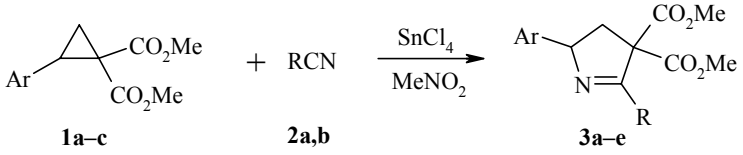
FIRST SYNTHESIS OF 2-ALKYL-5-ARYL-3,3-BIS(METHOXYCARBONYL)-4,5-DIHYDROPYRROLES

A. O. Chagarovskiy[1], E. M. Budynina[1], O. A. Ivanova[1], and I. V. Trushkov[1]*

Keywords: donor-acceptor cyclopropanes, nitriles, Δ^1-pyrrolines, cycloaddition.

Donor-acceptor cyclopropanes have attracted considerable interest in light of their high reactivity in various reactions including cycloaddition [1-3]. Until now, the cycloaddition of such cyclopropanes to nitriles has been studied only for 2-alkoxycyclopropanecarboxylates [4-8]. In the presence of Me_3SiOTf, these compounds form adducts, which, under the reaction conditions, tend to lose an alcohol molecule with the formation of pyrroles [5-8]. According to Yu and Pagenkopf [5], other cyclopropanes do not react with nitriles.



1a–c **2a,b** **3a–e**

1a, **3a**,**d** Ar = Ph; **1b**, **3b** Ar = 4-BrC_6H_4; **1c**, **3c**,**e** Ar = 3,4,5-$(MeO)_3C_6H_2$;
2a, **3a**,**c** R = Me; **2b**, **3b**,**d**,**e** R = Et

We studied the reaction of 2-arylcyclopropane-1,1-dicarboxylates **1a-c** with nitriles **2a** and **2b** and found that Δ^1-pyrrolines **3a-e** were formed when the reaction was carried out in nitromethane with $SnCl_4$ as the catalyst.

The IR spectra were taken on a UR-20 spectrometer for vaseline mulls. The ^1H and ^{13}C NMR spectra were taken on a Bruker Avance-400 spectrometer at 400 and 100 MHz, respectively for $CDCl_3$ solutions. The chemical shifts were measured relative to the solvent signals (^1H: δ 7.26 ppm, ^{13}C: δ 77.13 ppm). The electron impact mass spectra were taken on a Finnigan SSQ7000 GC-MS at 70 eV.

2-Arylcyclopropane-1,1-dicarboxylates **1** were prepared according to Corey and Chaykovsky [9].

Δ^1-Pyrrolines 3a-e. $SnCl_4$ (1.5 mmol) in $MeNO_2$ (2 ml) was added to a solution of nitrile **2** (3.75 mmol) and cyclopropane **1** (0.75 mmol) in (18 ml) $MeNO_2$. The reaction mixture was stirred for 3 h in an argon atmosphere at 55°C, poured into 50 ml aqueous sodium carbonate, and extracted with three 40-ml portions of

* To whom correspondence should be addressed, e-mail: itrushkov@mail.ru.

[1]Chemistry Faculty, M. V. Lomonosov Moscow State University, Moscow 119991 Russia.

Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp. 139-141, January, 2010. Original article submitted November 20, 2009.

 0009-3122/10/4601-0120

methylene chloride. The combined organic layer was washed with three 20-ml portions of aqueous Trilon B and three 20-ml water portions and then dried over anhydrous sodium sulfate. The solvent was evaporated off and the reaction product was isolated by chromatography on a silica gel column.

Dimethyl Ester of 2-Methyl-5-phenyl-4,5-dihydropyrrole-3,3-dicarboxylic Acid (3a) was obtained in 74% yield as a colorless oil, R_f 0.31 (4:1 petroleum ether–ethyl acetate). IR spectrum, ν, cm^{-1}: 1740 (C=O), 1670 (C≡N). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.31 (3H, d, ^5J = 2.3, CH_3); 2.37 (1H, dd, ^2J = 13.5, ^3J = 8.1, CH_2); 3.16 (1H, dd, ^2J = 13.5, ^3J = 7.3, CH_2); 3.76 (3H, s, OCH_3); 3.82 (3H, s, OCH_3); 5.12 (1H, ddd, ^3J = 8.1, ^3J = 7.3, ^5J = 2.3, CHAr); 7.24-7.29 (3H, m, Ar); 7.30-7.37 (2H, m, Ar). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 18.17 ($^1J_{CH}$ = 128, CH_3), 42.62 ($^1J_{CH}$ = 137, CH_2), 53.05 ($^1J_{CH}$ = 136, CH_3O), 53.18 ($^1J_{CH}$ = 136, CH_3O), 72.19 (C), 73.63 ($^1J_{CH}$ = 140, CHAr), 126.52 (2CH, Ar), 127.26 (CH, Ar), 128.54 (2CH, Ar), 142.30 (C, Ar), 168.24 (C), 168.38 (C), 169.23 (C). Mass spectrum, *m/z* (I_{rel}, %): 275 [M] (33), 215 (100), 203 (15), 184 (15), 170 (38), 131 (42), 130 (42), 121 (24), 115 (32). Found, %: C 65.30; H 6.15; N 4.92. $C_{15}H_{17}NO_4$. Calculated, %: C 65.44; H 6.22; N 5.09.

Dimethyl Ester of 5-(4-Bromophenyl)-2-ethyl-4,5-dihydropyrrole-3,3-dicarboxylic Acid (3b) was obtained in 64% yield as a pale-yellow oil, R_f 0.50 (4:1 petroleum ether–ethyl acetate). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.22 (3H, t, ^3J = 7.3, CH_3); 2.27 (1H, dd, ^2J = 13.4, ^3J = 8.1, CH_2); 2.50-2.60 (2H, qd, ^3J = 7.3, ^5J = 2.3, CH_2Me); 3.10 (1H, dd, ^2J = 13.4, ^3J = 7.3, CH_2); 3.70 (3H, s, OCH_3); 3.76 (3H, s, OCH_3); 5.04 (1H, ddd, ^3J = 8.1, ^3J = 7.3, ^5J = 2.3, CHAr); 7.12 (2H, d, ^3J = 8.0, Ar); 7.40 (2H, d, ^3J =8.0, Ar). ^{13}C NMR spectrum, δ, ppm: 10.89 (CH), 24.88 (CH_2Me), 42.70 (CH_2), 53.10 ($2CH_3O$), 72.19 (C), 72.80 (CHAr), 120.99 (C, Ar), 128.29 (2CH, Ar), 131.54 (2CH, Ar), 141.72 (C, Ar), 168.39 (CO_2Me), 168.88 (CO_2Me), 173.29 (C=N). Found, %: C 52.46; H 4.78; N 3.98. $C_{16}H_{18}BrNO_4$. Calculated, %: C 52.19; H 4.93; N 3.80.

Dimethyl Ester of 2-Methyl-5-(3,4,5-trimethoxyphenyl)-4,5-dihydropyrrole-3,3-dicarboxylic Acid (3c) was obtained in 89% yield as a colorless oil, R_f 0.64 (ether). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.20 (3H, br. s, CH_3); 2.38 (1H, dd, ^2J = 13.6, ^3J = 8.1, CH_2); 3.16 (1H, dd, ^2J = 13.6, ^3J = 7.1, CH_2); 3.69 (3H, s, OCH_3); 3.71 (3H, s, OCH_3); 3.73 (3H, s, OCH_3); 3.76 (6H, s, $2OCH_3$); 4.95 (1H, br. dd, ^3J = 7.1, ^3J = 8.1, CHAr); 6.41 (2H, s, 2CH, Ar). ^{13}C NMR spectrum, δ, ppm: 18.11 (CH_3), 42.29 (CH_2), 53.06 ($CO_2\underline{C}H_3$), 53.17 ($CO_2\underline{C}H_3$), 55.95 ($2OCH_3$), 60.64 (OCH_3), 72.02 (C), 73.66 (CH), 103.53 (2CH), 136.94 (C), 137.90 (C), 153.23 (2C), 168.08 ($\underline{C}O_2$Me), 168.58 (CO_2Me), 169.14 (C=N). Found: C 59.21; H 6.32; N 3.75%. $C_{18}H_{23}NO_7$. Calculated, %: C 59.17; H 6.34; N 3.83.

Dimethyl Ester of 2-Ethyl-5-phenyl-4,5-dihydropyrrole-3,3-dicarboxylic Acid (3d) was obtained in 65% yield as a pale-yellow oil, R_f 0.45 (4:1 petroleum ether–ethyl acetate). IR spectrum, ν, cm^{-1}: 1740 (C=O), 1660 (C=N). ^{1}H NMR spectrum, δ, ppm, (*J*, Hz): 1.28 (3H, t, ^3J = 7.3, CH_3); 2.38 (1H, dd, ^2J = 13.4, ^3J = 7.9, CH_2); 2.62 (2H, qd, ^3J = 7.3, ^5J = 2.3, CH_2Me); 3.16 (1H, dd, ^2J = 13.4, ^3J = 7.1, CH_2); 3.76 (3H, s, OCH_3); 3.82 (3H, s, OCH_3); 5.43 (1H, ddd, ^3J = 7.9, ^3J = 7.3, ^5J = 2.3, CHAr); 7.24-7.28 (3H, m, Ar); 7.32-7.37 (2H, m, Ar). ^{13}C NMR spectrum, δ, ppm: 10.96 (CH_3), 24.89 (CH_2Me), 42.99 (CH_2), 53.01 (CH_3O), 53.15 (CH_3O), 72.23 (C), 73.58 (CHAr), 126.55 (2CH, Ar), 127.25 (CH, Ar), 128.52 (2CH, Ar), 142.60 (C, Ar), 168.61 (CO_2Me), 169.41 (CO_2Me), 172.75 (C=N). Mass spectrum, *m/z* (I_{rel}, %): 289 $[M]^+$ (64), 274 (8), 230 (41), 229 (100), 170 (88), 145 (56), 121 (51), 115 (57). Found, %: C 66.47; H 6.84; N 4.82. $C_{16}H_{19}NO_4$. Calculated, %: C 66.42; H 6.62; N 4.84.

Dimethyl Ester of 2-Ethyl-5-(3,4,5-trimethoxyphenyl)- 4,5-dihydropyrrole-3,3-dicarboxylic Acid (3e) was obtained in 72% yield as an orange oil, R_f 0.58 (ether). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.28 (3H, t, ^3J = 7.3, CH_3); 2.38 (1H, dd, ^2J = 13.4, ^3J = 8.0, CH_2); 2.58-2.81 (2H, m, CH_2Me); 3.15 (1H, dd, ^2J = 13.4, ^3J = 7.4, CH_2);; 3.78 (3H, s, OCH_3); 3.83 (6H, s, OCH_3); 3.86 (6H, s, OCH_3); 5.02-5.08 (1H, m, CHAr); 6.49 (2H, s, Ar). ^{13}C NMR spectrum, δ, ppm: 11.01 (CH_3), 24.89 (CH_2Me), 42.74 (CH_2), 53.18 (CH_3O), 56.08 ($3CH_3O$), 60.81 (CH_3O), 72.17 (C), 73.75 (CHAr), 103.64 (2CH), 137.19 (C), 138.25 (C), 153.33 (2C), 168.54 (CO_2Me), 169.46 (CO_2Me), 172.82 (C=N). Found, %: C 59.90; H 6.75; N 3.71. $C_{19}H_{25}NO_7$. Calculated, %: C 60.15; H 6.64; N 3.69.

REFERENCES

1. H.-U. Reissig and R. Zimmer, *Chem. Rev.*, **103**, 1151 (2003).
2. M. Yu and B. L. Pagenkopf, *Tetrahedron*, **61**, 321 (2005).
3. F. De Simone and J. Waser, *Synthesis*, 3353 (2009).
4. M. Yu and B. L. Pagenkopf, *J. Am. Chem. Soc.*, **125**, 8122 (2003).
5. M. Yu and B. L. Pagenkopf, *Org. Lett.*, **5**, 5099 (2003).
6. M. Yu, G. D. Pantos, J. L. Sessler, and B. L. Pagenkopf, *Org. Lett.*, **6**, 1057 (2004).
7. C. L. Morales and B. L. Pagenkopf, *Org. Lett.*, **10**, 157 (2009).
8. B. Bajtos and B. L. Pagenkopf, *Eur. J. Org. Chem.*, 1072 (2009).
9. E. J. Corey and M. Chaykovsky, *J. Am. Chem. Soc.*, **87**, 1353 (1965).