Synthesis of 3,3-diarylpyrrolidines from diaryl ketones

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Abstract
3,3-Diarylsuccinic acids **4** were prepared from diaryl ketones by the Knoevenagel condensation with ethyl cyanoacete followed by KCN addition and hydrolysis. These were cyclised using primary amines to the respective diarylpyrrolidones **7**, which were finally reduced to 3,3-diarylpyrrolidines using $BH_3 \cdot THF$.

Keywords: 3,3-Diarrylpyrrolidines, 3,3-Diarylsuccinic acids

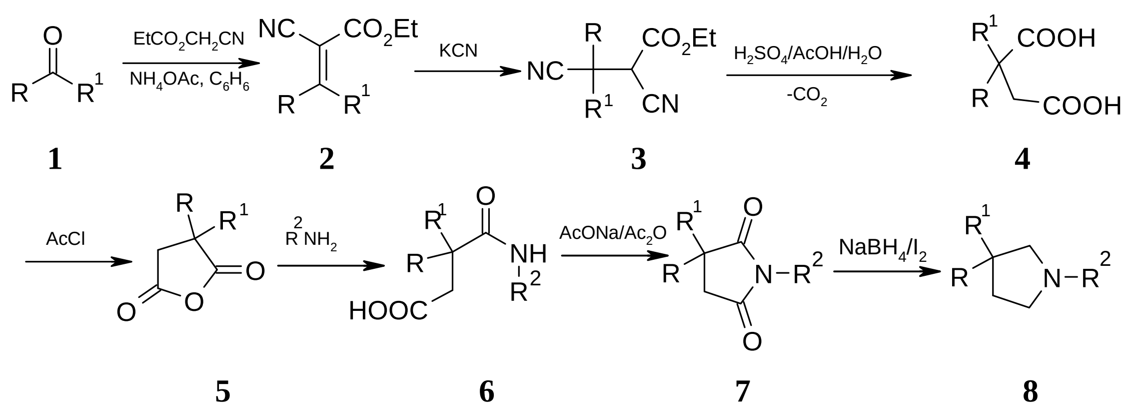
Introduction

Nitrogen-containing five membered rings are interesting synthetic targets as they are the basis of many natural and bioactive products.[1] Thus molecules such as 3,3-diaryloxindoles exhibit antibacterial, antiprotozoal and antiinflamatory activities.[2] Succinimides and hydantoins show antimuscarinic and anticonvulsant activity;[3] and the 3,3-diphenyl derivatives of these compounds are potent anticonvulsants.[4] In all the above-mentioned compounds, it is noteworthy to specify that the 3,3-diaryl derivatives are shown to be more biologically important. Pyrrolidines are another important class of bioactive molecules, which are extensively studied[5] and have been shown to inhibit glycosidases.[6] However, there is hardly any report in the literature on the general synthesis of 3,3-diarylpyrrolidines. The methods to 3,3-diarylpyrrolidines known in the literature include the preparation of 3,3-diphenylpyrrolidine from: a) diarylacetonitriles,[7] b) 4-phenoxy- or 4-bromo-2,2-diphenylbutylamine hydrochloride,[8] and c) 4-amino-3,3-diphenylbutan-1-ol hydrochloride.[9] Considering the importance of pyrrolidines and their derivatives[2, 10] as bioactive compounds, we have undertaken an investigation on the synthesis of their 3,3-diaryl derivatives from readily available benzophenones. We herein report the results of our studies.

Results and Discussion

The condensation of benzophenone **1a** with ethyl cyanoacetate under Knoevenagel conditions gave ethyl (α-cyano-β,β-diphenyl)acrylate **2a**[11] following the literature procedure, with a slight modification. We found that the use of a three-fold excess of ammonium acetate as a catalyst leads to the cyanoacrylate **2a** with a yield of 90% compared to the previously reported 41% yield. Under this improved condition, other diaryl ketones also reacted with ethyl cyanoacetate to yield the corresponding diaryl acrylates **2b–d** and **2h–i** in moderate to good yields. NMR spectra of all the diaryl acrylates (except **2a** and **2m**) indicated the presence of *E* and *Z* isomers in solution ($CDCl_3$). Since the double bond is fully substituted, it is difficult to determine the isomer ratio and to assign each signal to the respective isomer. Diarylacrylate **2m** derived from pyridyl phenyl ketone exists as a single isomer in $CDCl_3$ as seen from the ^{1}H NMR.

The subsequent conversion of **2a** into 2,2-diphenylsuccinic acid **4a** through the dicyanoester **3a** was achieved through hydrolysis and decarboxylation.[11] Diphenylsuccinic acid **4a** was cyclized to the anhydride **5a** by treatment with acetyl chloride. Subsequent reaction of **5a** with benzyl amine gave the succinimic acid **6a,** which was cyclized to succinimide **7a** in refluxing acetic anhydride (Scheme 1).[4] Other succinimides **7b–h** were also prepared following the above procedure. These were characterized by ^{1}H and ^{13}C NMR and were directly used for the reduction without further analytical characterization.



Scheme 1

2-Cyano-3,3-diarylacrylates, **2i** and **2m**, prepared from the corresponding benzophenones were treated with KCN and the intermediate dicyano derivatives obtained were subjected to acid hydrolysis. However, in these cases, we could not isolate the expected acids. Apart from our normal hydrolytic condition (H_2SO_4/H_2O/AcOH), attempts were made using HCl, but without any success. Other work up modifications like bringing the pH to neutral also did not help in isolating the succinic acids.

Succinimic acid **6j**, derived from 4-nitrobenzophenone and aniline, failed to ring close under the conditions tried. Apart from our normal procedure, we have tried heating **6j** neat to 150 ^{o}C, which eventually led to a complex mixture that could not be characterized. Whereas, anthrone and *o*-chloro benzophenone failed to undergo the condensation with ethyl cyanoacetate, *o,o*'-dichlorobenzophenone did react, surprisingly, but the isolated yield (<10%) was insufficient to proceed to subsequent steps.

Reduction of succinimides to the final pyrrolidine was carried out by BH_3.THF, which was generated *in situ* from $NaBH_4$ and I_2 following the method by Periasamy.[12] Thus, refluxing **7a** with an excess of BH_3-THF, generated from $NaBH_4$ and I_2, for 12h afforded 65% of 3,3-diphenylpyrrolidine **8a**. (Scheme 2) Other pyrrolidone diones **7b–h** also reacted similarly giving the corresponding pyrrolidines **8b–h** in reasonably good yields.

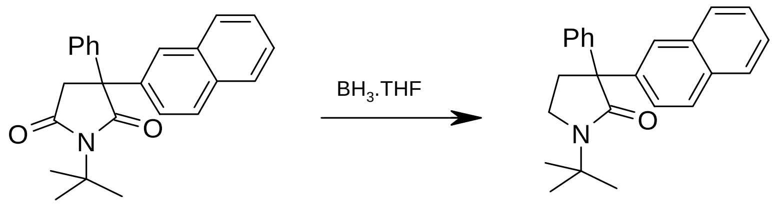
Table 1. 3,3-Diarylpyrrolidines Prepared and the Intermediates

Entry	R	R^1	R^2	Percentage isolated yield			
				2	4	7	8
a	Ph	Ph	$PhCH_2$	90	b	68	65
b	*p*-$F_3CC_6H_4$	Ph	$(Ph)_2CH$	57	b	70	72
c	*p*-$MeOC_6H_4$	Ph	CF_3CH_2	62	b	53	72
d	Ph	*p*-Br-C_6H_4	$PhCH_2$	87	b	67	59
e	Ph	Ph	cyclohexyl	90	b	62	67
f	Ph	Ph	*n*-butyl	90	b	63	66
g	Ph	Ph	Ph	90	b	72	70
h	2-Naphthyl	Ph	*t*-Bu	35	b	63	–
i	*p*-$Me_2NC_6H_4$	Ph	–	69	a	–	–
j	*p*-$O_2NC_6H_4$	Ph	Ph	42	b	a	–
k	*o*-ClC_6H_4	*o*-ClC_6H_4	–	10	–	–	–
l	*o*-ClC_6H_4	Ph	–	a	–	–	–
m	4-Pyridyl	Ph	–	30	a	–	–
n	Anthrone		–	a	–	–	–

(a) no reaction observed, (b) Crude product used in the next step without purification.

3-Phenyl-3-(2-naphthyl)-1-*tert*-butylpyrrolidine-2,5-dione **7h** was prepared starting from 2-naphthyl phenyl ketone in 61% yield. When the reduction of **7h** was tried using BH_3.THF, only the mono reduced product **9** was isolated in 89% yield (Scheme 2). The structure of **9** was confirmed from ^{1}H and ^{13}C NMR data. Use of a large excess (10 eq.) of the reagent and prolonged refluxing did not give the expected pyrrolidine. An attempted reduction using $LiAlH_4$

resulted in complete decomposition of the material. This could probably be due to two factors: 1) the steric hindrance by the bulky *t*-butyl group and (2) the reduced electrophilicity of the amide carbonyl by the electron releasing *t*-butyl group.



7h **9**

Scheme 2

In conclusion, we have elaborated a general synthesis of 3,3-diarylpyrrolidines from readily available benzophenones. Benzophenones with electron withdrawing as well as electron donating substituents could be used effectively for the preparation of respective succinic acids. However, under the specific acidic hydrolytic condition, the use of benzophenones containing basic nitrogens is not recommended. Generally, while any primary amine could be used for the preparation of pyrrolidones **7**, the final reduction restricts the use of amines like *t*-butylamine, which offers significant steric hindrance. Given the above-described caveats, this procedure has proven itself useful for the preparation of 3,3-diarylpyrrolidines.

Experimental Section

General Procedures. Melting points were determined using a Bristoline hot-stage microscope and are uncorrected. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra were recorded on a 300 MHz NMR spectrometer in chloroform-*d* solution. Column chromatography was performed on silica gel (230–400 mesh). Elemental analyses were performed on a Carlo Erba-1106 instrument.

General procedure for the preparation of 2-cyano-3,3-diarylacrylates (2). Diarylketone (50 mmol) was taken in benzene (50 mL) along with ethyl cyanoacetate (50 mmol). Ammonium acetate (150 mmol) was added in 2h intervals (50 mmol each time) and the mixture was refluxed for 24h with azeotropic water removal. The reaction mixture was cooled and washed with water (3x100 mL) followed by saturated solution of sodium chloride (100 mL). The organic layer was dried over sodium sulfate, concentrated and the crude mixture was purified by crystallization.

Ethyl (2-cyano-3,3-diphenyl)acrylate (2a).[1] Obtained as colorless crystals (benzene) (90%) mp 97.6–98.9 ^{o}C (Lit.[11] mp 95–97 ^{o}C) . ^{1}H NMR δ 1.14 (t, *J* = 7.2 Hz, 3H), 4.15 (q, *J* = 7.2 Hz, 2H), 7.15 (d, *J* = 8.1 Hz, 2H), 7.35–7.50 (m, 8H). ^{13}C NMR δ 13.7, 62.1, 104.0, 116.8, 128.2, 128.5, 129.2, 130.2, 130.3, 131.4, 138.2, 138.6, 162.6, 169.1.

Ethyl (2-cyano-3-(4-trifluoromethylphenyl)-3-phenyl)acrylate (2b). Obtained as a colorless liquid (57%, *E*/*Z* ~50:50).[1] ^{1}H NMR δ 1.05–1.09 (m, 6H), 4.06–4.13 (m, 4H), 7.06 (d, *J* = 7.8 Hz, 4H), 7.20-7.39 (m, 6H), 7.15 (d, J = 7.8 Hz, 4H), 7.56–7.62 (m, 4H). ^{13}C NMR δ 13.6, 62.4, 105.6, 116.1, 121.7, 125.1, 125.2, 125.3, 125.5, 125.6, 128.4, 128.7, 129.1, 129.3, 130.0, 130.4, 130.7, 131.7, 132.5, 133.0, 137.5, 137.7, 141.6, 161.9, 162.1, 167.0.

Ethyl (2-cyano-3-(4-methoxyphenyl)-3-phenyl)acrylate (2c). Obtained as a yellow liquid (62%, *E/Z* ~50:50) ^{1}H NMR δ 0.98 (t, J = 7.2 Hz, 3H), 1.19 (t, J = 7.2 Hz, 3H), 3.35 (s, 3H), 3.71 (s, 3H), 3.98 (q, J = 7.2 Hz, 2H), 4.12 (q, J = 7.2 Hz, 2H), 6.80 (d, J = 8.7 Hz, 2H), 7.04 (d, J = 8.7 Hz, 2H), 7.26–7.40 (m, 5H). ^{13}C NMR δ 13.4, 13.6, 24.4, 55.1, 55.2, 61.6, 62.5, 101.4, 113.1, 113.3, 113.6, 117.3, 127.8, 128.1, 129.1, 129.9, 130.0, 130.2, 130.3, 131.1, 131.6, 132.3, 138.7, 162.8, 168.7.

Ethyl (2-cyano-3-(4-bromophenyl)-3-phenyl)acrylate (2d). Obtained as yellow crystals (ethanol) (87%, *E/Z* ~50:50) mp 128–129 ^{o}C. ^{1}H NMR δ 1.11–1.22 (m, 6H), 4.11–4.22 (m, 4H), 7.01–7.04 (m, 2H), 7.13–7.30 (m, 6H), 7.35–7.57 (m, 11H), 7.30–7.13(m, 6H). ^{13}C NMR δ 13.6, 13.7, 62.2, 62.3, 104.2, 111.2, 116.5, 124.9, 126.2, 126.8, 128.3, 128.5, 129.2, 130.1, 130.5, 130.4, 131.4, 131.6, 131.8, 136.9, 137.3, 137.7, 137.9, 146.4, 162.2, 162.3.

Ethyl (2-cyano-3-naphthyl-3-phenyl)acrylate (2h). Obtained as yellow crystals (35%, *E/Z* ~50:50) mp 88.8–90.1 ^{o}C. ^{1}H NMR δ 1.07 (t, J = 7.2 Hz, 3H), 1.15 (t, J = 7.2 Hz, 3H), 4.15 (m, 4H), 7.18–7.24 (m, 2H), 7.36–7.64 (m, 14H), 7.77–7.96 (m, 8H). ^{13}C NMR δ 13.6, 62.1, 116.9, 117.0, 126.3, 126.4, 126.7, 126.8, 127.5, 127.6, 127.7, 127.8, 128.1, 128.2, 128.4, 128.5, 128.9, 129.3, 129.5, 130.3, 130.4, 131.1, 131.4, 132.4, 133.8, 134.3, 135.5, 135.9, 138.3, 138.6, 162.6, 169.1.

Ethyl (2-cyano-3-(4-N,N-dimethylaminophenyl)-3-phenyl)acrylate (2i). Obtained as pale brown crystals (ethanol) (69%) mp 128–129 ^{o}C. ^{1}H NMR δ 1.12 (t, J = 3.3 Hz, 3H), 4.10 (q, J = 3.3 Hz, 2H), 6.60–6.64 (m, 2H), 7.18–7.41 (m, 7H). ^{13}C NMR δ 13.7, 39.9, 61.4, 110.7, 118.9, 124.6, 127.8, 129.6, 130.8, 133.1, 139.7, 152.4, 152.7, 163.7.

Ethyl (2-cyano-3-(4-nitrophenyl)-3-phenyl)acrylate (2j). Obtained isomers as yellow crystals (ethanol, 42%, *E*/*Z* ~50%) mp 123.5–123.7 ^{o}C. ^{1}H NMR δ 1.22 (t, J = 7.2 Hz, 3H), 4.19 (q, 7.2 Hz, 2H), 7.13–7.58 (m, 7H), 8.24–8.30 (m, 2H). ^{13}C NMR δ 13.6, 13.7, 62.6, 105.7, 115.8, 115.9, 123.4, 123.7, 128.5, 128.8, 129.0, 129.7, 129.8, 130.9, 131.9, 137.0, 137.2, 144.2, 144.8, 148.4, 148.9, 161.0, 161.7.

Ethyl (2-cyano-3-(4-pyridyl)-3-phenyl)acrylate (2m). Obtained as yellow crystals (ethanol) (30%), mp 95–97 ^{o}C. ^{1}H NMR δ 1.20 (t, J = 7.2 Hz, 3H), 4.20 (q, J = 7.2 Hz, 2H), 7.32–7.52 (m, 6H), 8.44 (d, J = 1.2 Hz, 1H), 6.67 (dd, J = 1.5, 4.90 Hz, 1H). ^{13}C NMR δ 13.7, 62.5, 116.3, 123.0, 128.8, 130.0, 134.6, 136.5, 137.6, 149.0, 151.0, 162.0, 165.9.

General procedure for the preparation of 2,2-diaryl-pyrrolidine-2,5-diones (7)

a) Preparation of dicyanoesters, (3). A solution of ethyl (2-cyano-3,3-diaryl)acrylate (50 mmol) in 95% ethanol (50 mL) was added dropwise to a solution of KCN (100 mmol) in water (20 mL). The resulting mixture was heated and stirred at 90 ^{o}C for 2h. After cooling, conc. HCl was added until the pH of the solution becomes congo red on litmus. In most of the cases the dicyano derivative precipitated out (if not, it was extracted with ethyl acetate). The precipitate was washed with water (3x50 mL) and was used without any further purification for subsequent steps.

b) Preparation of diaryl succinic acids (4). Ethyl (α-cyano-β,β-diaryl)acrylate (50 mmol) was dissolved in acetic acid (30 mL) and refluxed with 80% H_2SO_4 (30 mL) for 12h. Cooled and poured into crushed ice, the resulting solid was filtered and washed with water (3x50 mL). This was directly taken in 20% KOH (50 mL) and refluxed for 72 h. The reaction mixture was cooled and acidified with con. HCl until the pH of the solution is congo red to precipitate the diaryl succinic acid (~40–50%), which was filtered, washed with water (3x100 mL) and dried in oven. No purification was attempted and the acid was used directly for subsequent reactions.

c) Preparation of succinic anhydrides (5). The succinic acid (20 mmol) was refluxed with acetyl chloride (10 mL) for 2h. The resulting mixture was concentrated under *vacuum* and the residue dissolved in ethyl acetate (50 mL). The organic layer was washed with water (3x50 mL), dried over sodium sulfate and concentrated to get the anhydride in quantitative yield (from the acid).

d) Preparation of 3,3-diaryl-pyrrolidine-2,5-diones (7). The anhydride (10 mmol) was treated with the corresponding primary amine (10 mmol) in refluxing acetone (20 mL) for 2h, concentrated, and the succinimic acid **6** was taken in acetic anhydride (20 mL) with sodium acetate (10 mmol). The mixture was heated at 70 ^{o}C for 2h. Acetic anhydride was removed under vacuum and the crude material was purified by column chromatography over silica gel using ethyl acetate/hexane (95:5). Yields of **7a–7h** refer to the yield from the corresponding diarysuccinic acids **4a–4h**.

3,3-Diphenyl-1-benzylpyrrolidine-2,5-dione (7a). Isolated as a colorless oil (68%) ^{1}H NMR δ 3.35 (s, 3H), 4.63 (s, 3H), 7.11–7.24 (m, 15H). ^{13}C NMR δ 42.7, 44.9, 56.9, 126.9, 127.0, 127.3, 127.5, 127.8, 128.4, 128.6, 128.7, 129.1, 135.5, 141.5, 174.6, 178.0.

3-Phenyl-3-(4-trifluoromethylphenyl)-1-benzhydrylpyrrolidine-2,5-dione (7b). Obtained as a colorless oil (70%) ^{1}H NMR δ 3.41 (d, J = 18.2 Hz, 1H), 3.53 (d, J = 18.3 Hz, 1H), 6.61 (s, 1H), 7.20–7.36 (m, 17H), 7.54 (d, J = 8.4 Hz, 2H). ^{13}C NMR δ 44.5, 56.7, 58.8, 125.5, 125.6, 125.7, 127.3, 127.8, 127.9, 128.0, 128.3, 128.4, 128.4, 129.0, 130.0, 137.0, 137.1, 140.7, 145.4, 173.8, 177.1.

3-Phenyl-3-(4-methoxyphenyl)-1-trifluoroethylpyrrolidine-2,5-dione (7c). Isolated as a colorless oil (53%) ^{1}H NMR δ 3.47 (d, J = 18.3 Hz, 1H), 3.55 (d, J = 18.3 Hz, 1H), 3.78 (s, 3H), 4.17 (d, J = 8.7, 1H), 4.23 (d, J = 8.4 Hz, 1H), 6.86 (d, J = 9 Hz, 2H), 7.18–7.37 (m, 7H). ^{13}C NMR δ 39.5, 39.9, 44.8, 114.2, 127.1, 127.7, 128.4, 128.9, 132.6, 141.4, 159.0, 173.4, 177.2.

3-Phenyl-3-(4-bromophenyl)-1-benzylpyrrolidine-2,5-dione (7d). Isolated as a pale yellow oil (67%). ^{1}H NMR δ 3.35 (d, J = 18.3 Hz, 1H), 3.43 (d, J = 18.3 Hz, 1H), 4.71 (s, 2H), 7.10 (d, J = 8.7 Hz, 2H), 7.16–7.19 (m, 2H), 7.24–7.31 (m, 8H), 7.40 (d, J = 8.7 Hz, 2H). ^{13}C NMR δ 42.7, 44.6, 56.4, 121.8, 127.1, 127.7, 128.0, 128.4, 128.6, 128.8, 129.1, 131.7, 135.3, 140.5, 141.1, 174.1, 177.5.

3,3-Diphenyl-1-cyclohexylpyrrolidine-2,5-dione (7e). Isolated as a pale yellow oil (62%). ^{1}H NMR δ 1.09−1.29 (m, 3H), 1.49−1.58 (m, 3H), 1.70−1.79 (m, 2H), 2.03−2.18 (m, 2H), 3.30 (s, 2H), 3.96 (tt, *J* = 4.2, 12 Hz, 1H), 7.15−7.23 (m, 10H). ^{13}C NMR δ 24.9, 25.7, 28.6, 44.9, 52.0, 56.3, 127.0, 127.3, 127.4, 128.7, 129.0, 141.9, 175.0, 178.3.

3,3-Diphenyl-1-butylpyrrolidine-2,5-dione (7f). Isolated as a colorless oil (63%). ^{1}H NMR δ 0.97 (t, *J* = 7.2 Hz, 3H), 1.35 (sextet, *J* = 7.2 Hz, 2H), 1.64 (quintet, *J* = 7.2 Hz, 2H), 3.50 (s, 2H), 3.65 (t, *J* = 7.5 Hz, 2H), 7.31−7.43 (m, 10H). ^{13}C NMR δ 13.5, 19.9, 29.5, 38.9, 45.0, 56.8, 127.3, 127.5, 128.7, 141.7, 175.0, 178.3.

3,3-Diphenyl-1-phenylpyrrolidine-2,5-dione (7g). Isolated as a colorless oil (72%). ^{1}H NMR δ 3.63 (s, 2H), 7.27−7.48 (m, 15H). ^{13}C NMR δ 45.0, 57.0, 126.5, 127.0, 127.4, 127.8, 128.7, 128.9, 129.1, 131.8, 141.5, 174.0, 177.3.

3-Phenyl-3-naphthyl-1-*tert*butylpyrrolidine-2,5-dione (7h). Isolated as a colorless oil (63%). ^{1}H NMR δ 1.62 (s, 9H), 3.39 (d, *J* = 18.3 Hz, 1H), 3.46 (d, *J* = 18.3 Hz, 1H), 7.27−7.33 (m, 6H), 7.46−7.49 (m, 2H), 7.74−7.81 (m, 4H). ^{13}C NMR δ 28.4, 45.1, 56.5, 58.9, 125.7, 125.9, 126.4, 127.4, 127.5, 128.2, 128.6, 128.7, 132.3, 132.9, 139.2, 142.1, 175.8, 179.2.

3,3-Diaryl-1-alkyl/arylpyrrolidines, (8a–h). Sodium borohydride (1.6g, 44 mmol) was taken in THF (50 mL) and cooled to 0 °C. I_2 (5.6g, 21mmol) in THF (25 mL) was added dropwise over 1h. To the $BH_3 \cdot THF$ thus prepared, 3,3-diarylpyrrolidine-2,5-dione (3g, 8.8 mmol) was added in THF (15 mL) and the mixture was refluxed overnight. The suspension was cooled in ice and 3N HCl (10 mL) was slowly added to destroy the excess hydride. The solution was made alkaline with 3N NaOH (25 mL) and extracted with ether (2x100 mL). The organic layer was washed with water (50 mL), dried over sodium sulfate and concentrated. The residue was dissolved in anhydrous Et_2O (25 mL) and $BF_3 \cdot Et_2O$ (10 mmol) was added at 0 °C. The mixture was stirred for 10 min followed by the addition of 3N NaOH (50 mL) and the amine was extracted into ether (3x100 mL). The combined organic extracts were washed with water (100 mL), brine (50 mL) and dried (Na_2SO_4). Evaporation of the solvent afforded the crude pyrrolidine, which was purified by column chromatography over silica gel using EtOAc/hexane (97:3).

3,3-Diphenyl-1-benzylpyrrolidine (8a). Obtained as white crystals (hexane/EtOAc) (65%) mp 133.6–135.1 °C. ^{1}H NMR δ 2.81–2.87 (m, 2H), 3.22–3.41 (m, 2H), 3.86 (dd, 2H, *J* = 12.6, 12.6 Hz), 4.05 (dd, *J* = 12.6, 12.6 Hz, 2H), 7.11–7.31 (m, 15H). ^{13}C NMR δ 36.5, 55.3, 60.0, 67.2, 70.1, 126.2, 126.4, 126.5, 127.8, 12.3, 128.7, 132.2, 132.6, 145.2, 146.6. Anal. Calcd For $C_{23}H_{23}N$: C, 88.13; H, 7.40; N, 4.47. Found: C, 87.86; H, 7.18; N, 4.17.

3-Phenyl-3-(4-trifluoromethylphenyl)-1-benzhydrylpyrrolidine (8b). Obtained as a white crystalline solid (from methanol) (72%) mp 115.7–116.0 °C. ^{1}H NMR δ 2.42–2.65 (m, 3H), 2.71–2.79 (m, 1H), 2.96 (d, *J* = 9.6 Hz, 1H), 3.09 (d, *J* = 9.6 Hz, 1H), 4.28 (s, 1H), 7.07–7.18 (m, 11H), 7.29–7.31 (m, 6H), 7.43 (d, *J* = 7.8 Hz, 2H). ^{13}C NMR δ 38.3, 52.1, 54.4, 64.7, 75.9, 124.9, 124.9, 126.2, 127.0, 127.0, 127.2, 127.3, 127.7, 128.2, 128.5, 128.5, 143.9, 143.9, 147.6, 153.0. Anal. Calcd For $C_{30}H_{29}F_3N$: C, 78.75; H, 5.73; N, 3.06. Found: C, 78.66; H, 6.25; N, 3.06.

3-Phenyl-3-(4-methoxyphenyl)-1-trifluoroethylpyrrolidine (8c). Obtained as white crystals (CH_2Cl_2) (72%) mp 64.1–64.8 ^oC. ^1H NMR δ 2.49 (t, J = 7.2 Hz, 2H), 2.99 (t, J = 7.0 Hz, 2H), 3.16 (dd, 2H, J = 9.6, 19.2 Hz), 3.42 (s, 2H), 3.74 (s, 3H), 6.79 (d, 2H, J = 8.7 Hz), 7.16 (d, 2H, J = 8.4 Hz), 7.22–7.28 (m, 5H). ^{13}C NMR δ 38.5, 53.5, 54.0, 55.1, 55.1, 66.0, 113.4, 123.6, 126.0, 127.0, 127.3, 128.1, 128.1, 139.8, 147.8, 157.7. Anal. Calcd For $C_{19}H_{23}F_3NO$: C, 68.03; H, 6.01; N, 4.18. Found: C, 67.87; H, 6.14; N, 4.15.

3-Phenyl-3-(4-bromophenyl)-1-benzylpyrrolidine (8d). Obtained as a colorless liquid (59%). ^1H NMR δ 2.29–2.40 (m, 2H), 2.60–2.67 (m, 1H), 2.72–2.79 (m, 1H), 2.95 (d, J = 9 Hz, 1H), 3.06 (d, J = 9 Hz, 1H), 6.97–7.22 (m, 14H). ^{13}C NMR δ 38.6, 52.9, 54.1, 60.3, 65.7, 119.5, 125.9, 126.8, 127.1, 128.1, 128.2, 128.3, 129.1, 130.9, 139.4, 148.1, 148.2. Anal. Calcd For $C_{23}H_{22}BrN$: C, 70.41; H, 5.65; N, 3.57. Found: C, 69.94; H, 5.750; N, 3.76.

3,3-Diphenyl-1-cyclohexylpyrrolidine (8e). Obtained as a colorless oil (67%). ^1H NMR δ 0.91–1.08 (m, 2H), 1.13-1.25 (m, 1H), 1.47-1.51 (m, 1H), 1.60-1.84 (m, 6H), 1.93-1.98(m, 1H), 2.18-2.26 (m, 1H), 2.74–3.03 (m, 2H), 3.23–3.32 (m, 1H), 3.85 (d, J = 12.3 Hz, 1H), 4.05 (d, J = 12.9 Hz, 1H), 7.02–7.28 (m, 10H). ^{13}C NMR δ 25.5, 25.8, 25.9, 28.5, 29.7, 54.7, 60.7, 70.6, 72.7, 126.2, 126.5, 126.6, 127.2, 127.9, 128.4, 128.8, 145.7, 146.8. Anal. Calcd For $C_{22}H_{27}N$: N, 4.59. Found: N, 4.43.

3,3-Diphenyl-1-butylpyrrolidine (8f). Obtained as a colorless oil (66%). ^1H NMR δ 0.75 (t, J = 7.2 Hz, 3H), 0.99–1.13 (m, 2H), 1.55–1.70 (m, 2H), 2.54 (t, J = 8.4 Hz, 2H), 2.72–2.95 (m, 3H), 3.34–3.41 (m, 1H), 3.86 (d, J = 12.9 Hz, 1H), 3.92 (d, J = 12.9 Hz, 1H), 7.03–7.29 (m, 10H). ^{13}C NMR δ 13.6. 20.3, 27.3, 36.2, 55.2, 61.6, 65.0, 70.9, 125.6, 126.3, 126.3, 126.4, 126.7, 127.1, 128.0, 128.4, 128.8, 144.9, 146.4. Anal. Calcd For $C_{20}H_{25}N$: N, 5.01. Found: N, 4.87.

3,3-Diphenyl-1-phenylpyrrolidine (8g). Obtained as white crystals (from CH_3OH) (70%) mp 111.1–112.0 ^oC. ^1H NMR δ 2.47 (t, J = 6.3 Hz, 2H), 3.22 (t, J = 6.3 Hz, 2H), 3.80 (s, 2H), 6.51 (d, J = 8.1 Hz, 2H), 6.60 (t, J = 7.2 Hz, 1H), 7.19–7.04 (m, 12H). ^{13}C NMR δ 37.2, 45.9, 53.8, 57.8, 111.3, 115.6, 126.3, 126.9, 128.3, 129.2, 146.4, 146.9. Anal. Calcd For $C_{22}H_{21}N$: C, 88.25; H, 7.07; N, 4.68. Found: C, 87.96; H, 7.39; N, 4.69.

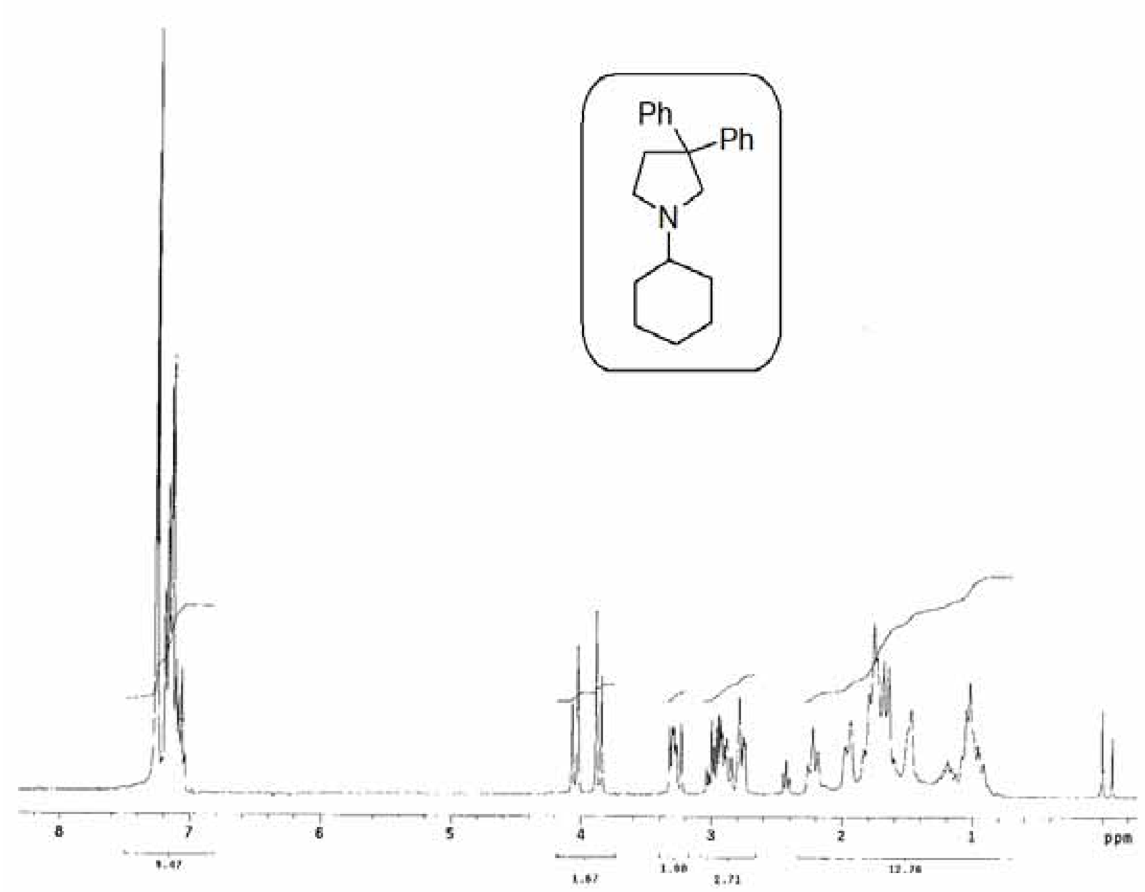


Figure 1. ^{1}H NMR of **8e**.

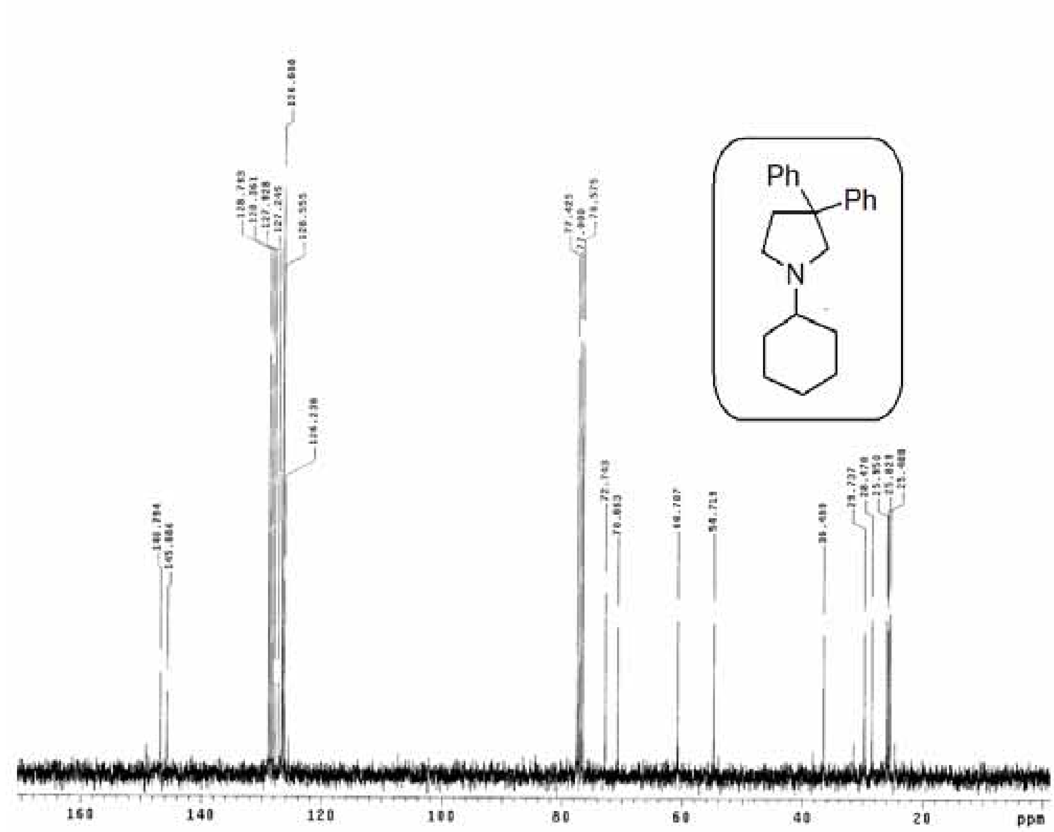


Figure 2. ^{13}C NMR of **8e**.

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