membered rings, respectively; 2,4-dichlorophenol, 5.0×10^{-3} M for the four-membered ring. The progress of the reactions was monitored by following the increase of transmittance at the above wavelengths. The time scale of the oscilloscope was chosen as to include 6 to 8 half-lives in a single trace. The experimental data were treated according to the Guggenheim method,[19] with Δ values in the order of 2–3 half-lives. In all cases the linearity of the kinetic plots was good, and no systematic drift was present.

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References and Notes

(1) Part 10: L. Mandolini, B. Masci, and S. Roelens, *J. Org. Chem.*, in press.
(2) Most of the experimental work on which this article is based has been carried out at the Fast Reaction Group of the University of Kent at Canterbury, U.K., directed by Professor E. F. Caldin, where the author spent two months, October and November 1975, as a visiting research fellow. A preliminary account of this work was presented at the Organic Reaction Mechanism Group, The Chemical Society, Exeter, U.K., July 1976.
(3) C. Galli, G. Illuminati, L. Mandolini, and P. Tamborra, *J. Am. Chem. Soc.*, **99**, 2591 (1977).
(4) P. A. Tregloan and G. S. Laurence, *J. Sci. Instrum.*, **42**, 869 (1965).
(5) As a general reference see J. Sicher, *Prog. Sterochem.*, **3**, 202 (1962).
(6) R. W. Taft, Jr., in "Steric Effects in Organic Chemistry", M. S. Newman, Ed., Wiley, New York, N.Y., 1956, p 672.
(7) G. Illuminati, L. Mandolini, and B. Masci, *J. Am. Chem. Soc.*, **97**, 4960 (1975).
(8) C. Galli, G. Illuminati, and L. Mandolini, *J. Am. Chem. Soc.*, **95**, 8374 (1973).
(9) R. Huisgen and H. Ott, *Tetrahedron*, **6**, 253 (1959).
(10) L. Ruzicka, *Chem. Ind. (London)*, **54**, 2 (1935).
(11) (a) G. Illuminati, L. Mandolini, and B. Masci, *J. Am. Chem. Soc.*, **96**, 1422 (1974); (b) *ibid.*, **99**, 6308 (1977).
(12) (a) R. Bird, A. C. Knipe, and C. J. M. Stirling, *J. Chem. Soc., Perkin Trans. 2*, 1215 (1973); (b) R. Bird and C. J. M. Stirling, *ibid.*, 1221 (1973).
(13) C. J. M. Stirling, *J. Chem. Educ.*, **50**, 844 (1973).
(14) Limits of uncertainty more realistic than the usually reported probable or standard errors should be considered. This is the reason why we have estimated the uncertainty on both $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ as $\pm 2\sigma$ (see footnote *c*, Table I). However, a 99% confidence limit of $\pm 3\sigma$ could have been taken as well.
(15) H. E. O'Neal and S. W. Benson, *J. Chem. Eng. Data*, **15**, 266 (1970).
(16) M. I. Page and W. P. Jencks, *Proc. Natl. Acad. Sci. U.S.A.*, **68**, 1678 (1971); M. I. Page, *Chem. Soc. Rev.*, **2**, 295 (1973).
(17) W. P. Jencks, "Catalysis in Chemistry and Enzymology", McGraw-Hill, New York, N.Y., 1969, pp 418–425.
(18) G. Davies, *Inorg. Chem.*, **10**, 1155 (1971).
(19) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism", 2nd ed, Wiley, New York, N.Y., 1961 p 49.

Convenient and Stereoselective Route to Basic Frameworks for Synthesis of Unsymmetrical Pentacyclic Triterpenes†

Tetsuji Kametani,*[1a] Yoshiro Hirai,[1a] Yuichi Shiratori,[1a] Keiichiro Fukumoto,[1a] and Fumio Satoh[1b]

Contribution from the Pharmaceutical Institute, Tohoku University, Aobayama, Sendai 980, Japan, and The Sendai Institute of Heterocyclic Chemistry, 53, Kawauchi-Sanjuninmachi, Sendai 980, Japan. *Received June 24, 1977*

Abstract: Convenient and stereoselective synthesis of 10-ethoxy-3-methoxy- (**1**) and 3-ethoxy-10-methoxy-6bβ,12bα,14aα-trimethyl-5,6,6aα,6b,7,8,12b,13,14,14a-decahydropicene (**2**), key intermediates for synthesis of alnusenone (**8**) and friedelin (**9**), respectively, has been described. The key step in both syntheses is an intramolecular cycloaddition of the *o*-quinodimethanes **33**, derived from the benzocyclobutenes **32a** and **32b**, to the olefinic system in their side chain to form the corresponding pentacyclic compounds (**4** and **6**). This paper also describes a short but nonstereoselective synthesis of the pentacyclic compounds **4** and **6**.

There are many reports on elegant syntheses of the pentacyclic triterpenes.[2] Key reactions in the synthesis of these natural products are a construction of the pentacyclic ring system, which has a correct stereochemistry, and a stereoselective introduction of methyl groups to the angular positions. Using the enolate trapping method,[3] Stork[4] and Ireland[5] have established the stereoselective total synthesis of lupeol and germanicol, respectively. Recently, Ireland reported the total synthesis of friedelin (**9**) from a pentacyclic diaromatic diether **2**, having the trans-anti-trans BCD ring structure and the correct array of angular methyl groups, as a useful key intermediate.[6] Alnusenone (**8**) has also been prepared by the same authors[7] from the pentacyclic diaromatic compound (**1**).

Since we have found previously that intramolecular cycloaddition[8] of *o*-quinodimethanes in the synthesis of estrone[9] and atisine intermediate[10] could proceed stereoselectively and regioselectively, we investigated a new and simple synthesis of pentacyclic triterpenoids in connection with our interest[11-13] in the synthetic application of cycloaddition of *o*-quinodimethanes derived from benzocyclobutenes.[14] This paper reports a simple synthesis of two key intermediates **1** and **2**, which have been transformed into alnusenone (**8**) and friedelin (**9**) by Ireland described above.

Our plan was designed on the fact that the portion surrounded by a dotted line in the pentacyclic compounds (cf. **1**) corresponds to an isoprene unit. The first idea is that the pentacyclic ring system (**3**), which is a basic framework of the key compounds in the total synthesis of alnusenone and friedelin by Ireland, would be formed in one step by an intermolecular double cycloaddition of the bis-*o*-quinodimethane (**26b**), generated from the bisbenzocyclobutene (**25b**), with isoprene. The second approach involves the intramolecular cycloaddition of the *o*-quinodimethane (**33**), having an olefinic group at an appropriate position, derived from the benzocyclobutene (**32**). In these trials, we used the 1-substituted 1-cyanobenzocyclobutenes because 1-substituted 1-methylcyclobutenes are transformed into the *o*-methylstyrene derivatives by [1.5]-sigmatropic hydrogen migration[15] in *o*-quinodimethane gen-

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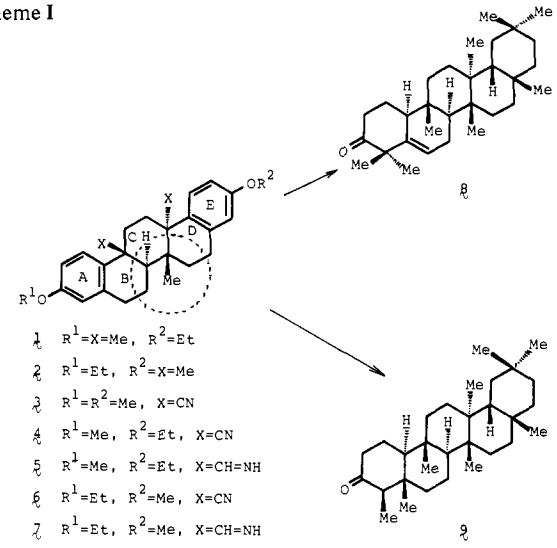
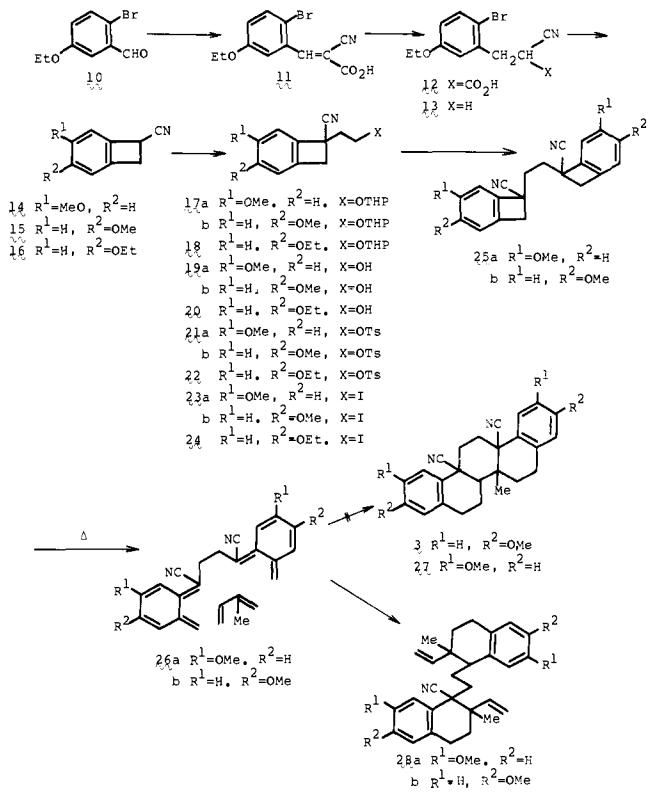
Scheme I



Scheme II



erated in situ. Keeping this in mind, we examined a simple and stereoselective synthesis of the diaromatic pentacyclic compounds from benzocyclobutenes having the appropriate substituent that could be converted into methyl group after a cycloaddition reaction.

Results and Discussion

The Double Cycloaddition Approach. Our first approach was a one-step construction of the diaromatic pentacyclic compounds (**3** and **27**) by an intermolecular double cycloaddition of the bis-*o*-quinodimethanes (**26**), derived from the 1,2-di(benzocyclobutenyl)ethanes (**25**), with isoprene. The preparation of the requisite bisbenzocyclobutenes **25** was straightforward as illustrated in Scheme II.

The tetrahydropyranyl ether[16] derived from ethylene bromohydrin was condensed with 1-cyano-5-methoxybenzocyclobutene (**14**)[17] in liquid ammonia in the presence of the freshly prepared sodium amide,[18] affording in 86% yield the 1-cyano-1-tetrahydropyranyloxyethyl-5-methoxybenzocyclobutene **17a,** which was hydrolyzed with methanolic hydrochloric acid at room temperature to give the alcohol **19a** in 93% yield. Treatment of the alcohol **19a** with *p*-toluenesulfonyl chloride in pyridine as usual[18] furnished the tosylate **21a** in 86% yield, which was converted into 2-(1-cyano-5-methoxybenzocyclobutenyl)ethyl iodide (**23a**) with sodium iodide in boiling acetone in 73% yield. Condensation of this iodide **23a** with 1-cyano-5-methoxybenzocyclobutene (**14**)[17] was carried out in the presence of the freshly prepared sodium amide in liquid ammonia to give the 1,2-di(1-cyano-5-methoxybenzocyclobutenyl)ethane (**25a**) [*m/e* 344 (M^+)] in 88% yield. Similarly, 1-cyano-1-tetrahydropyranyloxyethyl-4-methoxybenzocyclobutene (**17b**)[18] was converted into the iodide **23b,** in 64% overall yield, via the corresponding alcohol **19b** and tosylate **21b,** which was transformed to the 1,2-di(1-cyano-4-methoxybenzocyclobutenyl)ethane (**25b**), in 88% yield, by treatment with 1-cyano-4-methoxybenzocyclobutene.[10]

For conversion of the 1,2-di(benzocyclobutenyl)ethanes **25a** and **25b** into the corresponding pentacyclic compounds **3** and **27,** respectively, which constitute the framework of the key intermediates in the total synthesis of alnusenone (**8**) and friedelin (**9**) by Ireland, the bisbenzocyclobutenes **25a** or **25b** were heated with an excess of isoprene in a sealed tube at 180 °C for 4 h. However, the product was not the expected compound **3** or **27** which was formed by an intermolecular double cycloaddition of the bis-*o*-quinodimethane **26a** or **26b** to an equimolar amount of isoprene, but the bistetralin derivative **28a** or **28b** formed by a cycloaddition of 2 mol of isoprene with each part of the bis-*o*-quinodimethane, whose structure was determined by mass [*m/e* 480 (M^+)] and NMR spectra showing the resonance of vinyl protons.

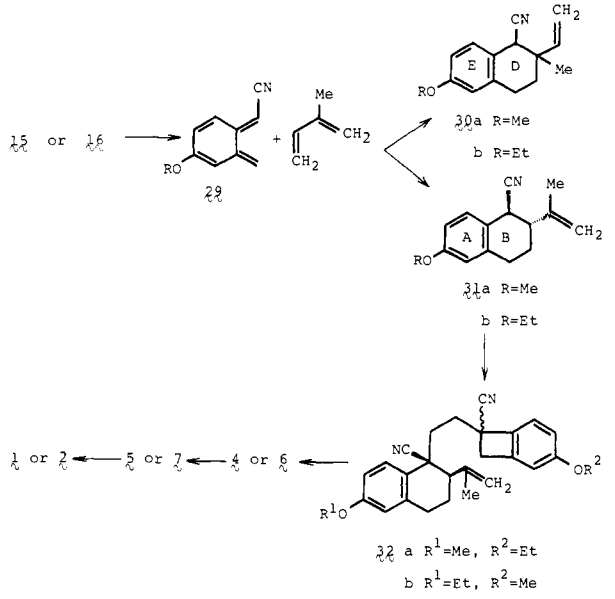
As attempts to convert **25a** and **25b** into the corresponding pentacyclic compounds **3** and **27** under several conditions failed, our attention then turned to the second approach which synthesizes pentacyclic compounds in a stepwise manner by an application of the intramolecular cycloaddition of the *o*-quinodimethanes derived from the benzocyclobutenes.

Stepwise and Stereoselective Synthesis. The second idea is that the cycloaddition of benzocyclobutenes to isoprene forms tetralin derivatives corresponding to A and B rings and then introduction of benzocyclobutene residue constructing C, D, and E rings, followed by an intramolecular cycloaddition of benzocyclobutene to the olefinic system derived from the isoprene unit, would give the pentacyclic compounds.

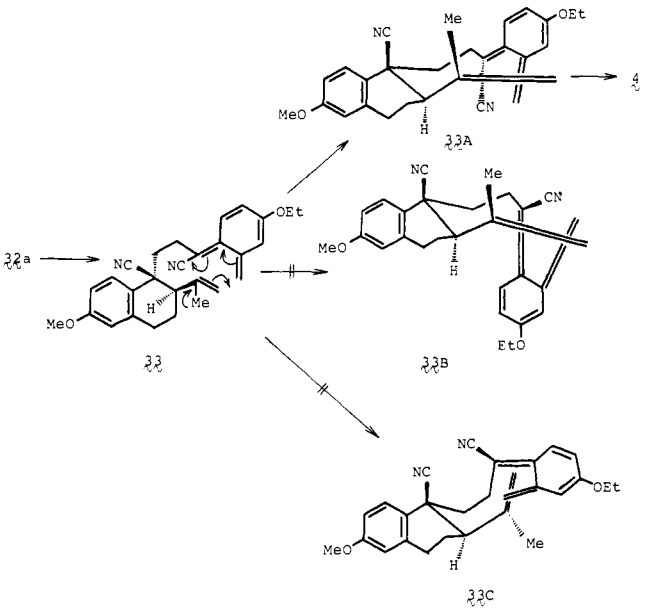
The synthesis of the starting benzocyclobutene derivative **24** was carried out by the usual method[16-18] as follow. A Knoevenagel reaction of 2-bromo-5-ethoxybenzaldehyde (**10**) with cyanoacetic acid in the presence of pyridine and ammonium acetate in boiling benzene using a Dean-Stark apparatus gave, in 82% yield, the α-cyanocinnamic acid **11,** which on reduction with sodium borohydride in the presence of sodium bicarbonate solution afforded the dihydrocinnamic acid **12** in 79% yield. Decarboxylation was achieved in *N,N*-dimethylacetamide at 170 °C, and the resulting *o*-bromophenylpropiononitrile **13,** which was formed in 83% yield, was treated with sodium amide prepared freshly in liquid ammonia to give, in 77% yield, the benzocyclobutene **16.** Condensation of 2-(2-bromoethoxy)tetrahydropyran with **16** afforded the 1-cyano-1-tetrahydropyranyloxyethylbenzocyclobutene **18,** which was converted into the 1-cyanobenzocyclobutenylethyl iodide **24** through the alcohol **20** and the tosylate **22** by the same method with a preparation of **23a** described above. The iodide **24** forms the unit which is necessary for making C, D, and E rings in the pentacyclic compound **1.**

On the other hand, the A and B ring system in **1** was synthesized from 1-cyano-4-methoxybenzocyclobutene (**15**)[10] as

Scheme III



Scheme IV



shown in Scheme III. Thus, heating the benzocyclobutene **15** with an excess of isoprene in a sealed tube at 180 °C for 2 h gave 1-cyano-2-isopropenyl-6-methoxytetralin (**31a**) [*m/e* 227 (M^+), δ 1.86 (3 H, s, Me-C=)], in 42% yield, in addition to a diastereoisomeric mixture of 1-cyano-6-methoxy-2-methyl-2-vinyltetralin (**30a**) [*m/e* 227 (M^+), δ 1.25 and 1.26 (Me-C≤)], in 42% yield by an intermolecular cycloaddition of the quinodimethane **29** with each olefinic system in isoprene. Both products (**30a** and **31a**) could be separated by silica gel column chromatography, and the NMR spectrum of **31a** showed a methine proton on C_1 at δ 4.0 as a doublet with J = 5 Hz indicating the relative configuration of the substituents at C_1 and C_2 to be trans. Similarly, the reaction of 1-cyano-4-ethoxybenzocyclobutene (**16**) with isoprene afforded a mixture of the 1-cyano-2-isopropenyltetralin **31b** (41% yield) and a diastereoisomeric mixture of the 1-cyano-2-methyl-2-vinyltetralin **30b** (43% yield).

Condensation of the 1-cyano-2-isopropenyltetralin **31a** with the iodide **24** was carried out in liquid ammonia in the presence of the freshly prepared sodium amide to furnish the key starting material **32a** [*m/e* 426 (M^+)] in 96% yield. In this stage, an alkylation of the tetralin derivative **31a** with the iodide **24** is expected to proceed from the less hindered side at the C_1 position to form the product **32a,** in which the relative configuration between the 1-cyano and 2-isopropenyl groups could be cis to each other. The second key starting compound **32b** for the pentacyclic product **2** in friedelin synthesis could be also prepared by the reaction of the tetralin derivative **31b** with the iodide **23b** in 86% yield by the same way.

Heating the benzocyclobutene **32a** in dry toluene in a sealed tube at 210–215 °C for 3 h[10] provided stereoselectively, in 58% yield, the pentacyclic dinitrile **4,** mp 203–204 °C [*m/e* 426 (M^+)], whose structure was easily determined by NMR spectral analysis, which showed a *C*-methyl resonance at δ 0.88 as a singlet but lacked olefinic protons and methylene protons on cyclobutene ring. This product **4** was reduced with diisobutylaluminum hydride[19] in benzene at room temperature for 12 h to give the diimine **5** [ν_{max} ($CHCl_3$) 1630 cm^{-1}] in 90% yield. Wolff-Kishner reduction of **5** with hydrazine hydrate and hydrazine dihydrochloride in triethylene glycol in the presence of potassium hydroxide at 160–165 °C by Nagata's method[20] gave the 6bβ,12bα,14aβ-trimethylated pentacyclic trimethyl derivative **1:** mp 152–153 °C [lit.[7] mp 152–153 °C] [ν_{max} ($CHCl_3$) 1608, 1578, and 1488 cm^{-1}; δ 0.63 (3 H, s, Me), 1.10 (3 H, s, Me), 1.20 (3 H, s, Me), 1.40 (3 H, t, J = 7 Hz, CH_2CH_3), 3.77 (3 H, s, Me), 4.05 (2 H, q, J = 7 Hz, CH_2CH_3), 6.50–6.87 (6 H, m, ArH)] in 44% yield, whose IR and NMR spectra and melting point were identical with those of the authentic sample[7] provided by Ireland. This product **1** has been converted to a pentacyclic triterpenoid, alnusenone (**8**), by Ireland.[7]

Similarly, thermolysis of the benzocyclobutene **32b** in a sealed tube at 210–215 °C for 3 h gave, in 60% yield, the pentacyclic compound **6** [mp 204–205 °C, *m/e* 426 (M^+), δ 0.93 (3 H, s, Me-C)]. This product was reduced with diisobutylaluminum hydride in benzene, followed by Wolff-Kishner reduction, modified by Nagata, of the resulting diimine **7** to afford, in 42% yield, the pentacyclic trimethyl compound **2,**[6] mp 146.5–147.5 °C [δ 0.63, 1.10, and 1.19 (each 3 H, s, Me-C)], which has also been converted into friedelin (**9**) by Ireland.[6]

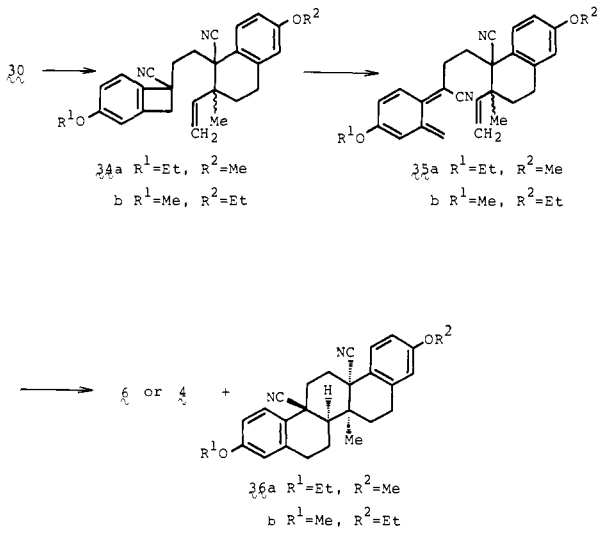
Regioselectivity in this cycloaddition would be due to an electron-attracting effect by the cyano group on *o*-quinodimethane and an electron-providing power of the methyl function in the olefin system as shown in the intermediate **33.**

The stereoselective formation of **4** and **6** in the thermolysis of **32a** and **32b** can be explained as follows. Conrotatory ring opening[21] of the cyclobutene unit in **32a** would form the sterically favored *o*-quinodimethane **33.** Synchronous intramolecular cycloaddition of **33** would most favorably proceed through the exo chair conformation **33A** to give **4** with the required stereochemical arrangement, rather than through the less stable "endo chair" form **33B** having a steric repulsion between tetralin and *o*-quinodimethane ring or "boat" form **33C** which would produce the trans-anti-cis-BCD and trans-syn-trans-BCD ring stereoisomers of **4.**

Thus, we could obtain the key compounds **1** and **2,** which have been converted to triterpenoid, alnusenone (**8**), and friedelin (**9**) by Ireland, in a convenient and stereoselective way, and this reaction provides an effective method for a general synthesis of the pentacyclic diaromatic diethers which would play an important role as a potential intermediate for pentacyclic triterpenoid synthesis.

Nonstereoselective Synthesis of Pentacyclic Compounds. The third approach is a use of the by-products **30a** and **30b** in the synthesis of the tetralins **31a** and **31b** from the benzocyclobutenes **15** and **16,** because these compounds **30a** and **30b** correspond to C, D, and E rings in pentacyclic compounds. In

Scheme V



this approach, the benzocyclobutenyl iodides, **23** and **24**, which have been applied as a precursor for E and D ring formation, are used as a starting material for the A and B ring formation.

Alkylation of a diastereoisomeric mixture of the 1-cyano-2-methyl-2-vinyltetralin **30a**, which could not be separated, with the iodide **24** in the presence of sodium amide as usual gave, in 86% yield, the 1,1,2,2-tetrasubstituted tetralin **34a** as a stereoisomeric mixture. This compound was subjected to a thermolysis in a sealed tube at 210–215 °C for 3 h to afford, in 59% yield, via the *o*-quinodimethane **35a**, a mixture of the pentacyclic compound **6** and its stereoisomer, which was separated in a ratio of 1:2 by high-pressure liquid chromatography. The latter fraction on this chromatography gave the expected product **6**, which was identical with the authentic sample, described above, in melting point and spectral comparisons. The stereochemistry of **36a** was assigned tentatively as the C_{6b}-methyl isomer of **6** as an intramolecular cycloaddition proceeds stereoselectively as described above. The pentacyclic dinitrile **4** having the correct stereochemical arrangement was also obtained by a thermolysis of **34b**, prepared from **30b** and **23b**, under the same conditions as a case of **6** through **35b**.

These products **6** and **4** have been converted into the pentacyclic trimethyl derivatives **1** and **2**, respectively; thus the third method affording a simple but nonstereoselective synthesis of pentacyclic compounds related to triterpenoids.

Experimental Section

General. All melting points are uncorrected. Infrared (IR) spectra were recorded on a Hitachi EPI-3 spectrophotometer. Nuclear magnetic resonance (NMR) spectra were measured on a JEOL JNM-PMX-60 spectrometer. Chemical shifts are reported as δ values relative to internal tetramethylsilane (Me_4Si). Mass spectra were taken on a Hitachi RMU-7 spectrometer. High-pressure liquid chromatography (HPLC) was carried out with a Hitachi 635 instrument equipped with 4 × 250 mm of Hitachi Gel 3011.

2-(1-Cyano-5-methoxybenzocyclobutenyl)ethyl Pyranyl Ether (17a). A solution of 1.59 g (10.0 mmol) of 1-cyano-5-methoxybenzocyclobutene (**14**)[17] in 10 mL of anhydrous tetrahydrofuran was added to a stirred sodium amide solution prepared from 260 mg (11.3 mmol) of sodium, 200 mL of liquid ammonia, and a catalytic amount of ferric chloride and then a solution of 2.09 g (10.0 mmol) of 2-(β-bromoethoxy)tetrahydropyran in 10 mL of anhydrous tetrahydrofuran was added to the above mixture. The stirring was continued for 0.5 h and 1 g of ammonium chloride was added to the resulting reaction mixture. After the ammonia had been evaporated off, the resulting mixture was extracted with ether. The extract was washed with 5% hydrochloric acid and brine, dried over anhydrous sodium sulfate, and evaporated to leave an oil, which was chromatographed on 35 g of silica gel using *n*-hexane–benzene (8:2) as eluent to afford 2.47 g (86%) of pyranyl ether **17a** as a colorless oil: IR ($CHCl_3$) 2230 cm^{-1}; NMR (CCl_4) δ 2.07–2.37 (2 H, t, CH_2CH_2O), 3.06 (3 H, s, OCH_3), 4.60 (1 H, broad s, >CH), 6.63–7.02 (3 H, m, ArH).

Anal. ($C_{12}H_{13}NO$) C, H, N.

2-(1-Cyano-5-methoxybenzocyclobutenyl)ethyl *p*-Toluenesulfonate (21a). A solution of 4 g (14.0 mmol) of the pyranyl ether **17a**, 4 mL of 10% hydrochloric acid, and 20 mL of methanol was stirred at room temperature for 3 h. This was mixed with 200 mL of chloroform and the organic layer was washed with water, dried over anhydrous sodium sulfate, and evaporated to leave an oil, which was chromatographed on 28 g of silica gel using *n*-hexane–benzene (2:8) as eluent to afford 2.64 g (93%) of the alcohol **19a** as a colorless oil: IR ($CHCl_3$) 2230 cm^{-1}; NMR (CCl_4) δ 2.09 (2 H, t, J = 6 Hz, CH_2CH_2O), 3.20 (1 H, d, J = 15 Hz, ArC*H*H), 3.40 (1 H, d, J = 15 Hz, ArCH*H*), 3.69 (3 H, s, OCH_3), 3.85 (2 H, t, J = 6 Hz, CH_2CH_2O), 6.60–7.03 (3 H, m, ArH); mass *m/e* 203 (M^+).

To a stirred solution of 2.13 g (10.5 mmol) of the alcohol **19a** in 16 mL of pyridine was added 4 g (20.1 mmol) of *p*-toluenesulfonyl chloride and the stirring was continued for 12 h at room temperature. The reaction mixture was poured into a mixture of 100 mL of concentrated hydrochloric acid and 100 g of ice. This was extracted with ether and the extract was washed with brine, dried over anhydrous sodium sulfate, and evaporated to leave a solid, which was recrystallized from methanol to give 3.2 g (86%) of the tosylate **21a** as colorless needles: mp 82.5–83 °C; IR ($CHCl_3$) 2240 cm^{-1}; NMR (CCl_4) δ 2.18 (2 H, t, J = 6 Hz, CH_2CH_2O), 2.35 (3 H, s, $ArCH_3$), 3.30 (1 H, d, J = 13 Hz, ArC*H*H), 3.52 (1 H, d, J = 13 Hz, ArCH*H*), 3.66 (3 H, s, OCH_3), 4.19 (2 H, t, J = 6 Hz, CH_2CH_2O), 6.60–7.01 (3 H, m, ArH), 7.22 (2 H, d, J = 7 Hz, ArH), 7.69 (2 H, d, J = 7 Hz, ArH).

Anal. ($C_{19}H_{19}NO_4S$) C, H, N.

2-(1-Cyano-4-methoxybenzocyclobutenyl)ethyl *p*-Toluenesulfonate (21b). The same treatment of 3 g (10.5 mmol) of the pyranyl ether **17b**[18] as above gave an oil, which was chromatographed on 30 g of silica gel using benzene as eluent to afford 2.01 g (94%) of the alcohol **19b** as a colorless oil: IR ($CHCl_3$) 3450 and 2230 cm^{-1}; NMR ($CDCl_3$) δ 2.12 (2 H, t, J = 6 Hz, CH_2CH_2O), 3.38 (1 H, d, J = 14 Hz, ArC*H*H), 3.75 (1 H, d, J = 14 Hz, ArCH*H*), 3.83 (3 H, s, OCH_3), 4.01 (2 H, t, J = 6 Hz, CH_2CH_2O), 6.70 (1 H, d, J = 2 Hz, C_3H), 6.80 (1 H, dd, J = 2 and 8 Hz, C_5H), 7.17 (1 H, d, J = 8 Hz, C_6H); mass *m/e* 203 (M^+).

The same treatment of 2 g (10.0 mmol) of the alcohol **19b** in 16 mL of pyridine with 4 g (20.1 mmol) of *p*-toluenesulfonyl chloride as above gave a solid, which was recrystallized from methanol to afford 3.2 g (91%) of the tosylate **21b** as colorless needles: mp 81–82.5 °C; IR ($CHCl_3$) 2240 cm^{-1}; NMR ($CDCL_3$) δ 2.30 (2 H, t, J = 6 Hz, CH_2CH_2O), 2.47 (3 H, s, $ArCH_3$), 3.30 (1 H, d, J = 14 Hz, ArC*H*H), 3.70 (1 H, d, J = 14 Hz, ArCH*H*), 3.76 (3 H, s, OCH_3), 4.30 (2 H, t, J = 6 Hz, CH_2CH_2O), 6.65 (1 H, d, J = 2 Hz, C_3H), 6.73 (1 H, dd, J = 2 and 8 Hz, C_5H), 7.10 (1 H, d, J = 8 Hz, C_6H), 7.33 (2 H, d, J = 8 Hz, ArH), 7.80 (2 H, d, J = 8 Hz, ArH); mass *m/e* 357 (M^+).

Anal. ($C_{19}H_{19}NO_4S$) C, H, N.

2-(1-Cyano-5-methoxybenzocyclobutenyl)ethyl Iodide (23a). A suspension of 2 g (5.6 mmol) of the tosylate **21a** and 2.6 g (17.3 mmol) of sodium iodide in 30 mL of acetone was heated under reflux for 3 h. After removal of the solvent, the resultant mixture was extracted with 60 mL of ether. The extract was washed with 5% sodium hydrosulfite solution and brine, dried over anhydrous sodium sulfate, and evaporated to give a solid, which was recrystallized from methanol to afford 1.27 g (73%) of the iodide **23a** as colorless needles: mp 83–84 °C; IR ($CHCl_3$) 2240 cm^{-1}; NMR (CCl_4) δ 2.26–2.70 (2 H, m, CH_2CH_2I), 3.00–3.60 (4 H, m, $ArCH_2$ and CH_2CH_2I), 3.70 (3 H, s, OCH_3), 6.60–7.16 (3 H, m, ArH); mass *m/e* 313 (M^+).

Anal. ($C_{12}H_{12}NOI$) C, H, N.

2-(1-Cyano-4-methoxybenzocyclobutenyl)ethyl Iodide (23b). The same treatment of 2 g (5.6 mmol) of the tosylate **21b** as above gave a solid, which was recrystallized from ether–*n*-hexane to afford 1.3 g (75%) of iodide **23b** as colorless needles: mp 42–43 °C; IR ($CHCl_3$) 2240 cm^{-1}; NMR ($CDCl_3$) δ 2.27–2.77 (2 H, m, CH_2CH_2I), 3.07–3.67 (4 H, m, $ArCH_2$ and CH_2CH_2I), 3.70 (3 H, s, OCH_3), 6.31 (1 H, d, J = 2 Hz, C_3H), 6.70 (1 H, dd, J = 2 and 8 Hz, C_5H), 7.06 (1 H, d, J = 8 Hz, C_6H); mass *m/e* 313 (M^+), which was used for the following reaction without further purification because of its instability.

1,2-Di(1-cyano-5-methoxybenzocyclobutenyl)ethane (25a). A solution of 0.67 g (4.2 mmol) of the benzocyclobutene **14** in 5 mL of anhydrous tetrahydrofuran was added to a stirred sodium amide solution prepared from 115 mg (5 mmol) of sodium, 100 mL of liquid ammonia, and a catalytic amount of ferric chloride and then 1.3 g (4.2 mmol) of the iodide **23a** in 5 mL of anhydrous tetrahydrofuran was added to the above mixture. The stirring was continued for 0.5 h and 1 g of ammonium chloride was added to the reaction mixture. After ammonia had been evaporated off, the resultant mixture was extracted with ether. The extract was washed with 5% hydrochloric acid and brine, dried over anhydrous sodium sulfate, and evaporated to leave a solid, which was recrystallized from methanol to afford 1.24 g (88%) of the bisbenzocyclobutene **25a** as colorless needles: mp 210–211 °C; IR ($CHCl_3$) 2240 cm^{-1}; NMR (CCl_4) δ 2.33 (4 H, s, $-CH_2CH_2-$), 3.18 (1 H, d, J = 13 Hz, ArC*H*H), 3.68 (1 H, d, J = 13 Hz, ArCH*H*), 3.75 (6 H, s, 2 OCH_3), 6.66–7.10 (6 H, m, ArH); mass *m/e* 344 (M^+).

Anal. ($C_{22}H_{20}N_2O_2$) C, H, N.

1,2-Di(1-cyano-4-methoxybenzocyclobutenyl)ethane (25b). The same treatment of 1 g (6.3 mmol) of the benzocyclobutene (**14**) with 1.95 g (6.2 mmol) of the iodide **23b** in the presence of sodium amide prepared from 160 mg (7.0 mmol) of sodium and 100 mL of liquid ammonia as above gave a solid, which was recrystallized from methanol to afford 1.91 g (88%) of the bisbenzocyclobutene **25b** as colorless needles: mp 177–178 °C; IR ($CHCl_3$) 2240 cm^{-1}; NMR ($CDCl_3$) δ 2.23 (4 H, s, $-CH_2CH_2-$), 3.20 (2 H, d, J = 14 Hz, ArC*H*H), 3.66 (2 H, d, J = 14 Hz, ArCH*H*), 3.76 (6 H, s, 2 OCH_3), 6.38 (2 H, d, J = 2 Hz, C_3H), 6.77 (2 H, dd, J = 2 and 8 Hz, C_5H), 7.08 (2 H, d, J = 8 Hz, C_6H); mass *m/e* 344 (M^+).

Anal. ($C_{22}H_{22}N_2O_2 \cdot 0.2H_2O$) C, H, N.

Thermal Reaction of 1,2-Di(1-cyano-5-methoxybenzocyclobutenyl)ethane (25a) with Isoprene. A mixture of 300 mg (0.87 mmol) of the bisbenzocyclobutene **25a** and 900 mg (13.2 mmol) of isoprene in 10 mL of toluene was heated at 180 °C in a sealed tube for 4 h. The crystals separated were collected by filtration and recrystallized from methanol to give 71 mg (17%) of the adduct **28a** as colorless leaves: mp 175–178 °C; IR ($CHCl_3$) 2240 cm^{-1}; NMR ($CDCl_3$) δ 1.10 (6 H, s, 2 CH_3), 3.76 (6 H, s, 2 OCH_3), 4.70–6.20 (6 H, m, 2 $CH{=}CH_2$), 6.60–7.17 (6 H, m, ArH); mass *m/e* 480 (M^+).

Anal. ($C_{32}H_{36}N_2O_2$) C, H, N.

Thermal Reaction of 1,2-Di(1-cyano-4-methoxybenzocyclobutenyl)ethane (25b) with Isoprene. The same treatment of 200 mg (0.58 mmol) of bisbenzocyclobutene **25b** with 230 mg (3.4 mmol) of isoprene in 10 mL of toluene as above and evaporation of the solvent gave a solid, which was recrystallized from methanol to afford 20 mg (7%) of the adduct **28b** as colorless needles: mp 174–175 °C; IR ($CHCl_3$) 2240 cm^{-1}; NMR ($CDCl_3$) δ 1.03 and 1.16 (6 H, 2 appeared s, 2 CH_3), 1.63–2.17 (4 H, m, 2 ArC$H_2$$CH_2$), 3.76 and 3.77 (6 H, 2 appeared s, 2 OCH_3), 4.80–5.33 (4 H, m, 2 $CH{=}CH_2$), 5.40–6.03 (2 H, m, 2 $CH{=}CH_2$), 6.57–7.20 (6 H, m, ArH); mass *m/e* 480 (M^+).

Anal. ($C_{32}H_{36}N_2O_2$) C, H, N.

2-Bromo-α-cyano-5-ethoxycinnamic Acid (11). A solution of 125 g (0.55 mol) of 2-bromo-5-ethoxybenzaldehyde (**10**), 47 g (0.55 mol) of cyanoacetic acid, 5 g (0.062 mol) of ammonium acetate, and 50 mL of pyridine in 500 mL of benzene was heated under reflux with a Dean-Stark apparatus until a theoretical amount of water was formed. The crystals separated were collected by filtration to give 168 g (82%) of pyridinium cinnamate. After acidification of the above pyridinium salts with 10% hydrochloric acid, the resultant yellowish solid was recrystallized from methanol to afford the cinnamic acid **11** as yellow needles: mp 210–211 °C; IR (KBr) 2220 and 1670 cm^{-1}; NMR ($CDCl_3 + CF_3CO_2H$) δ 1.50 (3 H, t, J = 7 Hz, OCH_2CH_3), 4.23 (2 H, q, J = 7 Hz, OCH_2CH_3), 7.12 (1 H, dd, J = 3 and 8 Hz, C_4H), 7.70 (1 H, d, J = 8 Hz, C_3H), 7.78 (1 H, d, J = 3 Hz, C_6H), 8.90 (1 H, s, ArC*H*=); mass *m/e* 296 (M^+).

Anal. ($C_{12}H_{10}NO_3Br$) C, H, N.

2-Bromo-α-cyano-5-ethoxyhydrocinnamic Acid (12). To a stirred suspension of 80 g (0.27 mol) of the cinnamic acid **11** in 500 mL of methanol and 200 mL of saturated sodium bicarbonate solution was added in small portions 25 g (0.66 mol) of sodium borohydride. After the stirring had been continued for 2 h, evaporation of the solvent gave a solid, which was acidified with 10% hydrochloric acid and extracted with ether. The extract was washed with brine, dried over anhydrous sodium sulfate, and evaporated to leave a solid, which was recrystallized from benzene to afford 64 g (79%) of the hydrocinnamic acid **12** as colorless prisms: mp 95.5–96 °C; IR ($CHCl_3$) 2255 and 1735 cm^{-1}; NMR ($CDCl_3$) δ 1.34 (3 H, t, J = 7 Hz, OCH_2CH_3), 3.00–3.50 (2 H, m, ArCH_2), 3.96 (2 H, q, J = 7 Hz, OCH_2CH_3), 6.65 (1 H, dd, J = 2 and 8 Hz, C_4H), 6.88 (1 H, d, J = 2 Hz, C_6H), 7.37 (1 H, d, J = 8 Hz, C_3H); mass *m/e* 298 (M^+).

Anal. ($C_{12}H_{12}NO_3Br$) C, H, N.

2-Bromo-5-ethoxyphenylpropiononitrile (13). A solution of 120 g (0.4 mol) of the hydrocinnamic acid **12** in 500 mL of *N,N*-dimethylformamide was heated at 170 °C for 3 h. The reaction mixture was poured into water and extracted with ether. The extract was washed with brine, dried over anhydrous sodium sulfate, and evaporated to leave an oil, which was distilled under reduced pressure to give 85 g (83%) of the nitrile **13** as a colorless oil: bp 165 °C (4 mmHg); IR ($CHCl_3$) 2255 cm^{-1}; NMR (CCl_4) δ 1.38 (3 H, t, J = 6 Hz, OCH_2CH_3), 2.30–3.27 (4 H, m, CH_2CH_2CN), 4.02 (2 H, q, J = 6 Hz, OCH_2CH_3), 6.61 (1 H, dd, J = 3 and 8 Hz, C_4H), 6.80 (1 H, d, J = 3 Hz, C_6H), 7.37 (1 H, d, J = 8 Hz, C_3H); mass *m/e* 254 (M^+).

Anal. ($C_{11}H_{12}NOBr$) C, H, N.

1-Cyano-4-ethoxybenzocyclobutene (16). A solution of 25 g (98.4 mmol) of the nitrile **13** in 20 mL of anhydrous tetrahydrofuran was added to a stirred sodium amide solution prepared from 10 g (434.8 mmol) of sodium, 500 mL of liquid ammonia, and a catalytic amount of ferric chloride. The stirring was continued for 3 h and 5 g (93.5 mmol) of ammonium chloride was added to the above reaction mixture. After ammonia had been evaporated off, the resultant mixture was partitioned between 300 mL of chloroform and 100 mL of water. The organic layer was separated, washed with 5% hydrochloric acid and water, dried over anhydrous sodium sulfate, and evaporated to leave a solid, which was recrystallized from ethanol to afford 15 g (88%) of the benzocyclobutene **16** as colorless prisms: mp 55.5–56 °C; IR ($CHCl_3$) 2246 cm^{-1}; NMR ($CDCl_3$) δ 1.40 (3 H, t, J = 7 Hz, OCH_2CH_3), 3.56 (2 H, distorted q, J = 2 Hz, ArCH_2), 4.01 (2 H, q, J = 7 Hz, OCH_2CH_3), 6.71 (1 H, d, J = 2 Hz, C_3H), 6.75 (1 H, dd, J = 2 and 9 Hz, C_5H), 7.11 (1 H, d, J = 9 Hz, C_6H); mass *m/e* 173 (M^+).

Anal. ($C_{11}H_{11}NO$) C, H, N.

2-(1-Cyano-4-ethoxybenzocyclobutenyl)ethyl Pyranyl Ether (18). The same treatment of 5 g (28.9 mmol) of the ethoxybenzocyclobutene **16** with 6.1 g (29.2 mmol) of 2-(β-bromoethoxy)tetrahydropyran in the presence of sodium amide prepared from 730 mg (31.7 mmol) of sodium and 200 mL of liquid ammonia as before gave an oil, which was chromatographed on 25 g of silica gel using *n*-hexane–benzene (8:2) as eluent to afford 8.2 g (94%) of the pyranyl ether **18** as a colorless oil: IR ($CHCl_3$) 2240 cm^{-1}; NMR (CCl_4) δ 1.36 (3 H, t, J = 6 Hz, OCH_2CH_3), 2.16 (2 H, t, J = 6 Hz, CH_2CH_2O), 3.93 (2 H, q, J = 6 Hz, OCH_2CH_3), 4.63 (1 H, s, CH), 6.60 (1 H, d, J = 2 Hz, C_3H), 6.70 (1 H, dd, J = 2 and 8 Hz, C_5H), 7.06 (1 H, d, J = 8 Hz, C_6H).

Anal. ($C_{18}H_{23}NO_3$) C, H, N.

2-(1-Cyano-4-ethoxybenzocyclobutenyl)ethyl Iodide (24). The same treatment of 6.9 g (22.9 mmol) of the pyranyl ether **18** with 5 mL of 10% hydrochloric acid in 20 mL of methanol as before gave an oil, which was chromatographed on 30 g of silica gel using benzene–*n*-hexane (8:2) as eluent to afford 4.65 g (93%) of the alcohol **20** as a colorless oil: IR ($CHCl_3$) 3480 and 2240 cm^{-1}; NMR (CCl_4) δ 1.33 (3 H, t, J = 6 Hz, OCH_2CH_3), 2.05 (3 H, t, J = 6 Hz, CH_2CH_2O), 3.21 (1 H, d, J = 14 Hz, ArC*H*H), 3.60 (1 H, d, J = 14 Hz, ArCH*H*), 3.91 (2 H, q, J = 6 Hz, OCH_2CH_3), 6.60 (1 H, d, J = 2 Hz, C_3H), 6.70 (1 H, dd, J = 2 and 8 Hz, C_5H), 7.06 (1 H, d, J = 8 Hz, C_6H). This was used for the following reaction without further purification.

To a stirred solution of 4 g (18.4 mmol) of the alcohol **20** in 50 mL of pyridine was added 9.6 g (50.5 mmol) of *p*-toluenesulfonyl chloride and the stirring was continued for 12 h. The reaction mixture was poured into a mixture of 100 mL of concentrated hydrochloric acid and 100 g of ice. The same workup as before gave an oil, which was chromatographed on 100 g of silica gel using *n*-hexane–benzene (6:4) as eluent to afford 4.5 g (91%) of the tosylate **22** as a colorless oil: IR ($CHCl_3$) 2240 cm^{-1}; NMR (CCl_4) δ 1.33 (3 H, t, J = 7 Hz, OCH_2CH_3), 2.20 (2 H, t, J = 6 Hz, CH_2CH_2O), 2.33 (3 H, s, $ArCH_3$), 3.18 (1 H, d, J = 14 Hz, ArC*H*H), 3.57 (1 H, d, J = 14 Hz, ArCH*H*), 3.90 (2 H, q, J = 7 Hz, OCH_2CH_3), 4.17 (2 H, t, J = 6 Hz, CH_2CH_2O), 6.50 (1 H, d, J = 2 Hz, C_3H), 6.56 (1 H, dd, J = 2 and 8 Hz, C_5H), 6.96 (1 H, d, J = 8 Hz, C_6H), 7.23 (2 H, d, J = 8 Hz, ArH), 7.70 (2 H, d, J = 8 Hz, ArH); mass *m/e* 371 (M^+). This was

used in the following reaction without further purification.

The same workup of 2.5 g (7.0 mmol) of the tosylate **22** with 3.2 g of sodium iodide in 50 mL of acetone as before gave a solid, which was recrystallized from methanol to afford 2 g (72%) of the iodide **24** as colorless needles: mp 82–83 °C; IR ($CHCl_3$) 2240 cm^{-1}; NMR (CCl_4) δ 1.35 (3 H, t, J = 7 Hz, OCH_2CH_3), 2.60–2.70 (2 H, m, CH_2CH_2I), 3.98 (2 H, q, J = 7 Hz, OCH_2CH_3), 6.67 (1 H, d, J = 2 Hz, C_3H), 6.74 (1 H, dd, J = 2 and 8 Hz, C_5H), 7.11 (1 H, d, J = 8 Hz, C_6H); mass *m/e* 327 (M^+).

Anal. ($C_{13}H_{14}NOI$) C, H, N.

Thermal Reaction of 1-Cyano-4-methoxybenzocyclobutene (15) with Isoprene. A mixture of 1 g (6.3 mmol) of the benzocyclobutene **15**[10] and 3 g (44.1 mmol) of isoprene was heated at 180 °C in a sealed tube for 2 h. The reaction mixture was chromatographed on 150 g of silica gel. Elution with *n*-hexane–benzene (8:2) gave 620 mg (43%) of the diastereoisomeric 1-cyano-6-methoxy-2-methyl-2-vinyltetralin (**30a**) as a colorless oil: IR ($CHCl_3$) 2245 and 1640 cm^{-1}; NMR (CCl_4) δ 1.25 and 1.26 (3 H, 2 s, CH_3), 3.45 (3 H, s, OCH_3), 4.80–5.30 (2 H, m, $CH{=}CH_2$), 5.60–6.20 (1 H, m, $CH{=}CH_2$), 6.60–7.15 (3 H, m ArH); mass *m/e* 227 (M^+).

Elution with *n*-hexane–benzene (7:3) gave 600 mg (42%) of 1-cyano-2-isopropenyl-6-methoxytetralin (**31a**) as a colorless oil: IR ($CHCl_3$) 2245 and 1600 cm^{-1}; NMR (CCl_4) δ 1.86 (3 H, s, $CH_2{=}C{-}CH_3$), 4.00 (1 H, d, J = 5 Hz, >CHCN), 5.00 (2 H, d, J = 5 Hz, $>C{=}CH_2$), 6.80–7.17 (3 H, m, ArH); mass *m/e* 227 (M^+), which was converted into 1-carbamoyl-6-methoxy-2-isopropenyltetralin for the characterization as follows. A solution of 30 mg of 1-cyanotetralin (**31a**) in 30 mL of 10% potassium hydroxide–methanol was heated under reflux for 3 h. After evaporation of the solvent, the resultant mixture was partitioned between 20 mL of benzene and 10 mL of water. The organic layer was separated, washed with water, dried over anhydrous sodium sulfate, and evaporated to leave a solid, which was recrystallized from ethanol to afford 25 mg (78%) of the objective amide as colorless needles: mp 163.5–164.5 °C; IR ($CHCl_3$) 3540 and 3420 cm^{-1}; NMR ($CDCl_3$) δ 1.70 (3 H, s, $CH_2{=}C{-}CH_3$), 1.80 (3 H, t, J = 6 Hz, $ArCH_2CH_2$), 2.70 (3 H, t, J = 6 Hz, $ArCH_2CH_2$), 3.65 (3 H, *s*, OCH_3), 4.53 (1 H, d, J = 1 Hz, $>C{=}CHH$), 4.67 (1 H, d, J = 1 Hz, $>C{=}CHH$), 5.10–5.86 (2 H, broad s, NH_2), 6.47 (1 H, d, J = 2 Hz, C_5H), 6.56 (1 H, dd, J = 2 and 7 Hz, C_7H), 6.96 (1 H, d, J = 7 Hz, C_8H).

Anal. ($C_{15}H_{19}NO_2$) C, H, N.

Thermal Reaction of 1-Cyano-4-ethoxybenzocyclobutene (16) with Isoprene. The reaction mixture obtained from the same workup of 1 g (5.8 mmol) of the benzocyclobutene **16** with 2.2 g (32 mmol) of isoprene as above was subjected to chromatography on 150 g of silica gel. Elution with *n*-hexane–benzene (9:1) gave 600 mg (43%) of the diastereoisomeric 1-cyano-6-ethoxy-2-methyl-2-vinyltetralin (**30b**) as a colorless oil: IR ($CHCl_3$) 2245 cm^{-1}; NMR (CCl_4) δ 1.30 (3 H, s, CH_3), 1.37 (3 H, t, J = 7 Hz, OCH_2CH_3), 1.63–2.07 (2 H, m, $ArCH_2CH_2$), 2.57–3.07 (2 H, m, $ArCH_2CH_2$), 3.63 and 3.73 (1 H, 2 s, >CHCN), 4.77–5.33 (2 H, m, $CH{=}CH_2$), 5.57–6.20 (1 H, m, $CH{=}CH_2$), 6.43–7.40 (3 H, m, ArH); mass *m/e* 241 (M^+).

Elution with *n*-hexane–benzene (7:3) gave 570 mg (41%) of 1-cyano-2-isopropenyl-6-methoxytetralin (**31b**) as a colorless oil: IR ($CHCl_3$) 2245 cm^{-1}; NMR (CCl_4) δ 1.37 (3 H, t, J = 7 Hz, OCH_2CH_3), 1.87 (3 H, s, $CH_2{=}C{-}CH_3$), 2.27–2.60 (1 H, m, C_2H), 2.67–3.03 (2 H, m, $ArCH_2CH_2$), 4.00 (2 H, q, J = 7 Hz, OCH_2CH_3), 4.03 (1 H, d, J = 4 Hz, >CHCN), 4.94 (1 H, s, $>C{=}CHH$), 5.00 (1 H, s, $>C{=}CHH$), 6.63 (1 H, d, J = 2 Hz, C_5H), 6.70 (1 H, dd, J = 2 and 7 Hz, C_7H), 7.11 (1 H, d, J = 7 Hz, C_8H); mass *m/e* 241 (M^+).

Anal. ($C_{10}H_{19}NO$) C, H, N.

1-(1-Cyano-4-ethoxybenzocyclobutenyl)-2-(1-cyano-1,2,3,4-tetrahydro-2-isopropenyl-6-methoxynaphthyl)ethane (32a). A solution of 150 mg (0.66 mmol) of the tetralin **31a** in 5 mL of anhydrous tetrahydrofuran was added to a stirred sodium amide solution prepared from 20 mg (0.87 mmol) of sodium, 100 mL of liquid ammonia, and a catalytic amount of ferric chloride and then a solution of 215 mg (0.66 mmol) of the iodide **24** in 5 mL of anhydrous tetrahydrofuran was added to the above mixture. The stirring was continued for 0.5 h before addition of 100 mg of ammonium chloride. The same workup as before gave an oil, which was chromatographed on 7 g of silica gel using *n*-hexane–benzene (1:1) as eluent to afford 270 mg (96%) of the benzocyclobutenyltetralin (**32a**) as a colorless oil: IR ($CHCl_3$) 2240 cm^{-1}; NMR (CCl_4) δ 1.37 (3 H, t, J = 7 Hz, OCH_2CH_3), 1.90 (3 H, broad s, $CH_2{=}C{-}CH_3$), 2.82 (2 H, distorted t, J = 7 Hz, $ArCH_2CH_2$), 3.10 (1 H, d, J = 14 Hz, ArCHH), 3.56 (1 H, d, J = 14 Hz, ArCHH), 3.73 (3 H, s, OCH_3), 3.93 (2 H, q, J = 7 Hz, OCH_2CH_3), 4.67–5.00 (2 H, m, $>C{=}CH_2$), 6.43–7.17 (6 H, m, ArH); mass *m/e* 426 (M^+).

Anal. ($C_{28}H_{30}N_2O_2$) C, H, N.

1-(1-Cyano-4-methoxybenzocyclobutenyl)-2-(1-cyano-1,2,3,4-tetrahydro-6-ethoxy-2-isopropenylnaphthyl)ethane (32b). The same workup of 200 mg (0.83 mmol) of the tetralin **31b** with 290 mg (0.93 mmol) of the iodide **23b** in the presence of sodium amide prepared from 28 mg (1.2 mmol) of sodium and 100 mL of liquid ammonia as above gave an oil, which was chromatographed on 10 g of silica gel using *n*-hexane–benzene (1:1) as eluent to afford 303 mg (86%) of the benzocyclobutenyltetralin **32b** as a colorless oil: IR ($CHCl_3$) 2240 cm^{-1}; NMR (CCl_4) δ 1.37 (3 H, t, J = 7 Hz, OCH_2CH_3), 1.87 (3 H, s, $CH_2{=}C{-}CH_3$), 2.61–2.97 (2 H, m, $ArCH_2CH_2$), 3.13 (1 H, d, J = 14 Hz, ArCHH), 3.60 (1 H, d, J = 14 Hz, ArCHH), 4.03 (2 H, q, J = 7 Hz, OCH_2CH_3), 4.63–5.10 (2 H, m, $>C{=}CH_2$), 6.43–7.17 (6 H, m, ArH); mass *m/e* 426 (M^+).

Anal. ($C_{28}H_{30}N_2O_2{\cdot}0.2H_2O$) C, H, N.

12bα,14aβ-Dicyano-10-ethoxy-5,6,6aα,6b,7,8,12b,13,14,14a-decahydro-3-methoxy-6bβ-methylpicene (4). A solution of 360 mg (0.85 mmol) of the benzocyclobutene **32a** in 50 mL of toluene was heated at 210–215 °C in a sealed tube for 3 h. After removal of the solvent, the resultant mixture was chromatographed on 10 g of silica gel using *n*-hexane–benzene (6:4) as eluent to afford a solid, which was recrystallized from benzene–*n*-hexane to give 210 mg (58%) of the picene **4** as colorless needles: mp 203–204 °C; IR ($CHCl_3$) 2240 cm^{-1}; NMR (CCl_4) δ 0.88 (3 H, s, CH_3), 1.37 (3 H, t, J = 7 Hz, OCH_2CH_3), 3.73 (3 H, s, OCH_3), 3.80 (2 H, q, J = 7 Hz, OCH_2CH_3), 6.33–6.80 (6 H, m, ArH); mass *m/e* 426 (M^+).

Anal. ($C_{28}H_{30}N_2O_2$) C, H, N.

12bα,14aβ-Dicyano-3-ethoxy-5,6,6aα,6b,7,8,12b,13,14,14a-decahydro-10-methoxy-6bβ-methylpicene (6). The same workup of 200 mg (0.47 mmol) of the benzocyclobutene **32b** as above gave 120 mg (60%) of the picene **6** as colorless needles: mp 204–205 °C; IR ($CHCl_3$) 2240 cm^{-1}; NMR ($CDCl_3$) δ 0.93 (3 H, s, CH_3), 1.41 (3 H, t, J = 7 Hz, OCH_2CH_3), 3.78 (3 H, s, OCH_3), 4.03 (2 H, q, J = 7 Hz, OCH_2CH_3), 6.57–7.56 (6 H, m, ArH); mass *m/e* 426 (M^+).

Anal. ($C_{28}H_{30}N_2O_2$) C, H, N.

10-Ethoxy-5,6,6aα,6b,7,8,12b,13,14,14a-decahydro-3-methoxy-6bβ,12bα,14aβ-trimethylpicene (1). To a stirred solution of 40 mg (0.094 mmol) of the dinitrile **4** in 10 mL of dry benzene was added 0.2 mL (0.35 mmol) of 25% diisobutylaluminum hydride–toluene solution at room temperature under nitrogen atmosphere. After the stirring had been continued for 12 h, the reaction mixture was poured into a mixture of 5 mL of 10% potassium hydroxide solution and 5 g of ice. The organic layer was separated and the aqueous layer was extracted with ether. The combined organic layer was washed with brine, dried over anhydrous sodium sulfate, and evaporated to give 36 mg (90%) of the diimine **5** as a solid, IR ($CHCl_3$) 1630 cm^{-1}.

A mixture of 28 mg (0.065 mmol) of the diimine **5**, 1 mL (20 mmol) of hydrazine hydrate, 150 mg (2.2 mmol) of hydrazine dihydrochloride, and 10 mL of triethylene glycol was heated at 140–150 °C under nitrogen atmosphere for 4 h and then 1 g (18 mmol) of powdered potassium hydroxide was added to the above mixture at 100 °C. Nitrogen gas was blown into the reaction mixture at 160–165 °C for 1 h and heating was continued for 7 h at the same temperature as above. The reaction mixture was poured into 30 mL of water and extracted with ether. The extract was washed with brine, dried over anhydrous sodium sulfate, and evaporated to leave a solid, which was recrystallized from dichloromethane–ether to afford 12 mg (44%) of the trimethylpicene **1** as colorless needles: mp 152–153 °C; IR ($CHCl_3$) 1608, 1578, 1488 cm^{-1}; NMR ($CDCl_3$) δ 0.63, 1.10, and 1.20 (each 3 H, each s, 3 CH_3), 1.40 (3 H, t, J = 7 Hz, OCH_2CH_3), 6.50–6.87 (6 H, m, ArH), whose physical data and melting point [lit.[7] mp 152–153 °C] were completely identical with those of the authentic one.[7]

3-Ethoxy-5,6,6aα,6b,7,8,12b,13,14,14a-decahydro-10-methoxy-6bβ,12bα,14aβ-trimethylpicene (2). The same workup of 100 mg (0.23 mmol) of the dinitrile **6** with 1 mL (1.06 mmol) of 15% diisobutylaluminum hydride–toluene solution as above gave 96 mg (96%) of the diimine **7**.

The same treatment of 60 mg (0.14 mmol) of the diimine **7** using 2 mL (40 mmol) of hydrazine hydrate, 300 mg (4.4 mmol) of hydrazine dihydrochloride, 30 mL of triethylene glycol, and 2 g (36 mmol) of powdered potassium hydroxide as above gave a solid, which

was recrystallized from dichloromethane-ether to afford 24 mg (42%) of the trimethylpicene **2** as colorless needles: mp 146.5–147.5 °C; NMR ($CDCl_3$) δ 0.63, 1.10, and 1.19 (each 3 H, each s, 3 CH_3), 1.40 (3 H, t, J = 7 Hz, OCH_2CH_3), 2.73–3.20 (4 H, m, 2 $ArCH_2CH_2$), 3.76 (3 H, s, OCH_3), 4.01 (2 H, q, J = 7 Hz, OCH_2CH_3), 6.50–7.33 (6 H, m, ArH).

Anal. ($C_{28}H_{36}O_2$) C, H.

1-(1-Cyano-4-ethoxybenzocyclobutenyl)-2-(1-cyano-1,2,3,4-tetrahydro-6-methoxy-2-methyl-2-vinylnaphthyl)ethane (34a). The same treatment of 300 mg (1.3 mmol) of the tetralin **30a** in 5 mL of tetrahydrofuran with 450 mg (1.4 mmol) of the iodide **24** in 5 mL of tetrahydrofuran in the presence of 40 mg (1.75 mmol) of sodium and 100 mL of liquid ammonia as before gave an oil, which was chromatographed on 15 g of silica gel in the same way as **32a** to afford 470 mg (84%) of the benzocyclobutenyltetralin **34a** as a colorless oil: IR ($CHCl_3$) 2240 cm^{-1}; NMR (CCl_4) δ 1.36 (3 H, t, J = 7 Hz, OCH_2CH_3), 1.36 (3 H, s, CH_3), 3.70 (3 H, s, OCH_3), 3.90 (2 H, q, J = 7 Hz, OCH_2CH_3), 4.73–5.40 (2 H, m, $CH{=}CH_2$), 5.80–6.43 (1 H, m, $CH{=}CH_2$), 6.44–7.36 (6 H, m, ArH); mass m/e 426 (M^+).

1-(1-Cyano-4-methoxybenzocyclobutenyl)-2-(1-cyano-1,2,3,4-tetrahydro-6-ethoxy-2-methyl-2-vinylnaphthyl)ethane (34b). The same workup of 970 mg (4 mmol) of the tetralin **30b** with 1.26 g (4 mmol) of the iodide **23b** in the presence of sodium amide prepared from 110 mg (4.8 mmol) of sodium and 200 mL of liquid ammonia as above gave 1.4 g (86%) of the benzocyclobutenyltetralin **34b** as a colorless oil: IR ($CHCl_3$) 2225 cm^{-1}; NMR (CCl_4) δ 1.36 (3 H, t, J = 7 Hz, OCH_2CH_3), 1.36 (3 H, s, OCH_3), 3.70 (3 H, s, OCH_3), 3.95 (2 H, q, OCH_2CH_3), 4.66–5.46 (2 H, m, $CH{=}CH_2$), 5.66–6.13 (1 H, m, $CH{=}CH_2$), 6.44–7.36 (6 H, m, ArH); mass m/e 426 (M^+).

Thermolysis of 34a. The same workup of 100 mg (0.23 mmol) of the benzocyclobutene **34a** in 20 mL of toluene gave an oil, which was chromatographed on 1 g of silica gel using n-hexane–benzene (6:4) as eluent to afford 59 mg (59%) of the diastereoisomeric pentacyclic products (**6** and **36a**) as a solid, which was subjected to preparative HPLC (solvent methanol–chloroform (9:1); flow rate 1.5 mL/min). The first fraction (retention time 7.6 min) gave **36a** as crystals, which were recrystallized from methanol–chloroform (9:1) to afford colorless needles: mp 222–223 °C; IR ($CHCl_3$) 2225 cm^{-1}; NMR ($CDCl_3$) δ 1.40 (3 H, t, J = 7 Hz, OCH_2CH_3), 3.77 (3 H, s, OCH_3), 4.00 (2 H, q, J = 7 Hz, OCH_2CH_3), 6.43–7.60 (6 H, m, ArH); mass m/e 426 (M^+).

Anal. ($C_{28}H_{30}N_2O_2$) C, H, N.

The second fraction (retention time 9.2 min) gave colorless needles, mp 204–205 °C, which were identical with the sample (**6**) synthesized before.

Thermolysis of 34b. The same workup of 170 mg (0.4 mmol) of the benzocyclobutene **36b** in 30 mL of toluene as above gave 140 mg (82%) of the diastereoisomeric pentacyclic products (**4** and **36b**) as a solid, which was subjected to preparative HPLC in the same manner as above. The first fraction (retention time 6 min) gave crystals, which were recrystallized from methanol–chloroform (9:1) to afford **36b** as colorless needles: mp 221–222 °C; IR ($CHCl_3$) 2220 cm^{-1}; NMR ($CDCl_3$) δ 1.33 (3 H, t, J = 7 Hz, OCH_2CH_3), 3.72 (3 H, s, OCH_3), 3.93 (2 H, q, J = 7 Hz, OCH_2CH_3), 6.33–7.33 (6 H, m, ArH); mass m/e 426 (M^+).

Anal. ($C_{28}H_{30}N_2O_2$) C, H, N.

The second fraction (retention time 6.8 min) gave colorless needles, mp 203–204 °C, which were identical with the sample (**4**) synthesized before.

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References and Notes

(1) (a) Tohoku University; (b) The Sendai Institute of Heterocyclic Chemistry.
(2) (a) T. K. Devon and A. I. Scott, "Handbook of Naturally Occurring Compounds", Vol. II, "Terpenes", Academic Press, New York, N.Y., 1972; (b) J. W. ApSimon and J. W. Hooper, "The Total Synthesis of Natural Products", Vol. 2, J. W. ApSimon, Ed., Wiley, New York, N.Y., 1973, p 559.
(3) G. Stork, P. Rosen, N. Goldman, R. V. Coombs, and J. Tsuji, *J. Am. Chem. Soc.*, **87**, 275 (1965).
(4) G. Stork, S. Uyeo, T. Wakamatsu, P. Grieco, and J. Labovitz, *J. Am. Chem. Soc.*, **93**, 4945 (1971).
(5) R. E. Ireland, S. W. Baldwin, D. J. Dawson, M. I. Dawson, J. E. Dolfini, J. Neubould, W. S. Johnson, M. Brown, R. J. Crawford, P. F. Hufdlik, G. H. Rasmussen, and K. K. Schmiegel, *J. Am. Chem. Soc.*, **92**, 5743 (1970).
(6) R. E. Ireland and D. M. Walba, *Tetrahedron Lett.*, 1071 (1976).
(7) R. E. Ireland, M. I. Dawson, S. C. Welch, A. Hagenbach, J. Bordner, and B. Trus, *J. Am. Chem. Soc.*, **95**, 7829 (1973).
(8) (a) W. Oppolzer, *J. Am. Chem. Soc.*, **93**, 3833 (1971); (b) *ibid.*, **93**, 3834 (1971); (c) *Tetrahedron Lett.*, 1001 (1974).
(9) T. Kametani, H. Nemoto, H. Ishikawa, K. Shiroyama, and K. Fukumoto, *J. Am. Chem. Soc.*, **98**, 3378 (1976).
(10) T. Kametani, Y. Kato, T. Honda, and K. Fukumoto, *J. Am. Chem. Soc.*, **98**, 8185 (1976).
(11) T. Kametani and K. Fukumoto, *Heterocycles*, **3**, 29 (1975), and references cited therein.
(12) T. Kametani, Y. Kato, F. Honda, and K. Fukumoto, *Heterocycles*, **4**, 241 (1976).
(13) T. Kametani, H. Nemoto, and K. Fukumoto, *J. Chem. Soc., Chem. Commun.*, 400 (1976).
(14) I. L. Klundt, *Chem. Rev.*, **70**, 471 (1970).
(15) T. Kametani, M. Tsubuki, Y. Shiratori, Y. Kato, M. Ihara, H. Nemoto, K. Fukumoto, F. Satoh, and H. Inoue, *J. Org. Chem.*, **42**, 2672 (1977).
(16) W. E. Parham and E. L. Anderson, *J. Am. Chem. Soc.*, **70**, 4187 (1948).
(17) T. Kametani, M. Kajiwara, and K. Fukumoto, *Chem. Ind. (London)*, 1165 (1973); *Tetrahedron*, **30**, 1053 (1974).
(18) T. Kametani, H. Nemoto, H. Ishikawa, H. Matsumoto, K. Shiroyama, and K. Fukumoto, *J. Am. Chem. Soc.*, **99**, 3461 (1977).
(19) A. E. G. Miller, J. W. Biss, and L. H. Schwartzman, *J. Org. Chem.*, **24**, 627 (1959).
(20) W. Nagata and H. Itazaki, *Chem. Ind. (London)*, 1194 (1964).
(21) R. B. Woodward and R. Hoffmann, "The Conservation of Orbital Symmetry", Academic Press, New York, N.Y., 1970.