Synthesis of Spiropyrrrolidines via 1, 3 Anionic Cycloaddition

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ABSTRACT

In this work, series of substituted α, β-unsaturated carbonyl compounds (A1-8) had been prepared using Claisen-Schmidt condensation. Also, series of substituted Schiff bases (N-arylidene-4-picolyamine) (B1-6) were prepared by the condensation of 4-picolyamine with various aromatic aldehydes.

The reaction of the above mentioned materials (A+B) afforded the desired products [Spiropyrrrolidines (S1-15)]. The reaction occurred through the formation of azallyl anion which acted as a nucleophile that has the ability to attack the exocyclic double bond of chalcones through the 1,3-anionic cycloaddition mechanism to form the product.

The structure for all synthesized compounds (chalcones, Schiff bases, pyrrolidines) had been confirmed by the spectral data obtained by (UV, IR, 1H-NMR) as well as the determination of physical properties.

Keywords: spiropyrrrolidine, 1,3-anionic cycloaddition.
INTRODUCTION

Spiro compounds having cyclic structure fused at a central carbon are of recent interest due to their interesting structural implications on biological system (Jayashankaran et al., 2005). The asymmetric characteristics of the molecule due to the chiral spiro carbon is one of the important criteria of the biological activities (Ghandi et al., 2009).

Spiro compounds represent an important class of naturally occurring substances characterized by highly pronounced biological properties (Raj and Raghnathan, 2005).

The most developed route for the synthesis of these compounds depends on the cycloaddition to an exocyclic bond. (Poornachandran and Raghunathan, 2010) (Fisera et al., 1994).

The 1,3-Anionic cycloaddition provides a way for the synthesis of many spiroheterocycles through the cycloaddition reaction of nonstabilised azomethine ylides with the Chalcones (Waldmann, 1995). Also highly substituted pyrrolidines have attracted much interest as they contribute the central structural element of many alkaloids and pharmacological active compounds (Luibineau et al., 1995) (Deshong and Leginus, 1983) (Manikandan et al., 2001) (Subramaniyan and Raghunathan, 2001) on the synthesis of novel spiropyrrrolidinyl derivatives we have examined the 1,3-Anionic cycloaddition reaction of E-2-arylidene-1-tetralones with the azomethine ylide generated by treatment the Schiff bases with sodium hydroxide.

EXPERIMENTAL

Melting points were determined by Electrothermal 9300 Engineering LTD Apparatus (the melting points are uncorrected), the boiling points were determined by inverted capillary in a thiele tube using paraffin colorless oil (Shriner et al., 1964). A shimadzu UV-Visible spectrophotometer UV-1650/PC connected to a computer with pentium 4 processor Quartz cells (1×1×3cm) were used to for UV measurements. Fourier –Transform Infrared (FT-IR) spectrophotometer, Tensor Co. Brucker, 2003 Germany, was used to run IR spectra. The nuclear magnetic resonance (1H-NMR) spectra were performed using (300MH₂) Brucker, tetramethyl silane (TMS) as an internal standard, and CDCl₃ as a solvent in Al Al-Bayt University, Jordan.

Preparation of chalcones (arylidene-cycloalkanone and derivatives (A1-8)

A solution of 2.2g of sodium hydroxide in 20 ml of water and 12.25 ml of ethanol were placed in a 50 ml round –bottomed flask provided with a mechanical stirrer. The flask is immersed in a bath of crushed ice. A (0.0215) mol of freshly distilled cycloalkanone was added. Stirring is then started and 0.043 mole of pure aldehyde was added. The temperature of the mixture is kept at about 25 °C (the limits are 15-30 °C) with vigorous stirring until
turns to a very thick consistency. The stirrer was stopped and the reaction mixture was left in an ice crushed bath or refrigerator overnight. The product was filtered using Buchner funnel or a sintered glass funnel, washed with cold water until the washings were neutral to litmus, and then with 20 ml of ice–cold ethanol. After drying in air, the crude chalcone was recrystallized from ethanol. The product was always handled with care as it caused a skin irritation (Vogel, 1989). The physical properties of synthesized compounds and spectral data illustrated in Tables 1 and 2. The melting points, infrared and ultraviolet data, were in a good agreement with the reported values. (Parikh, 1974).

**Preparation of Schiff bases** [N-Arylidene 4-picolyamine] (B1-B6)

In a 100 ml beaker, 0.01 mole of (4-picolyamine) was heated with 0.01 mole of substituted benzaldehyde and 10 ml of n-butanol for 10 minutes at (100 ºC). The reaction mixture was then cooled and filtered. The precipitate was dried and recrystallized from ethanol (the liquid products were purified by distillation). The physical properties and spectral data of Schiff bases (B1-6) illustrated in Table 3 and 4 respectively. The Infrared and ultraviolet data were in a good agreement with the reported values. (Bin et al., 2009).

Table 1: Names and some physical properties of substituted chalcones A (1-8).

| Compd. No. | Y       | Ar           | Reaction time /h | Color | m.p., °C | Yield % |
|------------|---------|--------------|------------------|-------|----------|---------|
| A1         | H       | 2-furfuryl   | 3                | Yellow| 71-73    | 75      |
| A2         | 6-Meo   | phenyl       | 3                | Yellow| 95-97    | 65      |
| A3         | 6-Meo   | 4-anisyl     | 4                | Yellow| 141-143  | 61      |
| A4         | 6-OCH₃  | p-nitro phenyl | 3             | Yellow| 98-101   | 58      |
| A5         | 6-OCH₃  | p-chloro phenyl | 4             | White | 91-93    | 60      |
| A6         | H       | phenyl       | 4,5              | Yellow| 105-107  | 80      |
| A7         | H       | 4-anisyl     | 3                | Yellow| 109-111  | 60      |
| A8         | H       | p-chloro phenyl | 3               | White | 72-75    | 83      |

Table 2: Spectral data of Chalcones (A1-8).

| Compd. No. | IR (KBr), ν cm⁻¹ | U.V. (CHCl₃) λₘₐₓ(nm) |
|------------|------------------|------------------------|
|            | C=O C=C C ---C C-O-C N _____ O | λₘₐₓ(nm)  |
| A1         | 1664 1620 1591 1233 | 352                   |
| A2         | 1604 1660 1586 ----- | 324                   |
| A3         | 1663 1593 1508 ----- | 338                   |
| A4         | 1681 1639 1506 ----- | 1333 Sym 1549A sym 390 |
| A5         | 1656 1606 1590 1226 | 304                   |
| A6         | 1660 1624 1589 ----- | 310                   |
| A7         | 1666 1600 1508 1222 | 342                   |
| A8         | 1662 1604 1514 ----- | 386                   |
Table 3: Physical properties of the Schiff bases (B1-6).

| Compd. No. | X            | Color & phase    | m.p. or b.P /°C | Yield % |
|------------|--------------|------------------|-----------------|---------|
| B1         | H            | Yellow precipitate| 70-72           | 76      |
| B2         | 4-OCH₃       | Orange liquid    | 205-208         | 62      |
| B3         | 4-NO₂        | Brown liquid     | 130-132         | 73      |
| B4         | 4-Cl         | Pale yellow precipitate | 62-64       | 69      |
| B5         | 3,4-di4-OCH₃ | Orange liquid    | 143-146         | 60      |
| B6         | 4-CH₃        | White precipitate| 40-43           | 75      |

Table 4: Spectral data of the Schiff bases (B1-6).

| Compd. No. | IR(KBr), v(cm⁻¹) | U.V λ_max/nm |
|------------|------------------|--------------|
|             | C=N | C-O-C | Asym N––O | Sym N––O | C-Cl |                  |
| B1         | 1594 | ----- | ----- | ----- | ----- | 280 |
| B2         | 1606 | 1251  | ----- | ----- | ----- | 288 |
| B3         | 1600 | ----- | 1519  | 1342  | ----- | 285 |
| B4         | 1633 | ----- | ----- | ----- | 752   | 292 |
| B5         | 1602 | 1251  | ----- | ----- | ----- | 284 |
| B6         | 1606 | ----- | ----- | ----- | ----- | 282 |

Condensation of chalcones with Schiff bases

A mixture of Schiff bases (0.01 mole) and chalcone (0.01 mole) was magnetically stirred in the presence of (3 ml) of (0.01mole) alcoholic sodium hydroxide solution (Popandova et al., 1989). The mixture was allowed to stand overnight, water (100 ml) was then added to the reaction mixture. The separated precipitate was washed with water until the filtrate became clear and neutral. The solid product was then dried and recrystallized from methanol-ethyl acetate (8:2). The physical properties and the spectral data were listed in Table (5 and 6) respectively.
Table 5: Physical properties of Spiropyrrolidines (S1-15)

| Compd. No. | Ar     | X       | Color              | m.p/ºC    | Yield % |
|------------|--------|---------|--------------------|-----------|---------|
| S1         | 2-furfuryl | H      | Pale orange        | 167-171   | 51      |
| S2         | 2-furfuryl | H      | Pale yellow        | 15-139    | 45      |
| S3         | 2-furfuryl | 4-OCH₃ | Pale red           | 110-115   | 56      |
| S4         | Phenyl   | H      | Brown              | 198-204   | 50      |
| S5         | Phenyl   | 4-Cl   | Yellowish brown    | 149-153   | 56      |
| S6         | Phenyl   | 4-OCH₃ | Brown              | 132-136   | 58      |
| S7         | 4-anisyl | H      | Pale brown         | 121-125   | 38      |
| S8         | Phenyl   | 4-NO₂  | Dark brown         | 220-225   | 41      |
| S9         | 4-Chloro phenyl | 4-OCH₃ | Dark orange       | 155-158   | 43      |
| S10        | 4-Chloro phenyl | H    | Pale brown        | 141-144   | 45      |
| S11        | 4-anisyl | 4-Cl   | Dark brown         | 110-113   | 36      |
| S12        | 4-anisyl | 4-NO₂  | Pale red           | 135-139   | 45      |
| S13        | 4-Cl     | 4-NO₂  | Dark brown         | 160-164   | 57      |
| S14        | Phenyl   | 3,4-diOCH₃ | Pale yellow | 176-180   | 47      |
| S15        | Phenyl   | 4-CH₃  | Pale brown         | 184-187   | 50      |

RESULTS AND DISCUSSION

α-β Unsaturated carbonyl compounds are very attractive starting materials. They are considered as precursors to build other important compounds (March, 1992) such as compounds (Katritzky, 1997) through their reaction with other different compounds.

In this paper, some chalcones ATs and FTs are synthesized by condensation reaction of α-β unsaturated ketones such as:

Substituted-2(arylidene)-1-tetralone(AT)

Substituted-2(α-furfurylidene)-1-tetralone(FT)

The chalcones (ATs and FTs) (A1-8) were then condensed with different Schiff bases (B1-6) of the formula

N-Arylidene-4-picoly amine
To afford the corresponding substituted spiropyrrolidines (S1-15). The prepared unsaturated ketones and Schiff bases were confirmed by spectroscopic means. The physical properties and the spectral data were in quite good agreement with the published values (Parich, 1974), Table (6 and 7).

The Schemes (1 a and b) show the synthetic route of compounds A, B and S

Scheme 1a: Reaction of 2-furfurylidene-1-tetralone (chalones FTs) with Schiff bases

Scheme 1b: The reaction of 2-arylidene-1-tetralone with Schiff bases (B1-6)(A6-8)
The structures of the synthesized compounds (or spiro pyrrolidens) have been confirmed by the spectral methods.

The $^1$H-NMR spectrum of compound A6 is taken as a representative sample for the discussion which showed a triplet signal appeared at $\delta$ 2.0 ppm for two protons attached to (C1), another triplet signal appeared at $\delta$ 2.2 ppm for two protons attached to (C2), a singlet significant band for the proton attached to (C3) showed at $\delta$ 6.3 ppm, while the aromatic protons showed a multiple bands at the range $\delta$ (6.4-7.2) ppm (Table 6).

The (FT-IR) spectra of compounds (A1-8) bands showed an absorption in the range of (1721-1656) cm$^{-1}$ which is related to the stretching vibration of the carbonyl group, while the absorption bands in the range of (1660-1593) cm$^{-1}$ related to the stretching vibration of (C=C)(double bond) (Table2).
### Table 6: $^1$H-NMR spectra data of 2-Arylidene-1-tetralones

![Chemical Structure](image)

| Compd. No. | $^1$H-NMR(CDCl$_3$) δppm |
|------------|---------------------------|
|            | C$_1$-H | C$_2$-H | C$_3$-H | (OCH$_3$) | Ar-H |
| A1         | 2.0 (t) (2H) | 2.4 (t) (2H) | 6.3 (s) (1H) | ----- | 5.5-7.1 (m) (7H) |
| A6         | 2.0 (t) (2H) | 2.2 (t) (2H) | 6.3 (s) (1H) | ----- | 6.4-7.2 (m) (9H) |
| A7         | 2.0 (t) (2H) | 2.1 (t) (2H) | 6.0 (s) (1H) | 2.9 (s) (1H) | 6.3-7.1 (m) (8H) |
| A8         | 2.0 (t) (2H) | 2.2 (t) (2H) | 6.3 (s) (1H) | ----- | 6.3-7.2 (m) (8H) |

The $^1$H-NMR spectra of compound B1 is taken as a representative model for the discussion, which showed a singlet signal at δ 4.6 ppm related to methylene protons (CH$_2$) (C$_1$), another singlet signal at δ 7.2 ppm related to (CH) benzyl proton (=CH), (Table 7).

The (FT-IR) showed absorption bands in the range of (1606-1594) cm$^{-1}$ related to the stretching vibration of the (C=N) bond, (Table 4).

### Table 7: $^1$H-NMR of (some Schiff bases)

| Compd. NO. | $^1$H-NMR(CDCl$_3$) δppm |
|------------|---------------------------|
|            | methylene group (C$_1$-H) | (C$_2$-H) | others | Ar-H |
| B1         | 4.6 (s) (2H) | 7.2 (s) (1H) | ----- | 7.3-8.4 (m) (9H) |
| B2         | 3.7 (s) (2H) | 7.4 (s) (1H) | O-CH$_3$ 4.8 (s) (3H) | 7.5-8.8 (m) (8H) |
| B3         | 4.7 (s) (2H) | 7.5 (s) (1H) | ----- | 7.7-8.4 (m) (8H) |
| B6         | 4.6 (s) (2H) | 7.2 (s) (1H) | CH$_3$ 2.3 (s) (3H) | 7.7-8.4 (m) (8H) |

The Schiff base[N-Arylidene-4-picolyamine] (B1-6) were reacted with chalcones (FTs) 2- (2-furfurylidene-1-tetralone) (A1) under basic conditions to afford the corresponding substituted spiro- pyrrolidenes (S1-3), also Schiff base [N-Benzylidene-4-picolyamine] (B1) and its substituted analogue [N- Arylidene-4-picolyamine] (B2-6) were reacted with 2-benzylidine-1-tetralone (A6) and substituted 2-benzylidine-1-tetralone (A7, A8) under basic conditions to afford the corresponding substituted spiro- pyrrolidenes (S4-15).
The $^1$H-NMR spectrum of compound S1 and S4 are taken as representative models for the discussion.

The Spectrum of compound (S1) showed significant bands at the following chemical shifts:

A broad singlet signal at $\delta$ 2.5 ppm related to N-H proton, a singlet signal at $\delta$ 4.7 ppm to C$_2$, protons a doublet signal at $\delta$ 3.8 ppm due to C$_4$ protons, another doublet signal at $\delta$ 4.4 ppm due to of C$_5$ protons.

The aromatic protons (16H) resonate at the range of $\delta$ (6.2-8.1) ppm.

Spectrum of compound (S4) showed significant bands at the following chemical shifts:

A singlet signal at $\delta$ 2.3 ppm related to N-H proton, a singlet signal at $\delta$ 4.6 ppm related to C$_2$ protons , a doublet signal at $\delta$ 3.6 ppm due C$_4$ protons, and a doublet signal at $\delta$ 4.4 ppm due to of C$_5$ protons.

The aromatic protons (18H) resonate within the range of $\delta$ (7.0-8.0) ppm.

The $^1$H-NMR spectra for the other synthesized pyrrolidines are listed in Table (8).

The (FT-IR) spectral (Table 9) exhibit the main absorption bands for compounds (S1-15).

A bands at the range of (1654-1715) cm$^{-1}$, related to the stretching vibration of the carbonyl group. a band at 3393-3446cm$^{-1}$ corresponds to the stretching vibration of N-H. In the case of the compounds (S1, S2, S3, S6, S7, S11, S12, S14), the absorption bands appeared at the range of (1218-1292) cm$^{-1}$ related to the bonds of C-O-C, but in case of compounds (S3, S8, S12, S13) the nitro groups, showed absorption bands in the range of (1313-1560) cm$^{-1}$ due to the symmetric and asymmetric stretching $\tilde{N}=\tilde{O}$ respectively (Table 9). Also in the case of compounds (S5, S9, S10, S13), the band at (741-772) cm$^{-1}$ is related to the C-Cl stretching vibration.

The UV spectra (Field et al., 2007) (Mistry, 2009) (Table 9) show a maximum absorption of compounds S(1-15) in the range of (266-352)nm, which indicates blue shift with respect to $\lambda_{max}$ of the Chalcones (ATs and FTs).
Table 8: $^1$H-NMR spectral data of some spiropyrrolidine compounds

| Compd. No. | C$_6$H | C$_7$H | C$_4$H | OCH$_3$ | C$_5$H | C$_2$H | Ar-H | N-H |
|------------|--------|--------|--------|---------|--------|--------|-------|-----|
| S1         | 2.3(t) (2H) | 2.4(t) 2H) | 3.8(d) 1H | ---- | 4.4(d) 1H | 4.7(S) 1H | 6.2-8.1(m) | 16H | 8.5(S) 1H |
| S4         | 2.2(t) (2H) | 2.3 (t) (2H) | 3.6(d) 1H | ---- | 4.4(d) 1H | 4.6(S) 1H | 7.0-8.0(m) | 18H | 8.4(S) 1H |
| S5         | 2.3(t) (2H) | 2.4(t) (2H) | 3.7(d) 1H | ---- | 4.3(d) 1H | 4.6(S) 1H | 7.0-7.9(m) | 17H | 8.4(S) 1H |
| S7         | 2.3(t) (2H) | 2.4(t) (2H) | 3.6(d) 1H | 3.5(S) 3H | 4.2(d) 1H | 4.7(S) 1H | 6.9-7.8(m) | 17H | 8.4(S) 1H |
| S8         | 2.1(t) (2H) | 2.3(t) (2H) | 3.7(d) 1H | ---- | 4.7(d) 1H | 4.8(S) 1H | 7.0-7.8(m) | 17H | 8.6(S) 1H |
| S10        | 2.3(t) (2H) | 2.4t (2H) | 3.6(d) 1H | ---- | 4.4(d) 1H | 4.7(S) 1H | 7.0-7.6(m) | 17H | 8.3(S) 1H |
| S11        | 2.1(t) (2H) | 2.3(t) (2H) | 3.7(d) 1H | 3.9(S) 3H | 4.6(d) 1H | 4.8(S) 1H | 6.7-8.0(m) | 16H | 8.6(S) 1H |
| S12        | 2.3(t) (2H) | 2.4(t) (2H) | 3.4(d) 1H | 3.7(S) 3H | 3.9(d) 1H | 4.7(S) 1H | 6.7-8.1(m) | 16H | 8.4(S) 1H |
| S13        | 2.1(t) (2H) | 2.4(t) (2H) | 3.7(d) 1H | ---- | 4.3(d) 1H | 4.6(S) 1H | 7.0-8.0(m) | 16H | 8.4(S) 1H |
| S14        | 2.1(t) (2H) | 2.2(t) (2H) | 3.7(d) 1H | 3.89(S) 3H | 4.5(d) 1H | 4.6(S) 1H | 7.0-8.1(m) | 16H | 8.2(S) 1H |
| S15        | 2.2(t) (2H) | 2.3(t) (2H) | 3.6(d) 1H | CH$_3$ 2.6(S) 3H | 4.5(d) 1H | 4.7(S) 1H | 7.0-8.1(m) | 17H | 8.2(S) 1H |
Table 9: U.V and IR Spectral data of pyrrolidines (S1-15).

| Compd. No. | C=O | C=C | N-H | Others | U.V λ_max (nm) |
|------------|-----|-----|-----|--------|---------------|
| S1         | 1681| 1530| 3415| C-O-C 1232 | 270,328       |
| S2         | 1654| 1592| 3446| C-O-C 1250 | 340           |
| S3         | 1652| 1594| 3393| C-O-C 1233, N=O sym 1313 asym 1560 | 352           |
| S4         | 1715| 1597| 3432| ----- | 282           |
| S5         | 1656| 1598| 3412| C-Cl 741  | 270           |
| S6         | 1661| 1598| 3414| C-O-C 1218 | 292           |
| S7         | 1657| 1598| 3413| C-O-C 1231 | 270           |
| S8         | 1666| 1579| 3418| N=O sym 1345 asym 1518 | 282           |
| S9         | 1650| 1576| 3438| C-Cl 772  | 266           |
| S10        | 1681| 1601| 3452| C-Cl 747  | 268           |
| S11        | 1666| 1590| 3430| C-O-C 1230 | 274           |
| S12        | 1665| 1592| 3439| C-O-C 1219, N=O sym 1324 asym 1543 | 270,318       |
| S13        | 1665| 1597| 3480| N=O sym 1334 asym 1494 C-Cl 752 | 286           |
| S14        | 1686| 1628| 3415| C-O-C 1258 | 292,350       |
| S15        | 1697| 1598| 3427| ----- | 268,402       |

REFERENCES

Bin, L.; Xi-Qun, L.; Wen-Jieomed, Z.; Me-Yun, Z. (2009). Synthesis of ionic liquid-supported Schiff bases, *ARKIVOC*, Xi, 165-171.
Deshong, P.; Leginus, M. (1983). Stereospecific synthesis of racemic daunosamine. Diastereofacial selectivity in a nitro compound cycloaddition. *J. Am. Chem. Soc.*, 105, 1686.
Fisera, L.; Sauter, F.; Frolich, J.; Feng, Y.; Ertl, P.; Mereiter, K., (1994). Synthesis of spiro-substituted 1,3-oxazines by a new sequence leading to spiroheterocycles. *Monatsh. Chem.*, 125, 909.
Field, L.D.; Sternhen, S.; Kalman, R. (2007). "Organic Structures from Spectra", 4th edn. John-Wiley and Sons. New York, pp.30-34.
Ghandi, M.; Yari, A.; Jamal, S.; Taheri, A. (2009). Synthesis of novel spiropyrrolidine through 1,3-dipolar cycloaddition, *Tetrahedron Letterers*, 50, 4724-472.
Jayashankaran, J.; Durga, R.; Raghunathan, R., (2005). A facile entry into a novel class of dispiroheterocycles through 1,3–dipolar cycloaddition. *ARKIVOC*, 32-39.
Katritzky, R.; Ress, C.W. (1997). Comprehensive heterocyclic chemistry. *Elsevier Sci. Ltd.*, 256-260.
Luibineau, A.; Bouchain, G.; Queneau, Y. (1995). Pyrrolidine and 1,3-oxazolidine formation from azomethine ylides influenced by change from classical conditions to microwave irradiation. *J. Chem. Soc, Perkin Trans I*, 2433.

Manikandan, S.; Mohamed Ashraf, M.; Raghunathan, R. (2001). A formal [3,2] cycloaddition strategy for the synthesis of unique class of dispiroheterocycles, *Synth. Commun.*, 31, 3593.

March, J.A. (1992). "Advanced Organic Chemistry". 4th edn., Mc Graw-Hill, Inc., New York, 896 p.

Mistry, B.D. (2009). A Handbook of Spectroscopic Data". Oxford book company.

Parich, V. M. (1974). "Absorption Spectroscopy of Organic Compounds". Addition-Wesley publishing company, Inc., pp. 247-252, pp. 51-59, pp. 60-64.

Popandova-Yambolieva, K.; Ivanov, C. (1989). Synthesis of new spiropyrrrolidines and Michael addition products using phase transfer catalyzed addition of schiff bases to 9-arylmethylenefluorenes. *Chemica. Scripta*. 29, 269-271.

Poornachandran, M.; Raghunathan, R. (2010). A novel access to dispirocyclohexanoneindan pyrrolidine, *Indian J. Chemistry*, 49B, 127-130.

Raj, A. A.; Raghunathan, R. (2003). Synthesis of spiropyrrrolidine via formal [3,2] cycloaddition of unusual enones and cis 3-benzoy l 1-1-cyclohexy 1-2-phenylaziridine. *Tetrahedron*, 59, 2907-2911.

Waldmann, H. (1995). "Organic Synthesis in Water". Thamson Science, Pappellallee, Weinheim, Germany, Synlett, 133p.

Shriner, R. L.; Fuson, R.C.; Curtin, D.Y., (1964). "The Systematic Identification of Organic Compounds". 5th edn., John Wiley and Sons Inc., New York. 29p.

Subramaniyan, G.; Raghunathan, R. (2001). Synthesis of highly substituted spiropyrrrolidines via 1,3-dipolar cycloaddition reaction of N-metalated azomethine ylides. *Tetrahedron*, 57, 2909.

Vogel, A. (1989). "Practical Organic Chemistry". Longmans, 5th edn. 1034 p.