H_{81}–H_{82} form an AA'BB' system. At room temperature, the spectrum shows three identical AA'BB' systems for the aromatic protons and four identical A_4 systems.[2]

The assignment of the aromatic protons was possible thanks to the small benzylic coupling between the ortho and the methylene protons; at room temperature[2] the value of the coupling constant cannot be measured but the ortho protons (H_{13}, H_{16}, H_{17}, H_{20}, H_{21} and H_{24}) are clearly broadened with regard to the meta protons. The ortho protons are the most deshielded (7.32 compared with 7.22 ppm for the meta protons).[2] At low temperature, the COSY experiment relates *some* aromatic and aliphatic protons: H_{13} with H_{121} (and H_{16} with H_{31}) and H_{20} with H_{71} (and the symmetrically related H_{21} with H_{82}). The COSY experiment also connects the AA' and BB' protons, on one hand, and the ABCD protons on the other; thus, the complete series of aromatic protons are assigned. At low temperature the ortho protons (averaged value, 7.329 ppm) are still more deshielded than the meta ones (averaged value, 7.226 ppm).

The assignment of the aliphatic protons is now straightforward. The two spin systems, the AA'BB' and the $[ABCD]_2$, were clearly identified through the COSY experiments, and then the complete spin analysis (neglecting the small benzylic couplings) provided the values of chemical shifts and coupling constants of Table I. With these values, both spin systems have been simulated and added (Figure 2b). The ROESY experiment confirms that protons H_{71} (and H_{82}) are close to protons H_{32} (H_{122}) and H_{41} (H_{111}), identifying them as the protons "inside" the cavity.

The chemical shifts of the aliphatic protons can be classified in two groups, those which appear at an averaged value of 2.79 ppm (H_{31}, H_{121}, H_{42}, H_{112}, H_{71} and H_{82}) and those which appear at 3.19 ppm (H_{32}, H_{122}, H_{41}, H_{111}, H_{72} and H_{81}) (at room temperature, all aliphatic protons appear at 3.03 ppm).[2] These values are probably related in a complex manner to the relative positions of aliphatic protons and aromatic rings (the three aromatic rings) since the dihedral angles of these protons with the adjacent aromatic rings also belong to two groups, with values of 23.3° (26.5°) and 39.2° (39.8°), respectively.

The geminal coupling constants, −13.4 Hz, are normal. The vicinal coupling constants follow a Karplus relationship,[4] with the vicinal dihedral angles: $J_{trans} \approx 13.3$ Hz for an angle of about 172.3°, where the equation gives 13.15 Hz. There are two kinds of J_{gauche} values, one at about 2.6 Hz and the other at about 6.7 Hz. They are related to dihedral angles of 71.7° (76.4°) and 56.4° (56.1°). This is consistent with the Karplus relationship, although the empirically generalized Karplus-type equation we have used[4] gives for 71.7° and 56.4° values of ^3J = 1.3 and 3.5 Hz (6.7/2.6 = 2.6; 3.5/1.3 = 2.7). Due to limitations of this model,[4] it has been necessary to use a simple carbon atom to represent the phenyl rings. This approximation, which gives an excellent result for J_{trans} is not entirely satisfactory for J_{gauche}. Nevertheless, the J_{gauche} values support the propeller C_2 conformation for compound 1 at 173 K.

In conclusion, the complete analysis and assignment of the 12 aliphatic protons of 1,2:5,6:9,10-tribenzododeca-1,5,9-triene proves that the only conformer present in solution is the propeller one.

Experimental Section

The synthesis of compound 1 has been described.[1,2]

NMR Spectroscopy. ^{1}H NMR spectra were recorded on a Varian UNITY-500 spectrometer operating at 499.84 MHz, using a 2:1 CD_2Cl_2–CS_2 mixture as solvent. Variable-temperature experiments for compound 1 were carried out in the following conditions: pulse angle 90°, acquisition time 3 s, sweep width 4912 Hz, and data size 32 K (digital resolution ± 0.3 Hz). The temperature was varied in the range 173–303 K. The conformational analysis was performed at 173 K, where the signals were narrow enough (bandwidth, ~2 Hz).

The homonuclear 2D chemical shift correlation experiments were carried out with the following conditions: (1) for vicinal correlations a double quantum filter phase-sensitive COSY was used with spectral widths of 1053.1 Hz in both dimensions, a relaxation delay of 1 s, number of increments = 256 and 1024 × 1024 points for the data matrix; (2) for long-range correlations, a relayed-COSY in the absolute mode was used with spectral widths of 2704.5 Hz in both dimensions, a relaxation delay of 1 s, τ delay used to achieve coherence = 100 ms, number of increments = 225 and 1024 × 1024 points for the data matrix.

The 2D phase-sensitive ROESY spectrum was measured covering the spectral width of 2704.5 Hz in both dimensions with a relaxation delay of 1 s, spin lock field strength of 2.1 KHz, and spin lock time of 150 ms, using 16 scans for each of the 225 increments and a final data matrix of 1K × 1K points.

The ^{1}H-NMR iterative analysis of the spectrum was performed using the PANIC program (for the ABCD system, rms error = 0.17, J and δ are given with ±0.1 Hz and for the AA'BB' system, rms error = 0.5, J and δ are given with ±0.5 and ±0.25 Hz, respectively).[5] The simulated spectrum (Figure 2b) has been obtained using a bandwidth of 2.3 Hz.

(4) Cerda-García-Rojas, C. M.; Zepeda, L. G.; Joseph-Nathan, P. *Tetrahedron Comput. Methodol.* **1990**, *3*, 113.

(5) PANIC 86, Bruker Program Library, Germany.

Stereospecific Synthesis of *gem*-Diphenylcyclopropanecarboxamides: Aminolysis of Spiro Cyclopropano Lactones by Acetonitrile and Triethylamine†

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Cyclopropanecarboxylic acid derivatives play an important role as effective agents in agriculture and medicine. Of these, *gem*-diphenylcyclopropanecarboxylic acids and amides are of considerable pharmaceutical interest as coronary vasodilators[1] and in the treatment of Parkinson's disease.[2] In a continuation of our studies on cyclopropanation of 4-ylideneoxazol-5-ones,[3] we report here the preparation of *gem*-diphenylcyclopropanecarboxylic acid amides starting from azalactones in a single step. Thus, treatment of (*Z*)-2-phenyl-4-ylideneoxazol-5-one **1a** with diphenyldiazomethane (DPDM)[4] in acetonitrile containing TEA under reflux gave a colorless solid melting at 164 °C in 90% yield. The structure of the solid was shown to be 1-benzamido-2,2,3-triphenylcyclopropane-1-carboxamide (**3a**) based on elemental analysis and spectral data. The structure of **3a** was further established by comparison with an authentic sample of the amide prepared unambiguously from the spirolactone **2a** and ammonia (Scheme I).

Mechanistically the spirolactone **2a** may be considered as a reasonable intermediate in the formation of **3a**. The initially formed **2a** from **1a** and DPDM could subsequently

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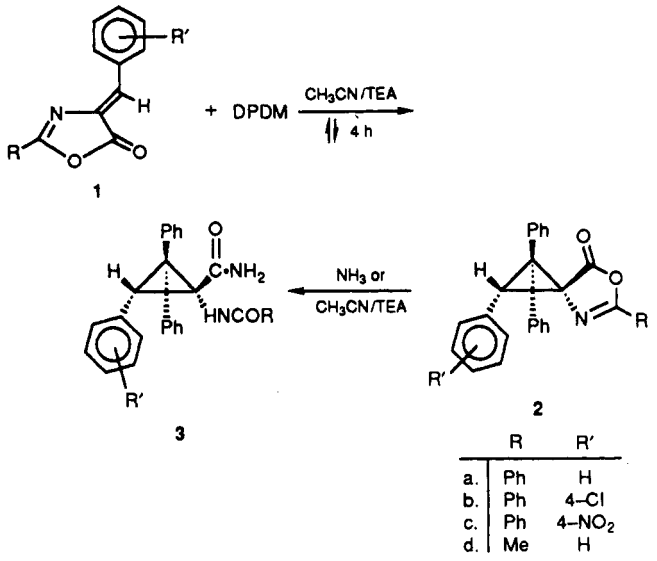
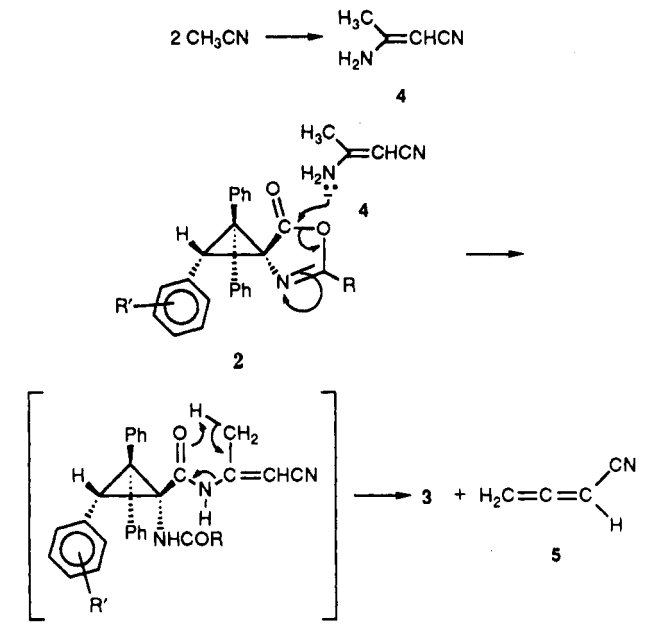
Scheme I



	R	R'
a.	Ph	H
b.	Ph	4-Cl
c.	Ph	4-NO_2
d.	Me	H

Scheme II



undergo aminolysis to give the observed product. It is pertinent to note that ammonia in any form was not used during the reaction. In order to explain the observed amide formation from the lactone **2a** generation of a similar aminolysis species has to be considered. The most probable source of aminolysis could be acetonitrile and TEA. Base-catalyzed dimerization of acetonitrile is known to give aminocrotononitrile **4**, and it is possible that **4** generated from acetonitrile in the presence of TEA can react with the spirolactone **2a** leading to the amide **3a** as shown in Scheme II. In fact, treatment of the spirolactone **2a** with acetonitrile in the presence of TEA gave a quantitative yield of **3a**. Further β-aminocrotononitrile generated from acetonitrile and sodium[5] reacted with **2a** to give **3a** in excellent yields.

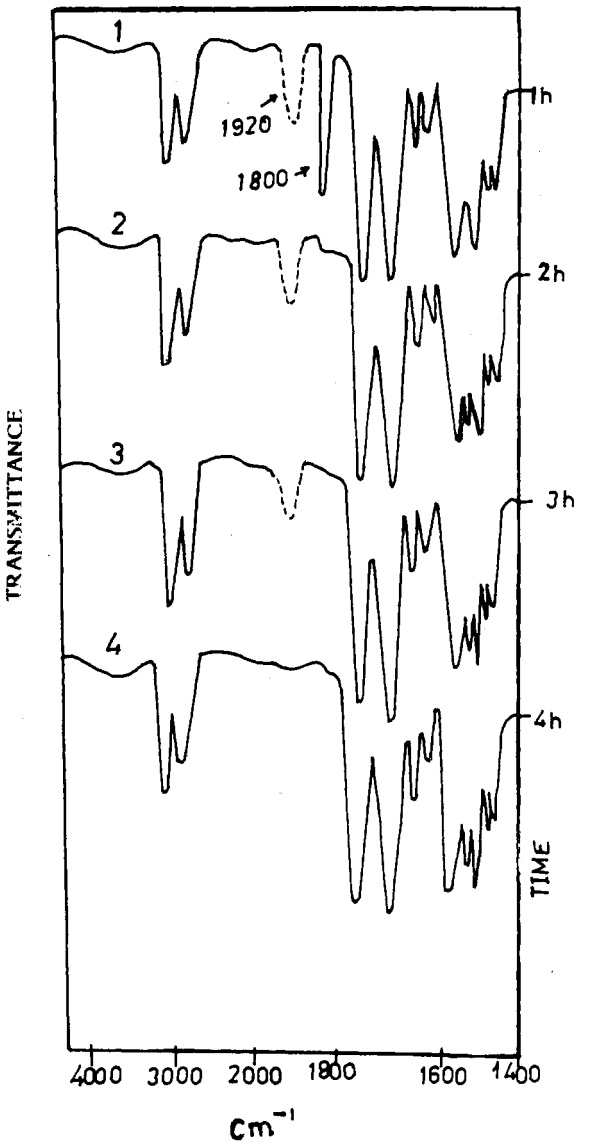


Figure 1.

The presence of cyanoallene, expected to be formed as in the mechanism in Scheme II, has been observed by monitoring the reaction progress spectroscopically (infrared).[6] The absorption at 1920 cm^{-1} assignable to the allene functionality[7] diminishes with the time (Figure 1) indicating the gradual loss of cyanoallene from the mixture.

Accepting the spirolactone **2a** as the intermediate in the formation of **3a**, the stereochemistry of **3a** can be deduced from that of **2a**. We have shown the stereochemistry of **2a** to be the *Z*-configuration on the basis of NOE studies,[3] and it is further confirmed by X-ray analysis, thus fixing the *Z*-configuration to the carboxamides **3a–3d**.[9]

It is observed that the unsaturated azalactone **1a** is uneffected under the reaction conditions, indicating that

(1) Cognacq, J. C. (Hexachimie). Ger. Offen. 2,359,796, 1974; *Chem. Abstr.* **1975**, *82*, P165725.
(2) Richard, B.; Russell, P. B.; Mehta, N. B. U.S. 3,098,076 (cl 260-294.7), 1963; *Chem. Abstr.* **1963**, *59*, P13954c.
(3) Lalitha, N.; Iyengar, D. S.; Bhalerao, U. T. *J. Org. Chem.* **1989**, *54*, 1771–1773.
(4) Attenburrow, J.; Cameron, A. F. B.; Chapman, J. H.; Evans, R. M.; Hems, B. A.; Jansen, A. B. A.; Walker, T. *J. Chem. Soc.* **1952**, 1104.
(5) Jaspar, J. C.; Alfred, T. *Can. J. Chem.* **1953**, *31*, 1211.
(6) The IR spectra of aliquots of the reaction mixture were recorded in $CHCl_3$, at 1-, 2-, 3-, and 4-h intervals. See Figure 1.
(7) (a) Oroshinik, M.; Karmas, G. *J. Am. Chem. Soc.* **1953**, 1050. (b) Walter Celmer, D.; Solomons, I. A. *J. Am. Chem. Soc.* **1953**, *75*, 1372. (c) Bellamy, L. J. *IR spectra of complex molecules*, 2nd ed.; John Wiley & Sons: New York, 1966.
(8) Grove, D. C.; Randall, W. A. *Antibiotic Monograph No. 2*; Medical Encyclopedia: New York, 1955; p 192.
(9) The new amides **3a–d** described in this paper have shown bacteriostatic action[8] against Gram-positive *Bacillus subtills*.

4 may not be nucleophilic enough to open the lactone, thereby involving the intermediacy of **2a** in the formation of **3a** directly. This is first observation of the aminolysis effected by CH_3CN/TEA particularly in azalactones. The present work offers a simpler method of converting saturated lactones to the corresponding amides under mild conditions without using ammonia. In order to explore the applications of this new reaction, succinic and maleic anhydrides were reacted with CH_3CN/TEA and gave the corresponding amidic acids in good yields.

Experimental Section

The *gem*-diphenylcyclopropanecarboxamides **3a–d** were prepared by the action of DPDM on oxazolones **1a–d** in the presence of TEA/CH_3CN.

Method A. 1-Benzamido-2,2,3-triphenylcyclopropane-1-carboxamide (3a). In a typical experiment oxazolone **1a** (2.49 g, 10 mmol) was mixed with DPDM (3.88 g, 20 mmol) and TEA (2.02 g, 20 mmol) in 20 mL of CH_3CN (freshly distilled from P_2O_5). The reaction mixture was refluxed for 4–6 h. When the pink color disappeared the reaction mixture was concentrated under vacuum, and the viscous residue was purified by column chromatography (silica gel 0.08 mm, benzene–hexane (2:1)) to give 1-benzamido-2,2,3-triphenylcyclopropane-1-carboxamide (**3a**) as a colorless solid (3.88 g, 89%): mp 164 °C; mass spectrum [M^+] 432; IR ($CHCl_3$) 3500, 3000, 1780, 1645, and 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.20 (s, 1 H, cyclopropyl-H), 7.24–7.61 (m, 20 H, ArH), and 8.22 (br, s, 3 H, NH and $CONH_2$). Anal. Calcd: C, 80.55; H, 5.55; N, 6.48. Found: C, 80.52; H, 5.45; N, 6.41.

Cyclopropanecarboxamides **3a–d** were also obtained by the same procedure.

Method B. Spirolactone **2a** (2.07 g, 5 mmol) was mixed with TEA (1.01 g, 10 mmol) in 20 mL of acetonitrile, and the mixture was refluxed for 4 h. The material was worked up as described in method A to give 2.0 g (93.5%) of **3a**.

Method C. Spirocyclopropane **2a** (1.5 g, 3.6 mmol) was heated with aqueous ammonia (10 mL, 20%) on a steam bath for 2 h. The solid was filtered and crystallized from benzene to give **3a** (1.4 g, 90.2%).

1-Benzamido-2,2-diphenyl-3-(4-chlorophenyl)cyclopropane-1-carboxamide (3b). A 4.37-g (10-mmol) portion of **2b** gave 3.732 g of **3c** (80% yield): mp 160 °C; mass spectrum m/z [M^+] 466.5; IR ($CHCl_3$) 3520, 3000, 1780, 1645, and 1030 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.10 (s, 1 H, cyclopropyl H), 7.20–7.85 (m, 14 H, ArH), 8.60 (br, s, 3 H).

1-Benzamido-2,2-diphenyl-3-(4-nitrophenyl)cyclopropane-1-carboxamide (3c). A 4.48-g (10-mmol) portion of **2c** gave 4.05 g of **3c** (85%): mp 162 °C; mass spectrum m/z [M^+] 477; IR ($CHCl_3$) 3520, 3000, 1780, 1650, 1520, 1320, and 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.35 (s, 1 H, cyclopropyl H), 7.20–7.85 (m, 14 H, ArH), 8.54 (br, s, 3 H).

1-Acetamido-2,2,3-triphenylcyclopropane-1-carboxamide (3d). A 3.41-g (10-mmol) portion of **2d** gave 2.96 g of **3d** (80%); mp 176 °C; mass spectrum m/z [M^+] 370; IR ($CHCl_3$) 3500, 3000, 1760, 1635, and 1035 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.87 (s, 1 H, cyclopropyl, H), 7.20–7.80 (m, 15 H, ArH), 2.83 (s, 3 H, MeH), and 8.40 (br, s, 3 H).

Acknowledgment. We thank Dr. A. V. Rama Rao for constant encouragement and CSIR for the award of research associateship to N.L. We also thank Prof. Y. S. Rao, Department of Chemistry, Kennedy-King College, Chicago, IL, for obtaining the X-ray data.

Supplementary Material Available: Details of the X-ray diffraction analysis of compound **2a** (2 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Additions and Corrections

Vol. 57, 1992

James C. Ciula and Andrew Streitwieser*. Dependence of Aggregation on the Basicity of Some Cesium Enolates in THF.

Page 432, eq 5 is incorrect because of a transcription error. The correct equation is

$$K_{a(obs)} = K_a(1 + (1 + 8K_{dimer}[Cs^+enolate^-]_{total})^{1/2})/2 \quad (5)$$

Table I was prepared from the correct equation. We thank Reinhard Hirsch for pointing out this error.