continued for an additional 1 h. The layers were separated, and the aqueous layer was extracted with methylene chloride (2 × 100 mL). The combined organic extracts were washed with water (2 × 150 mL), dried (anhydrous magnesium sulfate), and filtered, and the filtrate was concentrated in vacuo. Solid **6** (7.1 g, 83%) was thereby obtained. Recrystallization of this material from ethanol afforded pure **6** as colorless prisms: mp 151.0–151.5 °C; IR (KBr) 1572 (vs), 1355 (s), 1339 cm^{-1} (s); ^1H NMR ($CDCl_3$) δ 1.98 (m, 1 H), 2.35 (m, 1 H), 2.74 (m, 2 H), 3.01 (m, 1 H), 3.17 (m, 1 H), 3.7–4.0 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 37.37 (d), 38.89 (d), 39.05 (2 C, d), 45.51 (d), 46.62 (d), 46.70 (d), 47.74 (d), 63.17 (t), 65.27 (t), 65.36 (t), 65.90 (t), 113.79 (s), 118.47 (s), 124.26 (s).

Anal. Calcd for $C_{15}H_{16}N_2O_8$: C, 51.14; H, 4.58. Found: C, 51.02; H, 4.56.

8,8-Dinitropentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-4,11-dione (7). To a solution of **6** (3.0 g, 9.52 mmol) in methylene chloride (30 mL) was added concentrated sulfuric acid (5 mL), and the resulting mixture was stirred at room temperature for 2 h. The reaction mixture then was poured over crushed ice (50 g). Solid sodium bicarbonate was added portionwise with stirring (**CAUTION!**) until evolution of carbon dioxide had ceased. The resulting mixture was diluted with water (30 mL). The layers were separated, and the aqueous layer was extracted with methylene chloride (2 × 25 mL). The combined organic extracts were washed sequentially with 10% aqueous sodium bicarbonate solution (2 × 20 mL) and with water (20 mL). The organic layer was dried (anhydrous magnesium sulfate) and filtered, and the filtrate was concentrated in vacuo, thereby affording **7** (1.1 g, 50%). Recrystallization of this material from ethanol afforded pure **7** as colorless needles: mp 272 °C dec; IR (KBr) 1760 (s), 1725 (s), 1545 (s), 1345 cm^{-1} (m); ^1H NMR ($CDCl_3$) δ 2.54–2.70 (m, 2 H), 3.0–3.6 (m, 3 H), 3.75–4.2 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 29.81 (d), 38.51 (d), 39.98 (d), 41.28 (d), 43.19 (d), 44.36 (d), 44.81 (d), 46.36 (d), 121.90 (s), 203.10 (s), 204.10 (s).

Anal. Calcd for $C_{11}H_8N_2O_6$: C, 50.01; H, 3.01. Found: C, 49.53; H, 3.13.

8,8-Dinitropentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-4,11-dione Dioxime (8).[10] To a solution of **7** (1.00 g, 3.79 mmol) in methanol (50 mL) were added hydroxylamine hydrochloride (1.74 g, 25.0 mmol) and sodium acetate (4.1 g, 50 mmol), and the resulting mixture was refluxed for 2 h. The reaction mixture then was concentrated in vacuo; cold water (30 mL) was added to the residue, and the resulting mixture was extracted with methylene chloride (3 × 20 mL). The combined organic extracts were washed with water (20 mL), dried (anhydrous magnesium sulfate), and filtered. The filtrate was concentrated in vacuo, thereby affording **8** (0.82 g, 75%) as a colorless microcrystalline solid (mixture of geometric isomers): mp 155–160 °C; IR (KBr) 3400 (s), 1685 (w), 1540 (s), 1330 cm^{-1} (m). This material was used without further purification for the ensuing synthesis of **1**.

4,4,8,8,11,11-Hexanitropentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane (1). To a refluxing solution of **8** (950 mg, 3.28 mmol) in dry methylene chloride (50 mL) under nitrogen was added a solution of red nitric acid (98%)[1j] (20 mL, excess), urea (200 mg, 3.33 mmol), and ammonium nitrate (200 mg, 2.67 mmol) in methylene chloride (30 mL). A deep blue-green color developed initially; the color of the reaction mixture changed to brown as more nitric acid was added. After the addition of nitric acid had been completed, the reaction mixture was refluxed for 30 min, at which time 30% aqueous hydrogen peroxide solution (5 mL) was added cautiously to the refluxing mixture. The reaction mixture was thereby rendered colorless. After the addition of hydrogen peroxide had been completed, refluxing was continued for an additional 15 min. The reaction mixture then was allowed to cool to room temperature. The cooled reaction mixture was washed with ice–water (3 × 75 mL), dried (anhydrous magnesium sulfate), and filtered, and the filtrate was concentrated in vacuo. The residue was purified via column chromatography (silica gel stationary phase, 3:2 methylene chloride–hexane mixed solvent as eluent). The first fraction thereby collected afforded pure **1** (240 mg, 19%) as colorless microcrystalline solid: mp 199–200 °C; IR (KBr) 1565 (s), 1535 cm^{-1} (m); ^1H NMR (acetone-d_6) δ 3.85 (m, 4 H), 4.50 (m, 2 H), 4.70 (m, 2 H); ^{13}C NMR (acetone-d_6) δ 37.88 (d), 39.45 (d), 47.57 (d), 49.41 (d), 120.20 (s), 121.83 (s).

Anal. Calcd for $C_{11}H_8N_6O_{12}$: C, 31.70; H, 1.94. Found: C, 31.76; H, 1.94.

Single-crystal X-ray structural analysis of 1: $C_{11}H_8N_6O_{12}$, molecular weight 416.25, monoclinic, space group $P2_1/c$, a = 13.080 (3) Å, b = 17.842 (2) Å, c = 13.530 (3) Å, β = 106.67°, D_{calcd} = 1.83 g cm^{-3}, μ = 1.44 mm^{-1}, Z = 8 (two molecules per asymmetric unit). A total of 4094 independent reflections were measured out to $2\theta_{max}$ = 112° with a Nicolet R3MV diffractometer by using Cu$K\alpha$ radiation (λ = 1.5418 Å) with an incident beam graphite monochromator. The data were collected at 295 K from a colorless crystal by using the $\theta/2\theta$ scan technique with a variable 2θ scan rate depending upon the intensity of a reflection (10°/min minimum to 30°/min maximum). An empirical absorption correction was applied. The minimum and maximum transmission factors were found to be 0.675 and 0.752, respectively. The structure was solved by direct methods as implemented by the SHELXTL system of programs.[11] Least-squares refinement was performed on 588 parameters (coordinates for all atoms, anisotropic thermal parameters for non-hydrogen atoms, isotropic thermal parameters for hydrogen atoms) by using the 3601 reflections for which $|F_o| > 3\sigma|F_o|$ gave a final R factor of 0.060 (Rw = 0.077). The goodness of fit parameter was 3.20, and the final difference map was featureless.

Acknowledgment. Financial support of this study by the Air Force Office of Scientific Research (Grant AFOSR-88-0132), the Robert A. Welch Foundation (Grant B-963), the U.S. Army Armament Research, Development, and Engineering Center, Picatinny Arsenal, NJ (Contract DAAA21-86-C-0091), and the University of North Texas Faculty Research Committee is gratefully acknowledged. The X-ray crystallographic structure determination of **1** was supported in part by the Office of Naval Research Mechanics Division.

Registry No. **1**, 119183-92-5; **2**, 110243-30-6; (*E*)-**3**, 119183-93-6; (*Z*)-**3**, 119183-98-1; **4**, 119183-94-7; **5**, 119183-95-8; **6**, 119183-96-9; **7**, 119183-97-0; **8**, 119207-88-4.

Supplementary Material Available: A list of atomic coordinates and equivalent isotropic displacement parameters, bond lengths, bond angles, and H-atom coordinates and isotropic displacement parameters for **1** (5 pages). Ordering information is given on any current masthead page.

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Cyclopropanation of 2-Ylideneoxazol-5-one with Diphenyldiazomethane: Stereospecific Synthesis of Novel *gem*-Diphenylcyclopropyl Amino Acid Derivatives†

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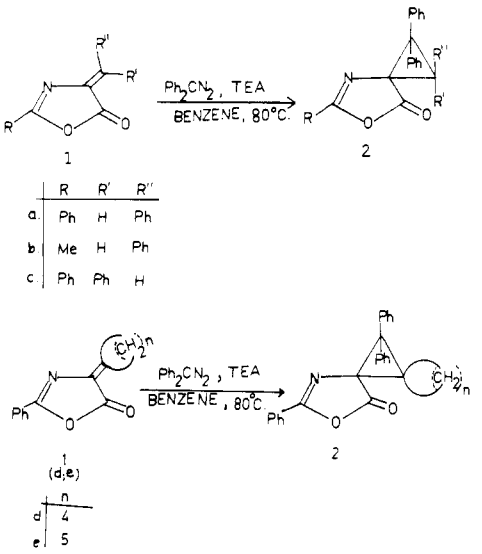
Aminocyclopropanecarboxylic acid derivatives are known to possess a wide spectrum of biological action.[1-4] Introduction of a *gem*-diphenyl group into the cyclopropane system leads to compounds that have shown pronounced action as plant growth regulatory, insecticidal, and anticancer activity. In our attempts to prepare cyclopropyl amino alcohol and acid derivatives for biological screening, we have achieved a stereospecific synthesis of

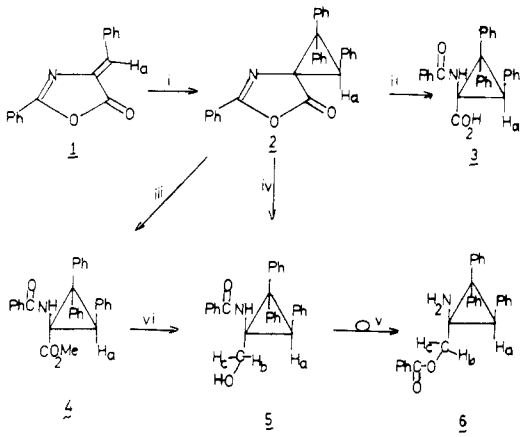
† RRL-H Communication No. 2098.

0022-3263/89/1954-1771$01.50/0

Scheme I



Scheme II[a]



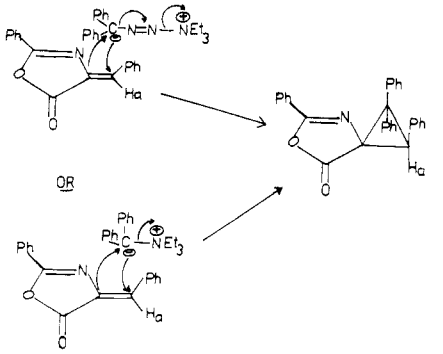
[a] (i) Ph_2CN_2, TEA, benzene, 80 °C; (ii) KOH, dioxane, 103 °C; (iii) MeOH, DMAP, 80 °C; (iv) LAH, THF, 27 °C; (v) HCl, dioxane, 27 °C; (vi) LAH, THF, 27 °C.

these compounds starting from easily accessible 2-ylideneoxazol-5-ones.

Reaction of (*Z*)-2-phenyl-4-benzylideneoxazol-5-one (**1a**) with diphenyldiazomethane (DPDM) in presence of triethylamine (TEA) gave a colorless crystalline solid melting at 170 °C. This product is assigned the spirocyclopropane structure **2** (Scheme I), with the same configuration as **1** on the basis of NMR spectra and chemical transformations (Scheme II). Spirocyclopropane oxazolone **2a** is converted to the (benzoylamino)cyclopropanecarboxylic acid **3** by alkali treatment and the corresponding methyl ester **4** by refluxing in methanol and 4-(dimethylamino)pyridine (DMAP). Reduction of **2a** with LAH gave the 1-benzamido-1-(hydroxymethyl)cyclopropane derivative **5**, which has smoothly transformed to the [(benzoyloxy)methyl]-aminocyclopropane derivative **6** by treating with hydrochloric acid. Other cyclopropanated compounds prepared in the present work are listed in the Experimental Section.

Stereochemical assignment of 1-benzamido-1-(hydroxymethyl)-2,2,3-triphenylcyclopropane (**5**) and the corresponding (benzoyloxy)methyl amine **6** has been made on the basis of NMR spectral data. The H_a proton in **2a** appears as a singlet at 3.85 ppm, and in **3a** at 4.28 ppm. When the carbonyl function is reduced to the corresponding alcohol **5** the H_a proton has suffered considerable upfield shift to 3.28 ppm, indicating a cisoid configuration between H_a and the carbonyl group. This is confirmed by NOE experiments. The methylene protons H_b and H_c appears as a doublet of doublets (3.66 and 4.13) (J_{gem} = 12 Hz). Irradiation of H_a proton in **5** and **6** caused significant enhancement of H_b and H_c proton signals (27–30%), while irradiation of H_b and H_c caused 27 and 35% enhancement of H_a proton signal, respectively.

The reaction of DPDM with oxazolones **1a–e** in the absence of TEA did not give the spirocyclopropanes; instead, it gave the decomposition products of DPDM.[5] It is suggested that the addition of diazoalkanes to an unsaturated system proceed either by insertion of the carbenoid moiety or by the formation of pyrazoline ring.[6,7] The diphenylcarbene produced under the influence of copper or copper salts[8] is not capable of reacting with oxazolones. Further, pyrazoline formation has not been detected in the reaction of DPDM with oxazolones. In view of these facts, the involvement of TEA may be visualized in the initial formation of an adduct either with DPDM or diphenylcarbene,[9] which can add to the ylidene double bond of the oxazolone in a Michael fashion with the concomitant elimination of nitrogen and/or TEA to give the spirocyclopropanes with retention of the stereochemistry of the original double bond.



The reaction of (*E*)-oxazolone **1c** with DPDM gave only the spirocyclopropane **2a** because of the rapid isomerization of **1c** to **1a** under the reaction conditions.[10] Spirocyclopropanes **2d** and **2e** were also obtained from the cycloalkylideneoxazolones by the same procedure. Some of the compounds described in the work have exhibited promising biological activity.[11]

Experimental Section

Instrumentation. All the melting points were taken on a Mettler FP51 capillary melting point apparatus and are uncorrected. Infrared spectra were measured with a Perkin-Elmer Model 710B recording spectrophotometer with polystyrene as a standard, reported values are given in the cm^{-1}. Mass spectra

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(11) Compounds **2a**, **2b**, and **4a** have shown significant antibacterial activity against *Bacillus subtilis*.

were measured on micromass 7070H model. ^1H NMR spectra were recorded on a Bruker AM 300 spectrometer at 300 MHz in $CDCl_3$ with tetramethylsilane as internal standard.

The spirolactones (**2a–e**) were prepared by the action of DPDM on oxazolones (**1a–e**) in the presence of TEA/benzene.

***cis*-1,2,2,5-Tetraphenyl-6-oxa-4-azaspiro[2.4]hept-4-en-7-one (2a).** In a typical experiment oxazolone **1a** (2.49 g, 10 mmol) was mixed with DPDM (20 mmol) and TEA (20 mmol) in 20 mL of benzene. The reaction mixture was refluxed for 10 h. When the pink color disappeared on the TLC, the reaction mass was concentrated in vacuo, and the resulting oily mass was passed through a column (silica gel of 200 mesh size using the eluent hexane–benzene, 1:1) to give the spirocyclopropane compound **2a** as a colorless solid (2.9 g): mp 170 °C; yield 70%; mass [M^+] 415; IR ($CHCl_3$) 3000, 1820, 1680, 1520, 1040; NMR ($CDCl_3$) δ 3.85 (1 H, s, H_a), 7.02–7.85 (20 H, m, Ar, H); ^{13}C NMR ($CDCl_3$) 78.939 (spirocarbon) 58.885 (Ph-*C*-Ph), 38.96 (Ph-*C*-H). Anal. Calcd: C, 83.58; H, 5.06; N, 3.37. Found: C, 83.28; H, 5.02; N, 3.42.

Spirocyclopropane lactones **2b–e** were also obtained by the same procedure.

***cis*-1-Benzamido-2,2,3-triphenylcyclopropanecarboxylic Acid (3).** Compound **2a** (2 mmol) was refluxed in 5 mL of 20% NaOH solution in 25 mL of dioxane for 45 min. The resulting reaction mixture was neutralized with 10% HCl, and the compound was extracted with methylene chloride. After the removal of the solvent the compound was obtained as a pure colorless solid (0.68 g, 80% yield): mass [M^+] 433; IR ($CHCl_3$) 3420, 1730, 1660; ^1H NMR ($CDCl_3$) δ 4.87 (1 H, m, H_a), 4.11 (1 H, s, D_2O exchanged), 7.32–7.8 (20 H, m, ArH).

Methyl 1-Benzamido-2,2,3-triphenylcyclopropanecarboxylate (4). Five millimoles of **2a** suspended in 60 mL of absolute methanol and 25 mmol of DMAP was stirred at 70–80 °C for 2 h. The solvent was removed in vacuo, and the residual mass was taken into CH_2Cl_2 and washed with 5% citric acid solution. The organic layer was dried over anhydrous magnesium sulfate and on concentration gave 1.9 g (85%) of crude ester: mass [M^+] 447; IR ($CHCl_3$) 3380, 1720, 1665; ^1H NMR ($CDCl_3$) δ 3.48 (3 H, s, Me*H*), 4.28 (1 H, s, H_a), 7.11–7.86 (20 H, m, Ar*H*).

1-Benzamido-1-(hydroxymethyl)-2,2,3-triphenylcyclopropane (5). To a stirred mixture of LAH (40 mmol) in dry THF (50 mL) was added **2a** (2 mmol) during 30 min under a nitrogen atmosphere. The resultant mixture was stirred for an additional 5 h at 28 °C. At the end of the reaction the contents were treated with ethyl acetate and THF (1:9) and hydrolyzed with 10% aqueous HCl at 0–5 °C. The resulting mass is filtered and extraced with benzene and dried over anhydrous Na_2SO_4. Concentration of the organic layer gave crystalline product (0.756 g; 90% yield) after standing overnight in the refrigerator: mp 182 °C; mass [M^+] 420; IR ($CHCl_3$) 3500, 3000, 1665, 1490, 1040; ^1H NMR ($CDCl_3$) δ 3.28 (1 H, s, H_a), 3.66 (1 H, d, methylene H_b), 4.13 (1 H, d, methylene H_c), 4.09 (1 H, s, hydroxy H). Anal. Calcd: C, 82.93; H, 5.99; N, 3.33. Found: C, 82.61; H, 5.91; N, 3.29.

1-Amino-1-[(benzoyloxy)methyl]-2,2,3-triphenylcyclopropane (6). A solution of **5a** (2 mmol) in dioxane (40 mL) was mixed with 10 N HCl (2 mL), and the mixture was stirred at room temperature for 10–12 h. The solvent was removed under reduced pressure, and the residue was extracted with ether. The ether layer was successively washed with water and 2% aqueous $NaHCO_3$ solution and dried over anhydrous Na_2SO_4. Removal of the solvent gave an oily residue, which on trituration with petroleum ether gave the product as fine crystals, which were stored under nitrogen atmosphere (0.672 g, 80% yield): mp 161 °C; mass [M^+] 420; IR ($CHCl_3$) 3240, 3000, 1720, 1030; ^1H NMR ($CDCl_3$) δ 1.55 (2 H, s, amino H), 3.06 (1 H, s, H_a), 4.29 (1 H, d, H_b), 4.32 (1 H, d, H_c), 6.53–7.21 (20 H, m, ArH). Anal. Calcd: C, 82.93; H, 5.99; N, 3.33. Found: C, 82.03; H, 5.92; N, 3.32.

Acknowledgment. We are thankful to Dr. A. V. Rama Rao, for encouragement. One of us (K.L.) is grateful to CSIR, New Delhi, for the award of Senior Research Fellowship and thankful to Dr. J. M. Rao and Dr. M. Pardhasaradhi for useful discussions, to Mr. Raju for carrying out NOE experiments, and Dr. J. Annapurna for carrying out the activity tests.

Registry No. **1a**, 17606-70-1; **1b**, 38879-46-8; **1c**, 15732-43-1; **1d**, 59759-76-1; **1e**, 52956-46-4; **2a**, 118896-81-4; **2b**, 118896-82-5; **2c**, 118896-83-6; **2d**, 118896-84-7; **2e**, 118896-85-8; **3**, 118896-86-9; **4**, 118896-87-0; **5**, 118896-88-1; **6**, 118896-89-2; Ph_2CN_2, 883-40-9.

Stereoselective Palladium-Catalyzed Synthesis of (*Z*)-Trimethyl(2-arylethenyl)silanes by Arylation of (*E*)-1,2-Bis(trimethylsilyl)ethylene. Effects of Added Halides Compared to Silver Salts

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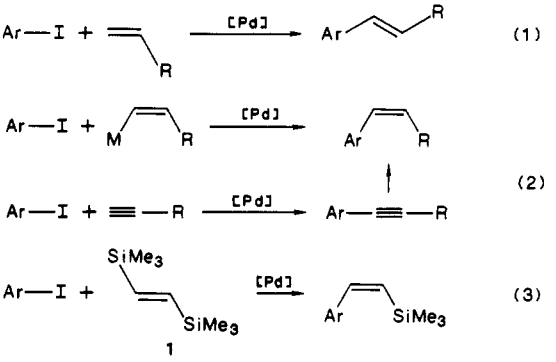
Introduction

Palladium-catalyzed vinylation of aryl halides (the Heck arylation) is of the utmost importance in organic synthesis.[1] Reactions with monosubstituted olefins furnish *E* β-arylated alkenes in high yields (eq 1), and there are to our knowledge no examples of synthetically useful arylations producing the *Z* isomers as the major products.[2] The *Z* isomers can easily be prepared by a stereoselective, palladium-catalyzed cross coupling reaction.[3] When aryl halides (or aryl triflates) are chosen as one of the counterparts,[4] coupling with the proper alkenylmetals[5] or, alternatively, acetylenes[6] followed by hydrogenation, gives the desired products (eq 2).

We here report a Heck-type reaction, which affords fair yields of (*Z*)-trimethyl(2-arylethenyl)silanes from (*E*)-1,2-bis(trimethylsilyl)ethylene (1) and aryl iodides (eq 3), and we have thereby taken advantage of a trimethylsilyl/palladium halide syn-elimination process.



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