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SYNTHESIS OF SUBSTITUTED PYRROLIDINES BY REACTION OF ARYL-SUBSTITUTED VINYLIDENECYCLOPROPANES WITH AROMATIC IMINES CATALYZED BY $BF_3 \cdot Et_2O$

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The reactions of 1,1-diaryl-2-(diphenylvinylidene)cyclopropanes and 1,1-diaryl-2-(2-phenyl-propenylidine)cyclopropanes with aromatic amines in the presence of $BF_3 \cdot Et_2O$ leads to the formation of pyrrolidine derivatives.

Keywords: vinylidenecyclopropanes, imines, pyrrolidines.

Vinylidenecyclopropanes have value as synthons in organic synthesis, in particular in the preparation of heterocyclic compounds [1-6]. Catalysis by Lewis acids has recently been reported in the reaction of vinylidenecyclopropanes with acetals to give indene derivatives [7]. It has previously been shown that the reaction of vinylidenecyclopropanes with aromatic imines or ethyl (arylimino)acetates in the presence of a Lewis acids gives pyrrolidine or 1,2,3,4-tetrahydroquinoline derivatives depending on the nature of the substituent on the multiple bond or in the cyclopropane ring [8, 9]. We have found that the reaction of aromatic imines with vinylidenecyclopropanes containing alkyl substituents in the cyclopropane ring and on the multiple bond gives only the formation of products which occurs *via* a cyclopropyl-allyl rearrangement stage, i.e. substituted pyrrolidines. Vinylidenecyclopropanes containing an aryl and alkyl substituent simultaneously in the cyclopropane ring and aryl substituents on the double bond gave products the formation of which occurs *via* an intramolecular Friedel-Crafts reaction stage, i.e. tetrahydroquinoline derivatives [8]. Vinylidene-cyclopropanes containing two aryl substituents in the cyclopropane ring have not been included in this reaction hence the aim of this work was a study of the reaction of vinylidenecyclopropanes containing aryl substituents in the cyclopropane ring and on the double bond with aromatic imines in the presence of $BF_3 \cdot Et_2O$.

It was found that treating the 1,1-diaryl-2-(diphenylvinylidene)cyclopropanes **1a,b** with the imines **2a,b** in the presence of $BF_3 \cdot Et_2O$ (15 mol %) in methylene chloride gave the 2-aryl-4-diarylmethylene-3-diphenylmethylene-1-phenylpyrrolidines **3a-d** in yields up to 27%. In all cases the target compounds were separated using preparative TLC. The structure and composition of compounds **3a-d** were established from their spectroscopic and elemental analytical data. The ^{1}H NMR spectra of these compounds show doublet signals for the methylene group protons at 4.2 and 4.6 ppm (J = 12 Hz) and a methine proton singlet at 5.0 ppm assigned to the pyrrolidine ring. The ^{13}C NMR spectra show the signals for atoms C-2 and C-5 of the pyrrolidine ring at 66 and 53 ppm respectively.

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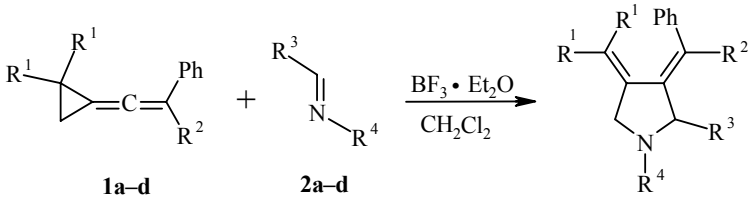
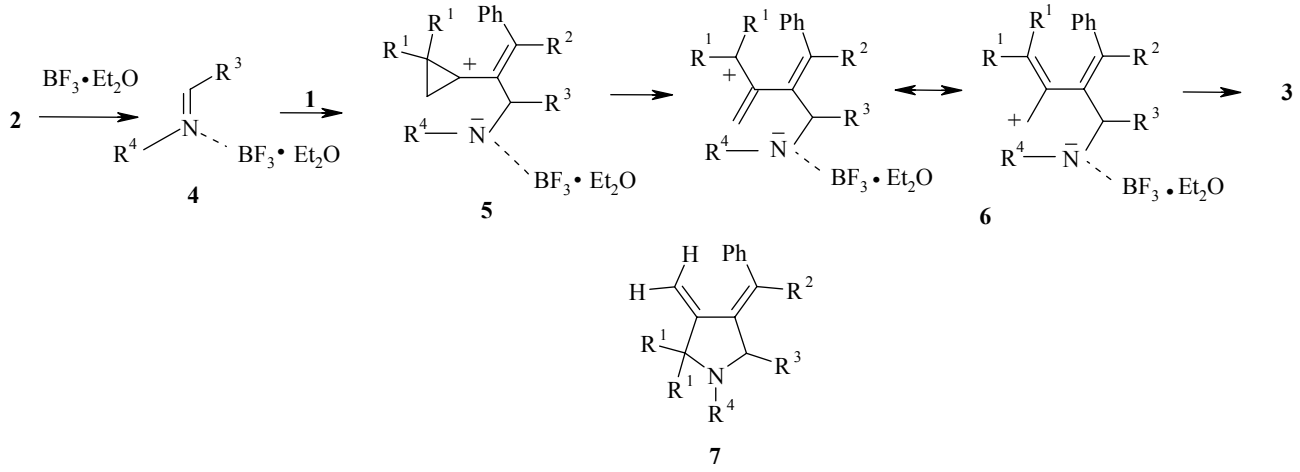


1a–d **2a–d** **3a–j**

1 a $R^1 = R^2 = Ph$; **b** $R^1 = 4\text{-}MeC_6H_4$, $R^2 = Ph$; **c** $R^1 = Ph$, $R^2 = Me$; **d** $R^1 = 4\text{-}MeC_6H_4$, $R^2 = Me$;
2 a $R^3 = R^4 = Ph$; **b** $R^3 = 4\text{-}ClC_6H_4$, $R^4 = Ph$; **c** $R^3 = 4\text{-}ClC_6H_4$, $R^4 = 4\text{-}MeOC_6H_4CH_2$;
d $R^3 = Ph$, $R^4 = 1$-naphtyl; **3 a** $R^1 = R^2 = R^3 = R^4 = Ph$; **b** $R^1 = R^2 = R^4 = Ph$, $R^3 = 4\text{-}ClC_6H_4$;
c $R^1 = 4\text{-}MeC_6H_4$, $R^2 = R^3 = R^4 = Ph$; **d** $R^1 = 4\text{-}MeC_6H_4$, $R^2 = R^4 = Ph$, $R^3 = 4\text{-}ClC_6H_4$;
e $R^1 = R^2 = Ph$, $R^3 = 4\text{-}ClC_6H_4$, $R^4 = 4\text{-}MeOC_6H_4CH_2$; **f** $R^1 = R^3 = R^4 = Ph$, $R^2 = Me$;
g $R^1 = R^4 = Ph$, $R^2 = Me$, $R^3 = 4\text{-}ClC_6H_4$; **h** $R^1 = 4\text{-}MeC_6H_4$, $R^2 = Me$, $R^3 = R^4 = Ph$;
i $R^1 = 4\text{-}MeC_6H_4$, $R^2 = Me$, $R^3 = 4\text{-}ClC_6H_4$, $R^4 = Ph$; **j** $R^1 = 4\text{-}MeC_6H_4$, $R^2 = Me$, $R^3 = Ph$, $R^4 = 1$-naphtyl

The reaction of the vinylidenecyclopropane **1a** with imine **2c** in the presence of $BF_3 \cdot Et_2O$ (15 mol %) yielded only 8% of the pyrrolidine **3e** from the reaction mixture. The ^1H NMR spectrum of compound **3e** showed doublet signals for the methylene group at 2.8 and 4.1 ppm (J = 13 Hz) and methine proton singlet at 4.4 ppm for the pyrrolidine ring and doublet signals for the benzyl substituent methylene protons at 3.3 and 3.6 ppm (J = 15 Hz). The shift of the signal for one of the methylene group protons of the pyrrolidine ring to the high field region (2.8 ppm) occurs as a result of the shielding effect of the benzyl group.

The reactions of the 1,1-diaryl-2-(2-phenylpropenylidene)cyclopropanes **1c,d** with the N-arylidene-anilines **2a,b** in the presence of $BF_3 \cdot Et_2O$ (15 mol %) in methylene chloride gives a complex mixture from which the 2-aryl-4-diarylmethylene-1-phenyl-3-[(*E*)-1-phenylethylidene]pyrrolidines **3f-i** could be separated in yields up to 30%. The structure and composition of compounds **3f-i** were proved using spectroscopic and elemental analytical data. The ^1H NMR spectra of these compounds show doublet signals for the methylene group protons at 4.1 and 4.5 ppm (J = 12 Hz) and methine proton at 5.5 ppm, the signal for the phenylethylidene methyl group being at 2.1 ppm. Through a comparison of the values of the chemical shift of the methyl group with literature data the phenylethylidene fragment at position 3 is assigned the *E*-configuration. It has previously been shown that, in similarly structured pyrrolidines **3f-i** with an *E*-configured phenylethylidene fragment, the methyl signal occurs in the range 1.9-2.3 ppm while in the *Z*-configuration it is shifted to 1.4-1.5 ppm as a result of the shielding effect of an aryl substituent in the diarylmethylene fragment at position 4 [10, 11]. The ^{13}C NMR spectra of compounds **3f-i** show signals for the pyrrolidine ring C-2 and C-5 atoms at 65 and 53 ppm respectively.



4 **5** **6** **7**

Treatment of the vinylidenecyclopropane **1d** with N-(1-naphthyl)imine **2d** in the presence of $BF_3 \cdot Et_2O$ (15 mol %) gives the pyrrolidine **3j** in 16% yield. The ^1H NMR spectrum of the compound shows doublet signals for methylene group protons at 4.2 and 4.4 ppm (J = 12 Hz) and methine proton singlet at 5.7 ppm from the pyrrolidine ring and the methyl group signal of the phenylethylidene fragment at 2.0 ppm.

The mechanism of formation of the pyrrolidines **3a-j** can be represented by the following scheme: in the first stage formation of the imine-Lewis acid complex **4** which then reacts with the starting vinylidenecyclopropane, while electrophilic attack occurs at the central carbon atom of the cumulated system to form the cyclopropyl cation **5** which subsequent undergoes cyclopropyl-allyl rearrangement to form intermediante **6** then cyclizing to the substituted pyrrolidine **3**. Formation of the isomeric pyrrolidines **7** was not observed.

EXPERIMENTAL

Elemental analysis was carried out using a Hewlett-Packard 185B CHN-analyzer. Melting points were determined on a Boetius block. ^1H and ^{13}C NMR spectra were recorded on a Bruker DPX-300 (300 and 75 MHz respectively) using $CDCl_3$. Chemical shifts are given relative to the residual solvent signal at 7.26 for ^1H NMR and 77.16 ppm for ^{13}C NMR [12].

Checking the purity and homogeneity of the compounds and monitoring the reaction course was carried out by TLC on Silufol UV-254 plates. Preparative TLC separations were performed on LSL_{254} 5/40 silica gel.

The vinylidenecyclopropanes **1a-d** were prepared by the method reported in [13].

3,4-Bis(diphenylmethylene)-1,2-diphenylpyrrolidine (3a). The vinylidenecyclopropane **1a** (170 mg, 0.46 mmol), imine **2a** (91 mg, 0.5 mmol), and absolute methylene chloride (3 ml) were placed in a 10 ml round bottomed flask in an argon stream. $BF_3 \cdot Et_2O$ (13 mg, 0.096 mmol) was added dropwise with stirring to the mixture obtained and it was stirred at room temperature under an argon atmosphere for 3 days. Solvent was evaporated and the residue was separated by preparative TLC using hexane and ethyl acetate (40: 1 by volume) as eluent. Yield 59 mg (23%); mp 160-162ºC (methanol). ^1H NMR spectrum, δ, ppm (J, Hz): 4.20 (1H, d, J = 12.4, CH_2); 4.66 (1H, d, J = 12.4, CH_2); 5.07 (1H, s, CH); 6.45-7.53 (30H, m, H_{arom}). ^{13}C NMR spectrum, δ, ppm: 53.1 (C-5), 66.4 (C-2); 111.9, 116.6, 126.6, 126.7, 127.7, 127.95, 127.96, 128.1, 128.37, 128.38, 128.59, 128.63, 129.4, 129.5, 129.8, 130.3, 133.3, 139.6, 139.8, 141.6, 142.06, 142.09, 143.1, 143.8, 146.1. Found, %: C 91.29; H 5.97; N 2.36. $C_{42}H_{33}N$. Calculated, %: C 91.43; H 6.03; N 2.54.

2-(4-Chlorophenyl)-3,4-bis(diphenylmethylene)-1-phenylpyrrolidine (3b) was prepared similarly to compound **3a** from the vinylidenecyclopropane **1a** and imine **2b** in 24% yield with mp 124-126ºC (methanol). ^1H NMR spectrum, δ, ppm (J, Hz): 4.20 (1H, d, J = 12.4, CH_2); 4.65 (1H, d, J = 12.4, CH_2); 5.04 (1H, s, CH); 6.38-7.60 (29H, m, H_{arom}). ^{13}C NMR spectrum, δ, ppm: 53.0 (C-5), 65.7 (C-2), 111.9, 116.8, 126.8, 126.9, 128.0, 128.1, 128.2, 128.5, 128.6, 128.8, 129.4, 129.5, 129.7, 129.8, 130.1, 132.9, 133.3, 139.96, 140.0, 140.2, 141.5, 141.9, 142.0, 142.6, 143.0, 145.9. Found, %: C 85.94; H 5.41; N 2.17. $C_{42}H_{32}ClN$. Calculated, %: C 86.06; H 5.50; N 2.39.

3-Diphenylmethylene-4-di(4-methylphenyl)methylene-1,2-diphenylpyrrolidine (3c) was prepared similarly to compound **3a** from the vinylidenecyclopropane **1b** and imine **2a** in 27% yield with mp 154-156ºC (methanol). ^1H NMR spectrum, δ, ppm (J, Hz): 2.17 (3H, s, CH_3); 2.41 (3H, s, CH_3); 4.17 (1H, d, J = 12.4, CH_2); 4.61 (1H, d, J = 12.4, CH_2); 5.02 (1H, s, CH); 6.32-6.71 (9H, m, H_{arom}); 6.83-6.97 (5H, m, H_{arom}); 7.02-7.29 (14H, m, H_{arom}). Found, %: C 91.07; H 6.32; N 2.31. $C_{44}H_{37}N$. Calculated, %: C 91.15; H 6.43; N 2.42.

2-(4-Chlorophenyl)-4-di(4-methylphenyl)methylene-3-diphenylmethylene-1-phenylpyrrolidine (3d) was prepared similarly to compound **3a** from the vinylidenecyclopropane **1b** and imine **2b** in 20% yield. ^1H NMR spectrum, δ, ppm (J, Hz): 2.17 (3H, s, CH_3); 2.41 (3H, s, CH_3); 4.18 (1H, d, J = 12.4, CH_2); 4.61 (1H,

d, J = 12.4, CH_2); 5.05 (1H, s, CH); 6.40-6.69 (9H, m, H_{arom}); 6.81-6.96 (5H, m, H_{arom}); 7.05-7.31 (13H, m, H_{arom}). Found, %: C 86.19; H 6.03; N 2.11. $C_{44}H_{36}ClN$. Calculated, %: C 86.04; H 5.91; N 2.28.

2-(4-Chlorophenyl)-3,4-bis(diphenylmethylene)-1-(4-methoxybenzyl)-pyrrolidine (3e) was prepared similarly to compound **3a** from the vinylidenecyclopropane **1a** and imine **2c** in 8% yield with mp 183-184ºC (methanol). ^{1}H NMR spectrum, δ, ppm (J, Hz): 2.75 (1H, d, J = 13.1, CH_2); 3.30 (1H, d, J = 17.4, CH_2); 3.58 (1H, d, J = 17.4, CH_2); 3.68 (3H, s, OCH_3); 4.05 (1H, d, J = 13.1, CH_2); 4.40 (1H, s, CH); 6.45 (4H, dd, J = 7.3, J = 8.0, H_{arom}); 6.79 (2H, d, J = 8.7, H_{arom}); 6.90-7.18 (6H, m, H_{arom}); 7.21-7.66 (14H, m, H_{arom}); 7.79 (2H, d, J = 7.3, H_{arom}). Found, % C 83.87; H 6.04; N 2.01. $C_{46}H_{40}ClNO$. Calculated, %: C 83.93; H 6.12; N 2.13.

1,2-Diphenyl-4-diphenylmethylene-3-[(*E*)-1-phenylethylidene]pyrrolidine (3f) was prepared similarly to compound **3a** from the vinylidenecyclopropane **1c** and imine **2a** in 21% yield with mp 162-164ºC (methanol). ^{1}H NMR spectrum, δ, ppm (J, Hz): 2.14 (3H, s, CH_3); 4.11 (1H, d, J = 11.6, CH_2); 4.52 (1H, d, J = 11.6, CH_2); 5.55 (1H, s, CH); 6.18 (2H, d, J = 6.5, H_{arom}); 6.58-7.55 (23H, m, H_{arom}). ^{13}C NMR spectrum, δ, ppm: 22.6 (CH_3), 53.3 (C-5); 65.5 (C-2); 111.9, 116.6, 126.2, 127.1, 127.4, 127.6, 127.8, 127.9, 128.1, 128.4, 128.6, 129.1, 129.4, 129.6, 129.8, 130.3, 132.4, 132.9, 135.9, 139.4, 141.7, 143.3, 143.6, 146.7. Found, %: C 90.59; H 6.29; N 2.65. $C_{37}H_{31}N$. Calculated, %: C 90.76; H 6.38; N 2.86.

2-(4-Chlorophenyl)-4-diphenylmethylene-1-phenyl-3-[(*E*)-1-phenylethylidene]pyrrolidine (3g) was prepared similarly to compound **3a** from the vinylidenecyclopropane **1c** and imine **2b** in 24% yield with mp 169-170ºC (methanol). ^{1}H NMR spectrum, δ, ppm (J, Hz): 2.10 (3H, s, CH_3); 4.08 (1H, d, J = 11.6, CH_2); 4.48 (1H, d, J = 11.6, CH_2); 5.49 (1H, s, CH); 6.16 (2H, d, J = 7.3, H_{arom}); 6.53-6.83 (7H, m, H_{arom}); 6.84-7.10 (6H, m, H_{arom}); 7.13-7.50 (9H, m, H_{arom}). ^{13}C NMR spectrum, δ, ppm: 22.6 (CH_3); 53.2 (C-5); 65.0 (C-2); 111.9, 117.0, 126.3, 126.5, 127.91, 127.93, 128.1, 128.2, 128.4, 128.5, 128.8, 129.3, 129.5, 129.6, 129.8, 132.0, 133.3, 135.4, 139.8, 141.6, 142.1, 143.2, 143.4, 146.5. Found, %: C 84.73; H 5.84; N 2.61. $C_{37}H_{30}ClN$. Calculated, %: C 84.79; H 5.77; N 2.67.

4-Di(4-methylphenyl)methylene-1,2-diphenyl-3-[(*E*)-1-phenylethylidene]pyrrolidine (3h) was prepared similarly to compound **3a** from the vinylidenecyclopropane **1d** and imine **2a** in 22% yield with mp 191-192ºC (methanol). ^{1}H NMR spectrum, δ, ppm (J, Hz): 2.11 (3H, s, CH_3); 2.22 (3H, s, CH_3); 2.41 (3H, s, CH_3); 4.12 (1H, d, J = 11.6, CH_2); 4.49 (1H, d, J = 11.6, CH_2); 5.49 (1H, s, CH); 6.07 (2H, d, J = 7.3, H_{arom}); 6.50-6.78 (7H, m, H_{arom}); 6.85-7.05 (5H, m, H_{arom}); 7.08-7.32 (5H, m, H_{arom}); 7.40 (2H, d, J = 8.0, H_{arom}); 7.46 (2H, d, J = 8.0, H_{arom}). ^{13}C NMR spectrum, δ, ppm: 21.4 (CH_3); 21.7 (CH_3); 22.6 (CH_3); 53.3 (C-5); 65.0 (C-2); 111.9, 116.9, 126.3, 127.9, 128.0, 128.5, 129.1, 129.2, 129.4, 129.6, 129.8, 131.1, 132.6, 133.2, 135.7, 135.9, 137.7, 138.8, 139.7, 140.4, 142.2, 143.5, 146.6. Found, %: C 90.32; H 6.67; N 2.53. $C_{39}H_{35}N$. Calculated, %: C 90.48; H 6.81; N 2.71.

2-(4-Chlorophenyl)-4-di(4-methylphenyl)methylene-1-phenyl-3-[(*E*)-1-phenylethylidene]pyrrolidine (3i) was prepared analogously to compound **3a** from the vinylidenecyclopropane **1d** and imine **2b** in 30% yield with mp 206-207ºC (methanol). ^{1}H NMR spectrum, δ, ppm (J, Hz): 2.13 (3H, s, CH_3); 2.21 (3H, s, CH_3); 2.41 (3H, s, CH_3); 4.13 (1H, d, J = 11.6, CH_2); 4.53 (1H, d, J = 11.6, CH_2); 5.53 (1H, s, CH); 6.07 (2H, d, J = 7.3, H_{arom}); 6.56 (2H, d, J = 8.0, H_{arom}); 6.65 (2H, d, J = 8.0, H_{arom}); 6.70 (2H, d, J = 7.3, H_{arom}); 6.93-7.52 (14H, m, H_{arom}). ^{13}C NMR spectrum, δ, ppm: 21.4 (CH_3); 21.7 (CH_3); 22.6 (CH_3); 53.3 (C-5); 65.5 (C-2); 111.9, 116.6, 126.1, 127.1, 127.5, 127.9, 128.0, 128.4, 129.1, 129.5, 129.8, 131.4, 132.2, 135.8, 136.1, 137.6, 138.9, 139.4, 140.6, 143.5, 143.7, 146.8. Found, %: C 84.71; H 6.71; N 2.39. $C_{39}H_{34}ClN$. Calculated, %: C 84.4; H 6.21; N 2.54.

4-Di(4-methylphenyl)methylene-1-(1-naphthyl)-2-phenyl-3-[(*E*)-1-phenylethylidene]pyrrolidine (3j) was prepared similarly to compound **3a** from the vinylidenecyclopropane **1d** and imine **2d** in 16% yield with mp 139-140ºC (methanol). ^{1}H NMR spectrum, δ, ppm (J, Hz): 2.00 (3H, s, CH_3); 2.25 (3H, s, CH_3); 2.31 (3H, s, CH_3); 4.24 (1H, d, J = 12.4, CH_2); 4.38 (1H, d, J = 12.4, CH_2); 5.72 (1H, s, CH); 6.37 (2H, d, J = 6.5,

H_{arom}); 6.65 (2H, d, J = 8.0, H_{arom}); 6.78-7.51 (16H, m, H_{arom}); 7.54 (1H, d, J = 7.3, H_{arom}); 7.63 (2H, d, J = 7.3, H_{arom}); 7.81 (1H, d, J = 8.0, H_{arom}); 8.24 (1H, d, J = 8.7, H_{arom}). Found, %: C 90.82; H 6.53; N 2.39. $C_{43}H_{37}N$. Calculated, %: C 90.96; H 6.57; N 2.47.

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