

Modern Friedel-Crafts chemistry. Part 32.[†]
Facile synthesis of some new fused heteropolycycles via direct intramolecular Friedel-Crafts cyclialkylations of suitable heteroarylalkanols

Ali A. Khalaf,* Ahmed M. El-Khawaga, Ibrahim M. Awad, and Hassan A. K. Abd El-Aal

Chemistry Department, Faculty of Science, Assiut University, Assiut, Egypt

E-mail: prof_khalaf@hotmail.com

DOI: <http://dx.doi.org/10.3998/ark.5550190.0011.a28>

Abstract

This study provides expedient methods for the synthesis of some novel fused heteropolycycles. Thus, a variety of fused di-, tri- and tetracyclic nitrogen and nitrogen-sulfur heteropolycycles **8**, **9**, **11-15** were smoothly synthesized by Friedel-Crafts intramolecular alkylations of heteroarylalkanols **1-7** in the presence of both Brønsted (PPA and PTSA) and Lewis (AlCl₃/CH₃NO₂) acid catalysts. The precursor alkanols were readily prepared by reaction of the corresponding carboxylic acid esters with methylmagnesium iodide. The structures of the compounds are established using both spectral and analytical data. A plausible carbocation mechanism is proposed to account for the results.

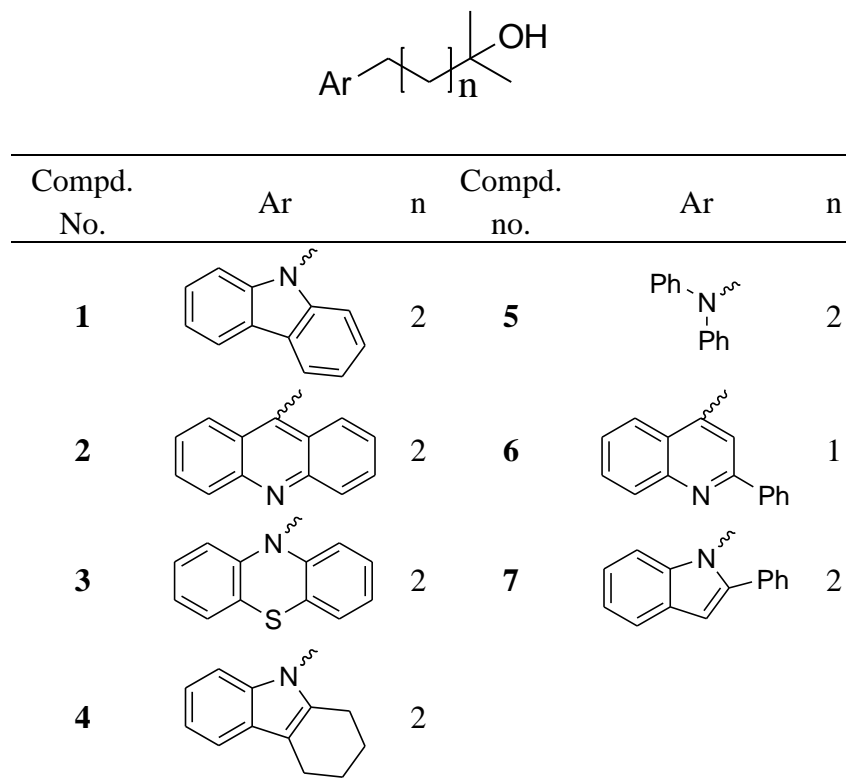
Keywords: Friedel-Crafts cyclialkylation, heteropolycycles, 4,4-dimethyl-5,6-dihydro-4*H*-pyrido[3,2,1-*jk*]carbazole, 3,3-dimethyl-2,3-dihydro-1*H*-benzo[*kl*]acridine, 5,5-dimethyl-2-phenyl-4,5-dihydrocyclopenta[*de*]quinoline, 3,3-dimethyl-2,3-dihydro-1*H*-pyrido[3,2,1-*kl*]phenothiazine

Introduction

A variety of methods have been developed for the synthesis of biologically and pharmacologically active heteropolycycles that bear quinoline or tetrahydroquinoline fragments.^{1,2} Among these methods, intramolecular Friedel-Crafts reactions (called cyclialkylations)³ prompted by both Brønsted and Lewis acid catalysts proved to introduce powerful pathways for the facile construction of not only homo- but also heteropolycycles.^{4,5}

In this paper, we introduce the construction of seven nitrogen and nitrogen-sulfur polycycles **8**, **9**, **11-15** containing fused quinoline, tetrahydroquinoline, acridine, phenothiazine and indole moieties via Friedel-Crafts cyclialkylations of seven new heteroarylalkanols **1-7** (Scheme 1).

† For preceding paper of the series see ref 19. Part of the Ph.D. Thesis of H. A. K. Abdel-Aal

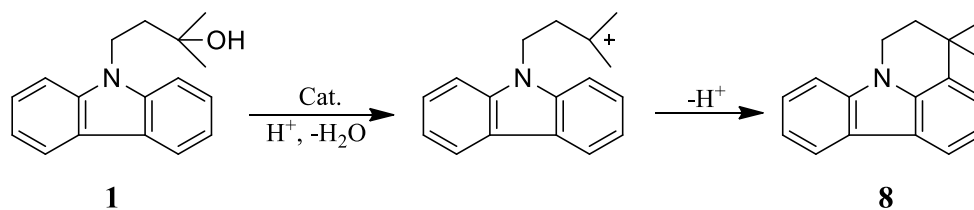


Scheme 1. Selected heteroarylalkanols **1-7**.

Results and Discussion

Synthesis and cyclialkylation of 4-(9H-carbazol-9-yl)-2-methylbutan-2-ol (1). This hitherto unknown 4-(9H-carbazol-9-yl)-2-methylbutan-2-ol **1** was synthesized in two consecutive steps starting from 3-(9H-carbazol-9-yl)propanoic acid⁶ by conversion to ethyl ester followed by reaction with methylmagnesium iodide.

Cyclialkylation of alcohol **1** in the presence of both polyphosphoric acid (PPA) and *p*-toluenesulfonic acid (PTSA) catalysts gave 4,4-dimethyl-5,6-dihydro-4H-pyrido[3,2,1-*jk*]carbazole **8** as sole product. The results are presented in Scheme 2 and Table 1 (Entries 1 and 2).



Scheme 2. Cyclialkylation of 4-(9H-carbazol-9-yl)-2-methylbutan-2-ol **1**.

Table 1. Cyclialkylation conditions and results of heteroarylalkanols **1-7**

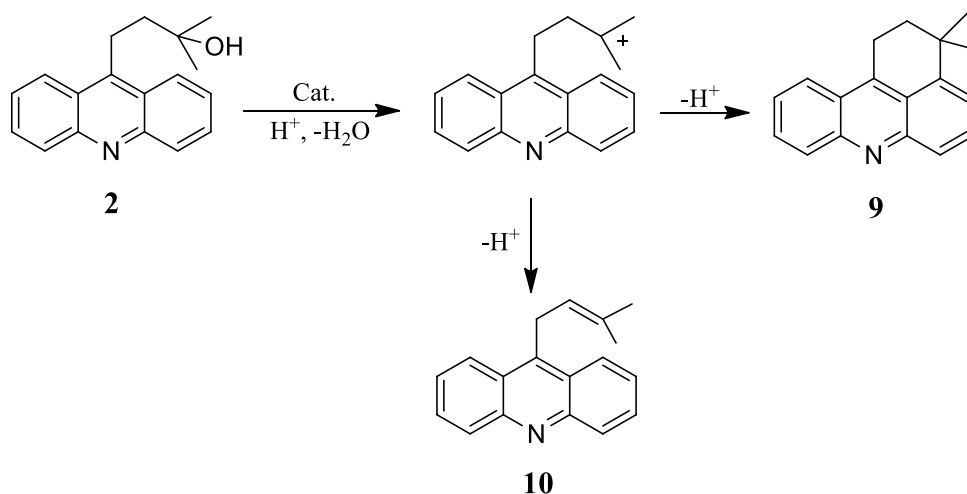
| Entry | Substrate no. | Catalyst type | Solvent | Temp C° | Time hr. | Yield % | Product composition (%) |
|----------------|---------------|--|------------------|---------|----------|---------|----------------------------------|
| 1 | 1 | PPA ^a | -- | 250 | 1 | 80 | 8 |
| 2 | 1 | PTSA ^b | PhH | reflux | 12 | 76 | 8 |
| 3 ^c | 2 | AlCl ₃ /CH ₃ NO ₂ | DCM ^d | RT | 2 | 80 | 9 (60), 10 (35) |
| 4 | 2 | PPA | -- | 250 | 24 | 79 | 10 |
| 5 | 3 | PPA | -- | 250 | 1 | 75 | 11 |
| 6 | 3 | PTSA | PhH | reflux | 24 | 82 | 11 |
| 7 | 4 | PPA | -- | 250 | 24 | 77 | 12 |
| 8 ^e | 4 | H ₃ PO ₄ | -- | 260 | 24 | 78 | 12 |
| 9 | 4 | PTSA | PhH | reflux | 20 | 81 | 12 |
| 10 | 5 | PPA | -- | 250 | 12 | 80 | 13 |
| 11 | 5 | PTSA | PhH | reflux | 24 | 78 | 13 |
| 12 | 6 | PPA | -- | 250 | 24 | 80 | 14 |
| 13 | 6 | PTSA | PhH | reflux | 24 | 77 | 14 |
| 14 | 7 | PPA | -- | 250 | 24 | 83 | 15 |
| 15 | 7 | PTSA | PhH | reflux | 24 | 81 | 15 |

^aWith PPA catalyst reactant proportions were: carbinol (0.5 g) and PPA (3 g). ^bWith PTSA catalyst reactant proportions were: carbinol (0.5 g), PTSA (3 g) and solvent (10 ml). ^cWith AlCl₃/CH₃NO₂ catalyst reactant proportions were: carbinol (0.002 mole), AlCl₃ (0.0024 mole), CH₃NO₂ (0.024 mole), solvent (10 ml). ^dDichloromethane. ^eWith H₃PO₄ catalyst proportions were: carbinol (0.5 g) and dry H₃PO₄ (4 g).

Synthesis and cyclialkylation of 4-(acridin-9-yl)-2-methylbutan-2-ol (**2**)

The title alcohol was synthesized by addition of methylmagnesium iodide to methyl 3-(acridin-9-yl)propanoate.⁷ Cyclialkylation of carbinol **2** was carried out using PPA and AlCl₃/CH₃NO₂ catalysts in methylene chloride solvent. The product from PPA was shown to be pure 3,3-dimethyl-2,3-dihydro-1H-benzo[*kl*]acridine **9**. With AlCl₃/CH₃NO₂ for 2 hours, however, the

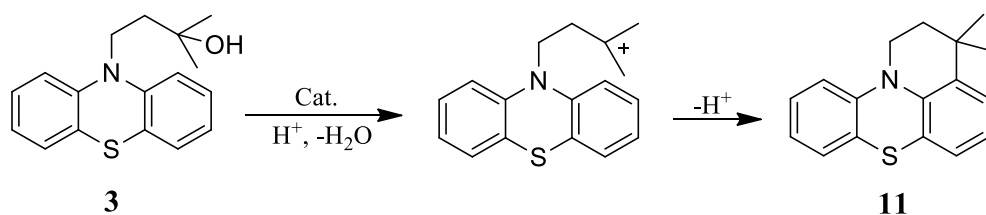
product was shown to be a mixture of tetracyclic product **9** (60%) and 9-(3-methylbut-2-en-1-yl)acridine **10** (35%) (Scheme 3; Table 1, Entries 3 and 4)



Scheme 3. Cyclialkylation of 4-(acridin-9-yl)-2-methylbutan-2-ol **2**.

Synthesis and cyclialkylation of 2-methyl-4-(10*H*-phenothiazin-10-yl)butan-2-ol (**3**)

Alkanol **3** was synthesized by treatment of ethyl 3-(10*H*-phenothiazin-10-yl)propanoate⁸ with methylmagnesium iodide in dry ether. Cyclialkylation of **3** in the presence of PPA and PTSA catalysts gave 3,3-dimethyl-2,3-dihydro-1*H*-pyrido[3,2,1-*kl*]phenothiazine **11** as a sole product (Scheme 4; Table 1, Entries 5 and 6).



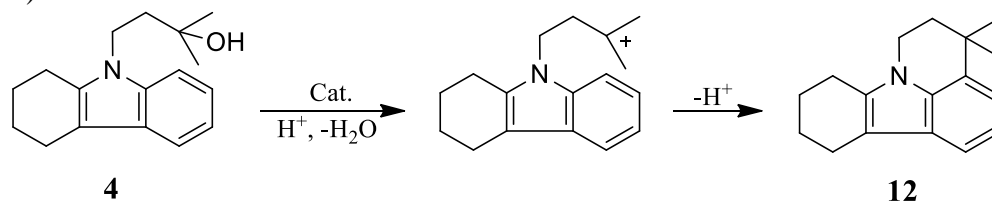
Scheme 4. Cyclialkylation of 2-methyl-4-(10*H*-phenothiazin-10-yl)butan-2-ol **3**.

Synthesis and cyclialkylation of 2-methyl-4-(1,2,3,4-tetrahydro-4*H*-carbazol-9-yl)butan-2-ol (**4**)

This alcohol was obtained in a series of two consecutive steps starting with 3-(1,2,3,4-tetrahydro-9*H*-carbazol-9-yl)propanoic acid.⁹ This acid was converted to its ethyl ester followed by addition of two equivalents of methylmagnesium iodide.

Cyclialkylation of carbinol **4** was carried out in the presence of PPA, H₃PO₄ and PTSA catalysts. The products of reactions with all three catalysts were identical and were shown to be

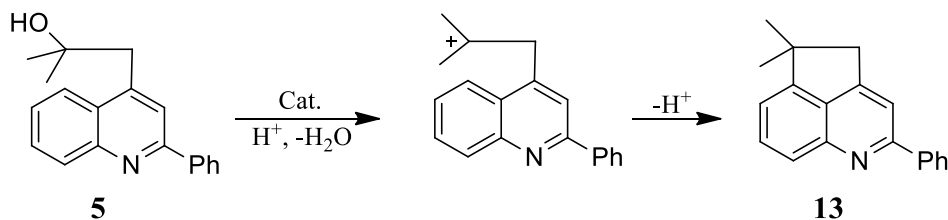
4,4-dimethyl-5,6,8,9,10,11-hexahydro-4*H*-pyrido[3,2,1-*jk*]carbazole **12** (Scheme 5; Table 1, Entries 7-9).



Scheme 5. Cyclialkylation of 2-methyl-4-(1,2,3,4-tetrahydro-4*H*-carbazol-9-yl)butan-2-ol **4**.

Synthesis and cyclialkylation of 2-methyl-1-(2-phenylquinolin-4-yl)propan-2-ol (**5**)

This alcohol was obtained in a series of five consecutive steps starting with (2-phenylquinolin-4-yl)methanol.¹⁰ A summary of the steps and of the involved product intermediates is given in the experimental section. Reaction of carbinol **5** in the presence of PTSA and PPA catalysts gave 5,5-dimethyl-2-phenyl-4,5-dihydrocyclopenta[*de*]quinoline **13** as a sole product (Scheme 6; Table 1, Entries 10 and 11).

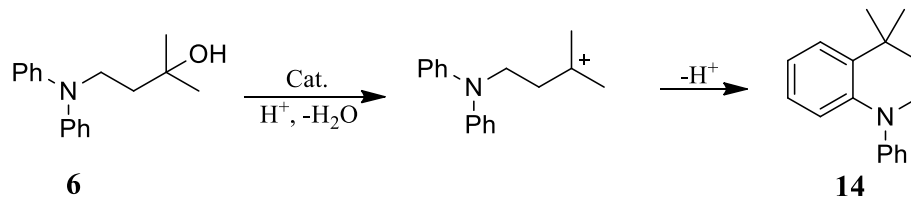


Scheme 6. Cyclialkylation of 2-methyl-1-(2-phenylquinolin-4-yl)propan-2-ol **5**.

Synthesis and cyclialkylation of 4-(diphenylamino)-2-methylbutan-2-ol (**6**)

This alcohol was obtained by addition of two equivalents of methylmagnesium iodide to ethyl 3-(diphenylamino) propanoate.¹¹

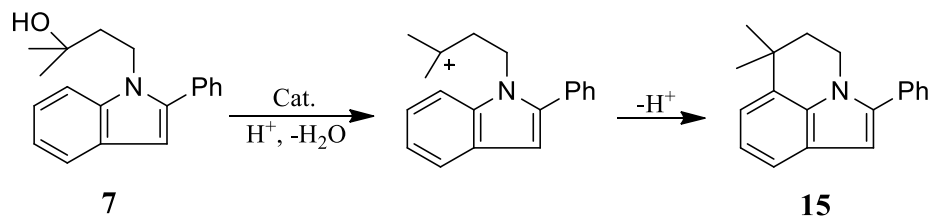
The cyclialkylation of alcohol **6** was carried out in the presence of both PPA and PTSA catalysts under different reaction conditions. The products with both catalysts were identical and were shown to be 4,4-dimethyl-1-phenyl-1,2,3,4-tetrahydroquinoline **14** (Scheme 7; Table 1, Entries 12 and 13).



Scheme 7. Cyclialkylation of 4-(diphenylamino)-2-methylbutan-2-ol **6**.

Synthesis and cyclialkylation of 2-methyl-4-(2-phenyl-1*H*-indol-1-yl)butan-2-ol (7)

The title alcohol was synthesized via two consecutive reaction steps starting from 3-(2-phenyl-1*H*-indol-1-yl)propanoic acid¹² by esterification to ethyl 3-(2-phenyl-1*H*-indol-1-yl)propanoate followed by reaction with two equivalents of methylmagnesium iodide. Cyclialkylation of alkanol **7** in the presence of either PPA or PTSA catalyst gave 6,6-dimethyl-2-phenyl-5,6-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline **15** as a sole product (Scheme 8; Table 1, Entries 14 and 15).



Scheme 8. Cyclialkylation of 2-methyl-4-(2-phenyl-1*H*-indol-1-yl)butan-2-ol **7**.

Conclusions

In conclusion, we have developed a facile and efficient approach to synthesize seven new heteropolycycles **8**, **9**, **11-15** via intramolecular Friedel-Crafts cyclialkylations of seven new heteroarylalkanols **1-7**. All together, the results of this study proved that Friedel-Crafts cyclialkylation can be considered as one of the most useful pathways to the synthesis of di-, tri- and higher condensed polycycles enclosing one or more heteroatoms.

Experimental Section

General. Melting points were measured on a digital Gallenkamp capillary melting point apparatus and are uncorrected. Infrared spectra were determined with a Shimadzu 470 Infrared spectrophotometer using KBr wafer and thin film techniques (ν cm⁻¹). ¹H NMR spectra were recorded by 90 MHz Varian NMR spectrometer using the appropriate deuteriated solvent with TMS as internal standard. Chemical shifts (δ) and *J* values are reported in ppm and Hz, respectively. Elemental analyses were performed on a Perkin-Elmer 2400 Series II analyzer. The mass spectra were performed by JEOL JMS 600 spectrometer at an ionizing potential of 70 eV using the direct inlet system. Reactions were monitored by thin layer chromatography (TLC) using precoated silica plates (Kieselgel 60, F 254, E. Merck) visualized with UV light. Flash column chromatography (FC) was performed on silica gel (230-400 mesh, E. Merck). All reagents were purchased from Merck, Sigma or Aldrich Chemical Co. and were used without further purification.

4-(9H-Carbazol-9-yl)-2-methylbutan-2-ol (1). Was obtained in a series of two consecutive steps starting with 3-(9H-carbazol-9-yl)propanoic acid.⁶ A summary of the steps and of the involved product intermediates is given in the following:

(i) Esterification of 3-(9H-carbazol-9-yl)propanoic acid with ethanol as usual¹³ in the presence H₂SO₄ gave ethyl 3-(9H-carbazol-9-yl)propanoate in the form of pale yellowish oil (79%): n_D^{25} 1.5722; IR (KBr) ν 3050, 2990, 1730, 1620, 1590, 1480, 1455, 1320, 1180, 745 cm⁻¹; ¹H NMR (90 MHz, CDCl₃, ppm), δ = 0.7 (3H, t, J = 9 Hz, CH₃), 2.4 (2H, t, J = 7.5 Hz, CH₂), 3.6 (2H, q, J = 9 Hz, CH₂), 4.2 (2H, t, J = 7.5 Hz, CH₂) and 6.8-7.8 (8H, m, Ar-H); MS (EI, 70 eV) m/z (%), 267 (M⁺, 22.8), 252 (M⁺-CH₃, 46.3), 239 (15.7), 238 (M⁺-C₂H₅, 74.5), 222 (100), 208 (9.6), 194 (15.7), 166 (45.6), 91 (8.4), 77 (4.2).

(ii) Addition of two equivalents of methylmagnesium iodide to ethyl 3-(9H-carbazol-9-yl)propanoate was followed by stirring overnight and decomposition by sat. aq. NH₄Cl soln. Extraction of the product with ether, drying over anhydrous magnesium sulfate, decantation and evaporation of the solvent gave (87%) of the crude solid product. Crystallization from methanol gave (83%) of pure 4-(9H-carbazol-9-yl)-2-methylbutan-2-ol **1** in the form of white crystals: m.p. 82 °C; IR (KBr) ν 3350, 3250, 3060, 2960, 2850, 1590, 1480, 1460, 1450, 1345, 1145, 915, 740, 670 cm⁻¹; ¹H NMR (90 MHz, CDCl₃, ppm), δ = 1.2 (6H, s, 2CH₃), 1.6 (1H, s, OH exchangeable with D₂O), 1.8 (2H, t, J = 7.5 Hz, CH₂), 4.3 (2H, t, J = 7.5 Hz, CH₂) and 7.1-8.2 (8H, m, Ar-H). Anal. Calcd. for C₁₇H₁₉NO (253): C, 80.63; H, 7.5; N, 5.53. Found: C, 80.22; H, 7.61; N, 5.82.

4-(Acridin-9-yl)-2-methylbutan-2-ol (2). Addition of two equivalents of methylmagnesium iodide to methyl 3-(acridin-9-yl)propanoate⁷ was followed by stirring overnight. Decomposition by sat. aq. NH₄Cl soln following standard procedure⁴ gave (93%) of crude solid product. Crystallization from methanol gave the product as yellow needles (86%): m.p. 110-11 °C; IR (KBr) ν 3350, 3220, 2980, 1610, 1550, 1515, 1480, 1365, 1145, 950, 740, 680 cm⁻¹; ¹H NMR (90 MHz, CDCl₃, ppm), δ = 1.2 (6H, s, 2CH₃), 1.4 (1H, s, OH exchangeable with D₂O), 1.7 (2H, apparent m, J = 6 Hz, CH₂), 3.6 (2H, apparent m, J = 6 Hz, CH₂) and 7.2-8.3 (8H, m, Ar-H). Anal. Calcd. for C₁₈H₁₉NO (265): C, 81.5; H, 7.16; N, 5.28. Found: C, 81.77; H, 6.85; N, 5.52.

2-Methyl-4-(10H-phenothiazin-10-yl)butan-2-ol (3). Addition of two equivalents of methylmagnesium iodide to ethyl 3-(10H-phenothiazin-10-yl)propanoate⁸ was followed by stirring for 15 hours and decomposition by sat. aq. NH₄Cl soln. Extraction following the standard procedure⁴ gave (78%) of the crude product which on crystallization from methanol gave (70%) of pure 2-methyl-4-(10H-phenothiazin-10-yl)butan-2-ol **3** in the form of pale brown crystals: m.p. 70-71 °C; IR (KBr) ν 3280, 3070, 2980, 1590, 1565, 1445, 1370, 1220, 1120, 1030, 720 cm⁻¹; ¹H NMR (90 MHz, CDCl₃, ppm), δ = 1.15 (6H, s, 2CH₃), 1.7 (2H, d, J = 9 Hz, CH₂), 2.3 (1H, s, OH exchangeable with D₂O), 3.75 (2H, t, J = 9 Hz, CH₂) and 6.7-7.3 (8H, m, Ar-H). Anal. Calcd. for C₁₇H₁₉NOS (285): C, 71.57; H, 6.66; N, 4.91; S, 11.22. Found: C, 71.92; H, 6.25; N, 5.2; S, 11.31.

2-Methyl-4-(1,2,3,4-tetrahydro-9H-carbazol-9-yl)butan-2-ol (4). Was obtained in two steps starting from 3-(1,2,3,4-tetrahydro-9H-carbazol-9-yl)propanoic acid⁹ as follows:

(i) Esterification of the above acid with ethanol and H_2SO_4 following the literature procedure¹³ gave (91%) of crude solid ester. Crystallization from n-hexane/benzene (7:3) mixture gave (86%) of pure ethyl 3-(1,2,3,4-tetrahydro-9*H*-carbazol-9-yl)propanoate as pale yellow crystals m.p. 54 °C; IR (KBr) ν 3050, 2995, 2910, 1725, 1610, 1463, 1440, 1420, 1375, 1180, 735 cm^{-1} ; ^1H NMR (90 MHz, CDCl_3 , ppm), δ = 1.2 (3H, t, J = 7.5Hz, CH_3), 1.8 (4H, d, cyclic 2CH_2), 2.7 (6H, m, cyclic 2CH_2 and C^2H_2), 4.2 (2H, q, J = 7.5Hz, CH_2), 4.2 (2H, t, J = 7.5Hz, C^3H_2) and 6.9-7.4 (4H, m, Ar-H); MS (EI, 70 eV) m/z (%), 272 (M^++1 , 9.2), 271 (M^+ , 20.3), 256 (M^+-CH_3 , 31.7), 242 ($\text{M}^+-\text{C}_2\text{H}_5$, 12.9), 226 ($\text{M}^+-\text{OC}_2\text{H}_5$, 100), 198 (43.4), 184 (24.3), 170 (39.2), 166 (33.5), 158 (5.3), 91 (4.9), 77 (3.5).

(ii) Addition of two equivalents of methylmagnesium iodide to ethyl 3-(1,2,3,4-tetrahydro-9*H*-carbazol-9-yl)propanoate followed by stirring for ten hours and decomposition by sat. aq. NH_4Cl soln following the standard procedure⁴ gave (95%) of crude solid product. Crystallization from methanol gave (87%) of 2-methyl-4-(1,2,3,4-tetrahydro-9*H*-carbazol-9-yl)butan-2-ol **4** in the form of brown crystals: m.p. 68 °C; IR (KBr) ν 3380, 3040, 2970, 2910, 1610, 1465, 1438, 1370, 1210, 1210, 1140, 740 cm^{-1} ; ^1H NMR (90 MHz, CDCl_3 , ppm), δ = 1.3 (6H, s, 2CH_3), 1.5 (1H, s, OH exchangeable with D_2O), 2.6-2.9 (6H, m, cyclic 2CH_2 and C^3H_2), 2.7 (4H, apparent s, unresolved cyclic 2CH_2), 4.0-4.3 (2H, t, J = 9Hz, C^4H_2) and 7.0-7.6 (4H, d, Ar-H). Anal. Calcd. for $\text{C}_{17}\text{H}_{23}\text{NO}$ (257): C, 79.37; H, 8.94; N, 5.44. Found: C, 79.1; H, 8.57; N, 5.72.

2-Methyl-1-(2-phenylquinolin-4-yl)propan-2-ol (5) was obtained in a series of five consecutive steps starting with (2-phenylquinolin-4-yl)methanol.¹⁰ A summary of the steps and of the involved product intermediates is given in the following:

(i) Following standard literature procedure and reactant ratios,¹⁴ a solution of thionyl chloride in dry benzene was added dropwise to an ice cooled stirred solution of (2-phenylquinolin-4-yl)methanol in dry benzene over a period of five minutes. The reaction mixture was left to stir for ten more minutes, treated with aqueous ammonia until alkaline then the precipitated hydrochloride was decomposed by water to give (88%) of a crude solid product. Crystallization from petroleum ether (60-80 °C) gave (83%) of pure 4-(chloromethyl)-2-phenylquinoline as white needles: m.p. 112 °C; IR (KBr) ν 3070, 2920, 2890, 1595, 1550, 1490, 1350, 1080, 765, 697 cm^{-1} ; ^1H NMR (90 MHz, CDCl_3 , ppm), δ = 4.7 (2H, s, CH_2) and 7.4-8.5 (10H, m, Ar-H); MS (EI, 70 eV) m/z (%), 255.6 (M^++2 , 7.3), 253.4 (M^+ , 15.6), 218 (100), 217 (M^+-HCl , 45.8), 203 (17.9), 176 (77.6), 166 (18.5), 141 (12.4), 127 (9.8), 90 (14.2), 77 (4.6).

(ii) A solution of 4-(chloromethyl)-2-phenylquinoline in ethanol was added during 30 minutes to a refluxing solution of potassium cyanide in water and ethanol mixture (1:3). After refluxing for four hours, excess alcohol was evaporated and the residue was diluted with water. Extraction of the product with ether, drying over anhydrous magnesium sulfate, decantation and evaporation of the solvent gave (84%) of crude solid product. Crystallization from acetone gave (75%) of pure (2-phenylquinolin-4-yl)acetonitrile in the form of white needles: m.p. 139 °C; IR (KBr) ν 3050, 2920, 2350, 1595, 1510, 1410, 1360, 1160, 1085, 785 cm^{-1} ; ^1H NMR (90 MHz, CDCl_3 , ppm), δ = 5.3 (2H, s, CH_2) and 7.4-8.5 (10H, m, Ar-H); MS (EI, 70 eV) m/z (%), 244 (M^+ , 7.2), 217 (M^+-HCN , 53.7), 203 (100), 166 (23.5), 140 (13.1), 126 (3.3), 90 (5.2), 77 (3.6).

(iii) Hydrolysis of (2-phenylquinolin-4-yl)acetonitrile to (2-phenylquinolin-4-yl)acetic acid was carried out by refluxing with ethanolic sodium hydroxide solution according to the literature procedure¹³ to give (91%) of crude solid product. Crystallization from aqueous ethanol gave (81%) of pure (2-phenylquinolin-4-yl)acetic acid as white needles: m.p. 188-9 °C; IR (KBr) ν 3060, 2900, 2370-2700, 1690, 1595, 1510, 1410, 1215, 785 cm^{-1} ; ¹H NMR (90 MHz, CDCl₃, ppm), δ = 3.9 (2H, s, CH₂) 7.2-8.0 ppm (10H, m, Ar-H) and 10.4 (1H, s, COOH); MS (EI, 70 eV) m/z (%), 263 (M⁺, 12.5), 246 (100), 218 (43.2), 204 (29.3), 169 (18.5), 166 (23.4), 90 (4.1), 77 (5.2).

(iv) Esterification of the above acid with methanol and H₂SO₄ following the standard method¹³ gave (83%) of crude ester. Crystallization from methanol gave (71%) of pure methyl (2-phenylquinolin-4-yl)acetate: m.p. 93-4 °C; IR (KBr) ν 3055, 2950, 1740, 1595, 1510, 1430, 1260, 1160, 787 cm^{-1} ; ¹H NMR (90 MHz, CDCl₃, ppm), δ = 3.5 (3H, s, CH₃), 4 (2H, s, CH₂) and 7.2-8.2 (10H, m, Ar-H); MS (EI, 70 eV) m/z (%), 278 (M⁺+1, 2.7), 277 (M⁺, 16.5), 262 (M⁺-CH₃, 100), 246 (12.4), 234 (M⁺-COCH₃, 100), 204 (39.4), 169 (8.4), 166 (18.2), 127 (5.4), 90 (4.2), 77 (2.4).

(v) Finally alcohol was prepared by addition of two equivalents of methylmagnesium iodide to methyl (2-phenylquinolin-4-yl)acetate in dry ether. The reaction mixture was left to stir overnight at room temperature then treated as usual⁴ to give (87%) of crude product which on purification by FC (basic alumina, benzene eluent) gave (82%) of pure 2-methyl-1-(2-phenylquinolin-4-yl)propan-2-ol **5** as a yellowish liquid: n_D^{25} 1.6512; IR (Film) ν 3590, 3430, 3030, 2985, 1590, 1510, 1460, 1375, 1200, 1140, 1020, 900, 780 cm^{-1} ; ¹H NMR (90 MHz, CDCl₃, ppm), δ = 1 (6H, s, 2CH₃), 2.2 (1H, s, OH exchangeable with D₂O), 3 (2H, s, CH₂) and 6.9-8.1 (10H, m, Ar-H). Anal. Calcd. for C₁₉H₁₉NO (277): C, 82.31; H, 6.86; N, 5.05. Found: C, 81.92; H, 7.26; N, 5.17.

4-(Diphenylamino)-2-methylbutan-2-ol (6). This alcohol was prepared by addition of two equivalents of methylmagnesium iodide to ethyl 3-(diphenylamino)propanoate.¹¹ The reaction mixture was left to stir overnight and then decomposed with sat. aq. NH₄Cl soln and the product was extracted with ether following the literature method⁴ to give (81%) of the crude oily product. Purification by flash chromatography (FC) of the liquid product [neutral alumina, 8:2, petroleum ether (60-80 °C)/benzene eluent] gave (79%) of pure 4-(diphenylamino)-2-methylbutan-2-ol **6** in the form of a colorless viscous oil: n_D^{25} 1.5426; IR (Film) ν 3400, 3060, 2990, 1585, 1480, 1360, 1220, 1055, 1020, 745, 692 cm^{-1} ; ¹H NMR (90 MHz, CDCl₃, ppm), δ = 1.3 (6H, s, 2CH₃), 1.7 (2H, t, J = 9Hz, CH₂), 2.7 (1H, s, OH exchangeable with D₂O), 3.8 (2H, t, J = 9Hz, CH₂) and 6.9-7.5 (10H, m, Ar-H). Anal. Calcd. for C₁₇H₂₁NO (255): C, 80.0; H, 8.23; N, 5.49. Found: C, 79.7; H, 8.3; N, 5.62.

2-Methyl-4-(2-phenyl-1H-indol-1-yl)butan-2-ol (7). This alcohol was synthesized in two consecutive reaction steps starting from 3-(2-phenyl-1H-indol-1-yl)propanoic acid.¹²

(i) Esterification of this acid by ethyl alcohol following the standard procedure¹³ gave (90%) of crude oily ester. Purification of the ester by FC (basic alumina, benzene eluent) gave (86%) of pure ester in the form of yellowish liquid: n_D^{25} 1.485; IR (Film) ν 3050, 2910, 1700, 1600, 1570,

1540, 1445, 1010, 745, 695 cm^{-1} ; ^1H NMR (90 MHz, CDCl_3 , ppm), δ = 1.0 (3H, t, J = 6Hz, CH_3), 2.5 (2H, t, J = 7.5Hz, C^2H_2), 3.9 (2H, q, J = 6Hz, CH_2), 4.4 (2H, t, J = 7.5Hz, C^3H_2), 6.5 (1H, s, CH) and 7.0-7.6 (9H, m, Ar-H); MS (EI, 70 eV) m/z (%), 293 (M^+ , 13.9), 278 ($\text{M}^+ - \text{CH}_3$, 21.5), 264 ($\text{M}^+ - \text{C}_2\text{H}_5$, 15.2), 248 (100), 220 (17.3), 187 (6.4), 166 (11.6), 90 (6.8), 77 (4.4).

(ii) The title alcohol was prepared by addition of two equivalents of methylmagnesium iodide to ethyl 3-(2-phenyl-1*H*-indol-1-yl)propanoate in dry ether followed by stirring for 20 hours and decomposition by sat. aq. NH_4Cl soln. Separation of the product following literature procedure⁴ gave (84%) of crude solid product. Crystallization from petroleum ether (60-80 °C)/benzene mixture gave (82%) of pure 2-methyl-4-(2-phenyl-1*H*-indol-1-yl)butan-2-ol **7** in the form of buff plates: m.p. 76-77 °C; IR (KBr) ν 3550, 3480, 3050, 2995, 1700, 1600, 1465, 1445, 1345, 1180, 920, 740, 695 cm^{-1} ; ^1H NMR (90 MHz, CDCl_3 , ppm), δ = 1.25 (6H, s, 2 CH_3), 1.7 (2H, t, J = 9Hz, C^3H_2), 4.2 (1H, s, OH exchangeable with D_2O), 4.4 (2H, t, J = 9Hz, C^4H_2), 6.6 (1H, s, CH) and 7.0-7.7 (9H, m, Ar-H). Anal. Calcd. for $\text{C}_{19}\text{H}_{21}\text{NO}$ (279): C, 81.72; H, 7.52; N, 5.01. Found: C, 81.52; H, 7.74; N, 4.83.

Cyclialkylation procedures

The procedures described earlier for cyclialkylation of arylalkanols with $\text{AlCl}_3/\text{CH}_3\text{NO}_2$ ¹⁵, PPA¹⁶, *p*-toluenesulfonic acid¹⁷ (PTSA) and H_3PO_4 ¹⁸ were essentially followed.

4,4-Dimethyl-5,6-dihydro-4*H*-pyrido[3,2,1-*jk*]carbazole (8). Greenish plates: m.p. 65 °C; IR (KBr) ν 3050, 2975, 1620, 1580, 1490, 1445, 1430, 1330, 1060, 1025 cm^{-1} ; ^1H NMR (90 MHz, CDCl_3 , ppm), δ = 1.2 (6H, s, 2 CH_3), 1.9 (2H, t, J = 6Hz, CH_2), 4.1 (2H, t, J = 6Hz, CH_2) and 7.0-8.2 (7H, d, Ar-H); MS (EI, 70 eV) m/z (%), 235 (M^+ , 85.8), 219 ($\text{M}^+ - \text{CH}_3 - \text{H}$, 100), 205 (0.8), 204 ($\text{M}^+ - 2\text{CH}_3 - \text{H}$, 25.1), 191 (5.7), 177 (1.4), 166 (12.5), 151 (1.6), 109 (5.3), 90 (0.3), 77 (0.1), 66 (0.2). Anal. Calcd. for $\text{C}_{17}\text{H}_{17}\text{N}$ (235): C, 86.8; H, 7.23; N, 5.95. Found: C, 86.59; H, 7.05; N, 6.2.

3,3-Dimethyl-2,3-dihydro-1*H*-benzo[*kl*]acridine (9). Faint yellow oil: n_{D}^{25} 1.6344, $R_{\text{F}2}$ 0.26 (7.2:2.8, n-hexane/benzene eluent); IR (Film) ν 3050, 2910, 1600, 1540, 1520, 1460, 1340, 742 cm^{-1} ; ^1H NMR (90 MHz, CDCl_3 , ppm), δ = 1.45 (6H, s, 2 CH_3), 2.0 (2H, t, J = 7.5Hz, CH_2), 3.5 (2H, t, J = 7.5Hz, CH_2) and 7.35-8.4 (7H, m, Ar-H); MS (EI, 70 eV) m/z (%), 247 (M^+ , 20.1), 245 ($\text{M}^+ - 2\text{H}$, 68.5), 232 ($\text{M}^+ - \text{CH}_3$, 3.4), 217 ($\text{M}^+ - 2\text{CH}_3$, 39.1), 203 (49.1), 191 (100), 189 (9.4), 178 (23.4), 166 (17.7), 151 (9.0), 90 (11.4), 77 (2.5), 66 (2.1). Anal. Calcd. for $\text{C}_{18}\text{H}_{17}\text{N}$ (247): C, 87.44; H, 6.88; N, 5.66. Found: C, 87.2; H, 6.95; N, 5.46.

9-(3-Methylbut-2-en-1-yl)acridine (10). Yellow plates: $R_{\text{F}1}$ 0.31 (7.2:2.8, n-hexane/benzene eluent); m.p. 61-62 °C; IR (KBr) ν 3050, 2910, 1460, 755 cm^{-1} ; ^1H NMR (90 MHz, CDCl_3 , ppm), δ = 1.6 (6H, 2s, 2 CH_3), 2.6 (2H, d, J = 9Hz, CH_2), 5.0 (1H, t, J = 6Hz, CH) and 7.0-8.3 (8H, m, Ar-H); MS (EI, 70 eV) m/z (%), 247 (M^+ , 6.6), 245 ($\text{M}^+ - 2\text{H}$, 100), 232 ($\text{M}^+ - \text{CH}_3$, 9.3), 231 (25.9), 217 ($\text{M}^+ - 2\text{CH}_3$, 57.3), 205 (18.0), 203 (32.8), 192 (49.5), 177 (6.0), 166 (5.4), 150 (7.4), 91 (2.5), 77 (5.8), 66 (1.3). Anal. Calcd. for $\text{C}_{18}\text{H}_{17}\text{N}$ (247): C, 87.44; H, 6.88; N, 5.66. Found: C, 87.53; H, 6.74; N, 5.52.

3,3-Dimethyl-2,3-dihydro-1H-pyrido[3,2,1-*kl*]phenothiazine (11). Yellowish viscous oil: n_D^{25} 1.644; IR (Film) ν 3070, 2985, 1600, 1570, 1460, 1430, 1320, 740 cm^{-1} ; ^1H NMR (90 MHz, CDCl_3 , ppm), δ = 1.25 (6H, s, 2 CH_3), 1.7 (2H, t, J = 6Hz, CH_2), 3.4 (2H, t, J = 6Hz, CH_2) and 6.6-7.4 (7H, d, Ar-H); MS (EI, 70 eV) m/z (%), 267 (M^+ , 100), 252 ($\text{M}^+ - \text{CH}_3$, 8.2), 251 ($\text{M}^+ - \text{CH}_3 - \text{H}$, 42.6), 236 ($\text{M}^+ - 2\text{CH}_3 - \text{H}$, 15.5), 223 (16.2), 203 (15.2), 191 (2.6), 177 (2.8), 166 (9.1), 91 (0.5), 77 (2.1), 65 (0.2). Anal. Calcd. for $\text{C}_{17}\text{H}_{17}\text{NS}$ (267): C, 76.4; H, 6.36; N, 5.24; S, 11.98. Found: C, 76.21; H, 6.52; N, 5.14; S, 11.7.

4,4-Dimethyl-5,6,8,9,10,11-hexahydro-4H-pyrido[3,2,1-*jk*]carbazole (12). Yellowish viscous oil: n_D^{25} 1.6352; IR (Film) ν 3050, 2910, 1610, 1490, 1450, 1320, 740 cm^{-1} ; ^1H NMR (90 MHz, CDCl_3 , ppm), δ = 1.25 (6H, 2s, 2 CH_3), 1.8 (6H, unresolved m, CH_2 and 2 CH_2 of tetrahydrocarbazole ring), 2.6 (4H, broad m, 2 CH_2), 3.8 (2H, t, J = 6Hz, cyclic NCH_2) and 6.6-7.3 (3H, m, Ar-H); MS (EI, 70 eV) m/z (%), 241 ($\text{M}^+ + 2$, 4.9), 240 ($\text{M}^+ + 1$, 26.5), 239 (M^+ , 100), 223 ($\text{M}^+ - \text{CH}_3 - \text{H}$, 31.8), 209 ($\text{M}^+ - 2\text{CH}_3$, 12.9), 195 (81.5), 181 (87.7), 166 (38.8), 90 (11.1), 77 (41.6), 66 (2.5). Anal. Calcd. for $\text{C}_{17}\text{H}_{21}\text{N}$ (239): C, 85.35; H, 8.78; N, 5.85. Found: C, 85.11; H, 8.72; N, 5.84.

5,5-Dimethyl-2-phenyl-4,5-dihydrocyclopenta[*de*]quinoline (13). Yellowish viscous oil: n_D^{25} 1.634; IR (Film) ν 3050, 2900-2980, 1590, 1510, 1450, 1355, 1170, 760 cm^{-1} ; ^1H NMR (90 MHz, CDCl_3 , ppm), δ = 1.7 (6H, s, 2 CH_3), 4.6 (2H, s, CH_2) and 7.4-8.3 (9H, d, Ar-H); MS (EI, 70 eV) m/z (%), 261 ($\text{M}^+ + 2$, 58.6), 259 (M^+ , 6.6), 244 ($\text{M}^+ - \text{CH}_3$, 3.1), 228 ($\text{M}^+ - 2\text{CH}_3 - \text{H}$, 6.0), 215 (11.5), 201 (65.3), 177 (100), 166 (7.3), 90 (0.1), 77 (1.2), 66 (0.6). Anal. Calcd. for $\text{C}_{19}\text{H}_{17}\text{N}$ (259): C, 88.03; H, 6.56; N, 5.4. Found: C, 87.68; H, 6.54; N, 5.27.

4,4-Dimethyl-1-phenyl-1,2,3,4-tetrahydroquinoline (14). White crystals: m.p. 82 °C from methanol; IR (KBr) ν 3040, 2950, 1590, 1490, 1310, 755, 690 cm^{-1} ; ^1H NMR (90 MHz, CDCl_3 , ppm), δ = 1.3 (6H, s, 2 CH_3), 1.7 (2H, t, J = 6Hz, CH_2), 3.5 (2H, t, J = 6Hz, CH_2) and 6.6-7.3 (9H, d, Ar-H); MS (EI, 70 eV) m/z (%), 237 (M^+ , 5.9), 236 ($\text{M}^+ - \text{H}$, 39.4), 221 ($\text{M}^+ - \text{CH}_3 - \text{H}$, 56.9), 207 ($\text{M}^+ - 2\text{CH}_3$, 3.6), 193 (11.6), 179 (18.2), 168 (100), 166 (34.1), 90 (16.0), 77 (4.9), 65 (5.7). Anal. Calcd. for $\text{C}_{17}\text{H}_{19}\text{N}$ (237): C, 86.07; H, 8.01; N, 5.9. Found: C, 85.85; H, 7.92; N, 6.1.

6,6-Dimethyl-2-phenyl-5,6-dihydro-4H-pyrrolo[3,2,1-*ij*]quinoline (15). Reddish viscous oil: n_D^{25} 1.624; IR (Film) ν 3060, 2970, 1600, 1568, 1480, 1440, 1360, 1070, 740, 695 cm^{-1} ; ^1H NMR (90 MHz, CDCl_3 , ppm), δ = 1.25 (6H, 2s, 2 CH_3), 1.8 (2H, t, J = 6Hz, CH_2), 4.1 (2H, t, J = 6Hz, CH_2), 6.35 (1H, s, CH) and 6.7-7.5 (8H, m, Ar-H); MS (EI, 70 eV) m/z (%), 262 ($\text{M}^+ + 1$, 22.9), 261 (M^+ , 86.8), 246 ($\text{M}^+ - \text{CH}_3$, 100), 231 ($\text{M}^+ - 2\text{CH}_3$, 10.3), 217 (10.9), 192 (84.0), 177 (5.7), 167 (6.4), 166 (7.2), 90 (5.8), 77 (74.2), 66 (1.7). Anal. Calcd. for $\text{C}_{19}\text{H}_{19}\text{N}$ (261): C, 87.35; H, 7.27; N, 5.36. Found: C, 87.57; H, 7.44; N, 5.06.

Acknowledgements

The authors wish to thank Assiut University, Assiut, Egypt for all the facilities and support received while performing and writing this work.

References

1. Kouznetsov, V.; Palma, A. R.; Ewert, C. A.; Varlamov, A.V. *J. Heterocycl. Chem.* **1998**, *35*, 761.
2. Katritzky, A. R.; Rachwal, S.; Rachwal, B. *Tetrahedron* **1996**, *52*, 15031.
3. (a) Roberts, R. M.; Khalaf, A. A. *Friedel-Crafts Alkylation Chemistry. A Century of Discovery*; Marcel Dekker: New York, 1984. (b) Olah, G. A.; Krishnamurti, R.; Prakash, G. K. S. In *Comprehensive Organic Synthesis*; Trost, B. M.; Fleming, I. Eds.; Pergamon Press: Oxford, 1991; Vol. 3, Chapter 1.8, p 293. (c) Barclay, L. R. C. In *Friedel-Crafts and Related Reactions*; Olah, G. A. Ed.; Interscience: New York, 1964; Vol. II, Chap. 22 and references therein.
4. (a) Khalaf, A. A.; Roberts, R. M. *J. Org. Chem.* **1969**, *34*, 3571; *ibid*, **1966**, *31*, 89; *ibid*, **1972**, *37*, 4227; *ibid*, **1971**, *36*, 1040 and references therein. (b) Khalaf, A. A., *Rev. Roum Chim.* **1973**, *18*, 297; *ibid*, **1974**, *19*, 1373.
5. (a) Beck, J. B.; Booher, R. N.; Brown, A. C.; Kwok, R.; Pohland, A. *J. Am. Chem. Soc.* **1967**, *89*, 3934. (b) Conley, R. T.; Knopka, W. N. *J. Org. Chem.* **1964**, *29*, 496. (c) Plostnieks, J. U. S. Patent 3,706,522, 1973; *Chem. Abstr.* **1973**, *78*, 29641f.
6. Smith, P. A. S. *J. Am. Chem. Soc.* **1952**, *74*, 1096.
7. Howland, L.; Jensen, H. *J. Am. Chem. Soc.* **1926**, *48*, 1988.
8. Cauquil, G.; Cassadevall, A. *Compt. Rend.* **1947**, *225*, 578.
9. Smith, N. L. *J. Am. Chem. Soc.* 1950, *72*, 4313.
10. Rosenmund, K. W.; Zymalkowski, F. *Chem. Ber.* **1952**, *85*, 152.
11. Amacker, T. M., Brit. Patent 653,452, May 16, 1951.
12. Farbenind, I. G. A. –G., Fr. Patent 47,563, June 4, 1937.
13. Jones, R. G.; Soper, Q. F.; Behrens, O. K.; Corse, J. W. *J. Am. Chem. Soc.* 1948, *70*, 2843.
14. Brown, B. R.; Hammick, D. L.; Thewlis, B. H. *J. Chem. Soc.* **1951**, 1145.
15. Khalaf, A. A.; Makki, M. S. I. T.; Kabli, R. A. *J. Indian Chem.Soc.* **1997**, *74*, 148.
16. Khalaf, A. A.; Awad, I. M.; El-Emary, T. I.; Abd El-Aal, H. A. K. *J. Indian Chem. Soc.* **2008**, *85*, 6.
17. Khalaf, A. A.; Makki M. S. I. T.; Kabli, R. A. *J. Indian Chem. Soc.* **1997**, *74*, 148.
18. Khalaf, A. A.; Awad, I. M.; El-Emary, T. I.; Abd El-Aal, H. A. K. *J. Indian Chem. Soc.* **2006**, *83*, 10.
19. Khalaf, A. A.; El-Khawaga, A. M.; Awad, I. M.; Abd El-Aal, H. A. K. *Arkivoc* **2009**, (xiv), 314.