** 1917 (1965).
(6) The generation of the aryne of cyclopentadiene anion has also been claimed,[7] but the evidence (trapping with tetracyclone) is similar to that proven to be equivocal with several five-membered hetarynes.[4b]
(7) J. C. Martin and D. R. Bloch, *J. Am. Chem. Soc.*, **93,** 451 (1971).
(8) A. Albert, "Heterocyclic Chemistry-An Introduction", 2d ed., Athlone Press, University of London, 1968.
(9) E. K. Fields and S. Meyerson, *J. Org. Chem.*, **31,** 3307 (1966).
(10) K. Peter, C. Vollhardt, and R. G. Bergman, *J. Am. Chem. Soc.*, **95,** 7538 (1973).
(11) H. Hageman and U. Wiersum, *Chem. Brit.*, 206 (1973).
(12) M. G. Reinecke and J. G. Newsom, *Abstracts of 29th Southwest Regional Meeting of the American Chemical Society*, El Paso, Texas, Dec 1973, p 69.
(13) (A) D. Callander, P. Coe, and J. Tatlow, *Chem. Commun.*, 143 (1966); (B) G. Brieger and T. Nestrick, *Chem. Rev.*, **74,** 567 (1974); (C) L. Friedman and D. Lindow, *J. Am. Chem. Soc.*, **90,** 2329 (1968); (D) G. Wittig and L. Pohmer, *Chem. Ber.*, **89,** 1334 (1965); subjection of the benzyne–furan adduct to FVT under the conditions of Table I (N_2 as a carrier gas) gives 1-naphthol in 40% yield, L. J. Chen, unpublished results from this laboratory; (E) S. Cristol and R. Cuple, *J. Org. Chem.*, **31,** 585 (1966).
(14) H. T. Raudsepp and H. E. Raudsepp, *Tr. Tallin. Politekh. Inst., Ser. A*, **254,** 34 (1967); *Chem. Abstr.*, **70,** 96458 (1969).
(15) A. Peters and D. Walker, *J. Chem. Soc.*, 1525 (1957).
(16) By way of contrast the 3,4-thiophene anhydride is recovered unchanged from FVT even at 700° in agreement with a recent report.[3f]

Manfred G. Reinecke,* James G. Newsom
Department of Chemistry, Texas Christian University
Fort Worth, Texas 76129
Received January 27, 1976

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

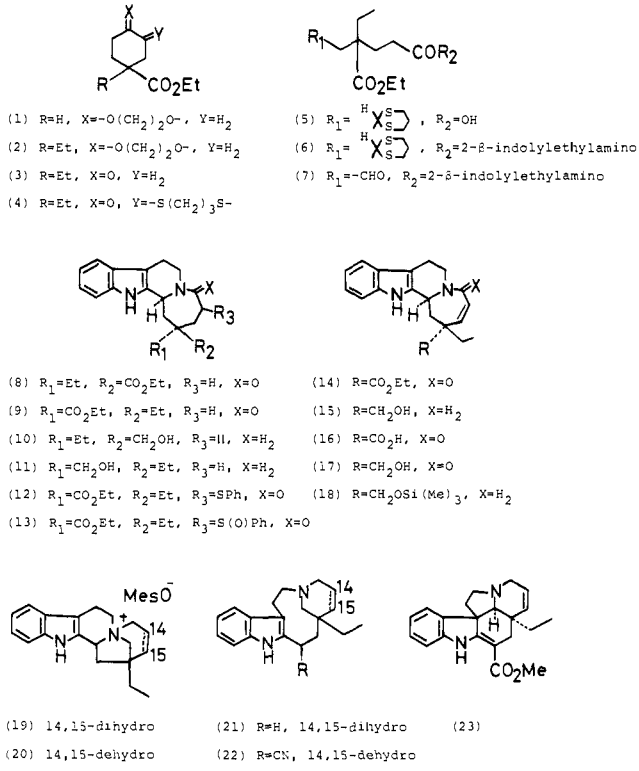
Sir:

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, $_H\times\overset{S}{\underset{S}{}}$).

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, $_H\times\overset{S}{\underset{S}{}}$), 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-



sponding amino alcohol **11** (mp 219–221°, ir (Nujol) 3320 cm^{-1}; NMR ($CDCl_3$ + Me_2SO-d_6) (δ) 0.83 (3 H, t, J = 7.0 Hz)) in 98% yield. The α-ethyl amino alcohol **10** was converted (CH_3SO_2Cl-pyridine, 0°, 3 h) to the mesylate which was refluxed in chloroform for 3 h to give the amorphous quaternary salt **19**,[10] NMR (D_2O) (δ) 0.71 (3 H, t, J = 6.5 Hz), 2.93 (3 H, s), almost quantitatively. Similarly the β-ethyl isomer **11** afforded the isomeric quaternary salt **19**, mp 206–208° dec, NMR (D_2O) (δ) 1.04 (3 H, t, J = 6.8 Hz), 2.90 (3 H, s), quantitatively. Reduction of both isomeric salts with sodium in liquid ammonia[10] provided *dl*-quebrachamine (**21**) in about 80% yield, respectively (total yield 22.3% from **2**).

Tabersonine precursor **22** was obtained from β-ethyllactam **9** via ten steps in 13.7% total yield (3.4% from 2). The β-ethyllactam **9** was converted (LDA–PhSSPh)[11] into the sulfide **12** in 91%: mp 166–167°; NMR ($CDCl_3$) (δ) 6.00 (1 H, d, J = 8.3 Hz). Oxidation and pyrolysis ((1) MCPBA; (2) toluene, reflux, 30 min)[12] transformed **12** into the α,β-unsaturated lactam **14** (mp 167–168°; ir (Nujol) 3260, 1720, 1648, 1598 cm^{-1}; NMR ($CDCl_3$) (δ) 6.08 (1 H, d, J = 12.0 Hz), 6.28 (1 H, dd, J = 12.0, 2.0 Hz)) in 95% yield from the sulfide **12** via the sulfoxide **13**. Since $LiAlH_4$ reduction failed to afford the desired unsaturated amino alcohol **15** as a major product (~5%), an alternative five-step method was developed. The unsaturated lactam **14** was hydrolyzed with potassium hydroxide to give the carboxylic acid **16** (mp 179.5–180°; ir (Nujol) 3400, 3050–2300, 1690, 1620, 1563 cm^{-1}; NMR ($CDCl_3$) (δ) 6.00 (1 H, d, J = 12.5 Hz), 6.48 (1 H, d, J = 12.5 Hz)) in 95% yield and the latter was converted to the unsaturated lactam alcohol **17** (mp 233–234°; ir (Nujol) 3350, 3240, 1630, 1579 cm^{-1}; NMR ($CDCl_3$+ Me_2SO-d_6) (δ) 5.88 (1 H, d, J = 10.5 Hz), 6.15 (1 H, d, J = 10.5 Hz)) by treating with ethyl chloroformate and triethylamine at room temperature, followed by $NaBH_4$ in aqueous tetrahydrofuran.[13] The unsaturated lactam alcohol **17** was silylated (Me_3SiCl–Et_3N, 20°) to give the silylether **18** which on reduction ($LiAlH_4$, THF, 0°) yielded the desired unsaturated amino alcohol **15** (mp 201–203.5°; ir (Nujol) 3400–3100 cm^{-1}; NMR ($CDCl_3$) (δ) 0.92 (3 H, t, J = 7.0 Hz), 2.00 (2 H, d, J = 9.0 Hz), 3.48 (1 H, d, J = 11.0 Hz), 3.74 (1 H, d, J = 11.0 Hz), 4.55 (1 H, t, J = 9.0 Hz), 5.50 (1 H, dd, J = 11.0, J = 2.8 Hz), 5.96 (1 H, ddd, J = 11.0, 6.0, J = 3.0 Hz)) in 58% yield from **14.**

Conversion of the unsaturated alcohol **15** to the known quaternary salt **20**[14] (mp 261° dec,[15] NMR (D_2O) (δ) 0.67 (3 H, t, J = 7.0 Hz), 1.41 (2 H, q, J = 7.0 Hz), 2.46 (3 H, s), 5.95 (1 H, d, J = 10.0 Hz)) was carried out as its saturated one **11** in quantitative yield. To confirm its formation, according to Ziegler and co-worker,[14] the salt **20** was transformed into 14,15,16,17-tetrahydroquebrachamine (58.2%) by $LiAlH_4$ and into 16-cyano-14,15-didehydroquebrachamine (**22**), (27.4%)[16] by potassium cyanide. Since the latter (**22**) has been converted to *dl*-tabersonine (**23**),[14] this constitutes an alternative synthesis of **23.**

The relatively simple sequence described here provides an efficient route to the non-tryptamine moiety of the Aspidosperma type and related indole alkaloids.

Acknowledgment. This research was supported by the grants from the Ministry of Education and by a Grant-in-Aid from Takeda Scientific Research Foundation.

References and Notes

(1) J. A. Marshall and D. E. Seits, *J. Org. Chem.*, **39**, 1814 (1974).
(2) M. Hesse, "Indolalkaloide in Tabellen", Springer Verlag, Berlin, 1964 and 1968.
(3) H. Musso, K. Naumann, and K. Grychtol, *Chem. Ber.*, **100**, 3614 (1967).
(4) D. S. Watt, *Tetrahedron Lett.*, 707 (1974).
(5) R. B. Woodward, I. J. Pachter, and M. L. Scheinbaum, *J. Org. Chem.*, **36**, 1137 (1971).
(6) J. C. A. Chivers and S. Smiles, *J. Chem. Soc.*, 697 (1928).
(7) Satisfactory mass spectroscopic data and analytical data were obtaine for all new compounds.
(8) M. Fetizon and M. Jurion, *J. Chem. Soc., Chem. Commun.*, 382 (1972).
(9) Stereochemcial assignment of the products will be described in the full paper.
(10) J. P. Kutney, N. Abdurahman, C. Gletsos, P. LeQuesne, E. Piers, and I. Vlattas, *J. Am. Chem. Soc.*, **92**, 1727 (1970).
(11) The same conversion was carried out on the α-ethyl isomer **8**, but a trace amount of desired sulfide was obtained with high recovery of the starting material.
(12) B. M. Trost and T. N. Salzmann, *J. Am. Chem. Soc.*, **95**, 6840 (1973).
(13) K. Ishizumi, K. Koga, and S. Yamada, *Chem. Pharm. Bull.*, **16**, 492 (1968).
(14) F. E. Ziegler and G. B. Bennett, *J. Am. Chem. Soc.*, **95**, 7458 (1973).
(15) Discrepancy from the reported value (mp 285° dec) might indicate a stereoisomeric relationship. However, this was not an important problem, because the isomeric center was lost in the following step.
(16) 10% of the corresponding carboxamide derivative was also obtained.

Seiichi Takano,* Susumi Hatakeyama, Kunio Ogasawara
Pharmaceutical Institute, Tohoku University
Aobayama, Sendai, Japan 980
Received December 31, 1975

Nocardicin A and B, Novel Monocyclic β-Lactam Antibiotics from a *Nocardia* Species

Sir:

In view of their outstanding antimicrobial activity, the β-lactam antibiotics have attracted great interest in recent years.[1] In the present communication we report the structure of two unique monocyclic β-lactam antibiotics, nocardicin A (**1**) and B (**2**), which are structurally and biologically related to the penicillins and cephalosporins.

Nocardicin A (**1**)[2] ($C_{23}H_{24}O_9N_4$, mp 214–216° dec, $[\alpha]_D$ −135.0° (H_2O),[3] pK_a 3.2, 4.5, 10.0, 11.6, and 12.7 (potentiometry), positive ninhydrin test) was isolated as a major component from a strain of *Nocardia*.[4] Acetylation of **1** with Ac_2O in MeOH (0°) and subsequent methylation with CH_2N_2 gave the monoacetyl-tetramethyl derivative **3**, while acetylation of **1** with Ac_2O in H_2O (pH ca. 9, room temperature), followed by methylation with CH_2N_2 gave the triacetyl-dimethyl derivative **4.** Hence one amino, two carboxyl, and two weakly acidic hydroxyl groups are present in **1.**

The ^1H NMR analysis of **1** (Na salt in D_2O) revealed all