# Base Catalyzed Synthesis of Novel Fused-Imidazoles from *N*-Vinyl-1*H*-imidazole

Ashraf A. Aly

Chemistry Department, Faculty of Science, El-Minia University, El-Minia, A. R. Egypt

Reprint requests to Dr. Ashraf A. Aly. Fax: +2086346876. E-mail: ashraf160@yahoo.com

Z. Naturforsch. **60b,** 106 – 112 (2005); received March 26, 2004

Syntheses of various classes of fused-imidazoles are reported. The key to their successful synthesis depends on the reaction of *N*-vinyl-1*H*-imidazole with the $\pi$-deficient compounds under basic conditions. Reaction of the target imidazole with 1,1,2,2-tetracyanoethylene and dimethyl acetylenedicarboxylate afforded pyrrolo[1,2-*a*]imidazoles. On the other site, reaction of the target imidazole with 2-dicyanomethyleneindane-1,3-dione, 2,3-dicyano-1,4-naphthoquinone gave indanylimidazolo-[1,2-*a*]azepine and imidazolo[2,1-*a*]phenanthridine derivatives, respectively. Under basic reaction condition, various classes of imidazolo[2,1-*a*]isoquinolines were obtained by the reaction of *N*-vinyl-1*H*-imidazole with 2,3,5,6-tetrachloro-1,4-benzoquinone, 2,3-dichloro-1,4-naphthoquinone, 2,3-dichloro-5,6-dicyano-1,4-benzoquinone and 3,4,5,6-tetrachloro-1,2-benzoquinone.

*Key words:* *N*-Vinyl-1*H*-imidazole, Base Catalysis, $\pi$-Deficients, Fused-Imidazoles

## 1. Introduction

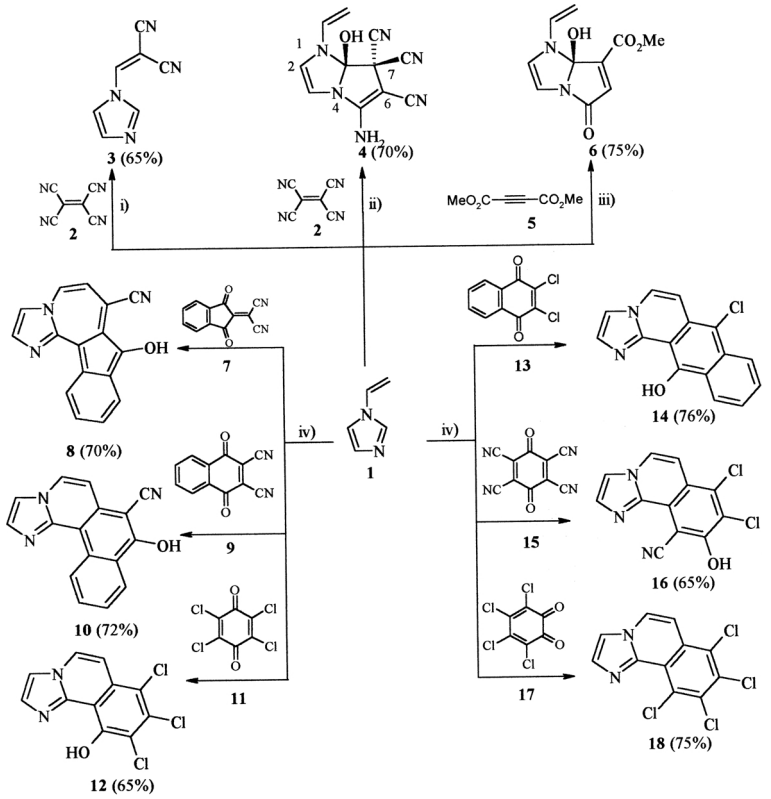
Vinyl substituted heterocyclic compounds have been used as dienes in Diels-Alder reactions to synthesize compounds of medicinal interest [1]. Although *N*-vinyl-1*H*-imidazole is a cheap purchase chemical, its chemistry has been little investigated due the ease of its polymerization [2 – 6]. Vinyl hetero-analogues (1-vinyl-pyrroles, -indoles, -pyrazoles and -carbazoles) require either the use of a highly reactive dienophile or extreme conditions to undergo Diels-Alder across the *cis*-diene of the ring system [1, 7]. It was reported on the dipolarophilic character of *N*-vinyl-1*H*-imidazole in 1,3-dipolar cycloadditions [8], whereas the target molecule behaved as a dienophile in its reaction with 5,5'-bi-1,2,4-triazines [9]. Moreover, mineral and/or Lewis acids catalyze the transformation of vinylimidazoles to produce polymers across the double bond *via* charge-transfer complexation [10]. However, base catalyzed addition of *N*-vinyl-imidazoles is used to initiate the nucleophilic reactions of C-2 [11, 12]. It was also shown that basic conditions enhancing *pseudo*-Michael reactions of substituted imidazoles bearing substituents in position-1 (aryl or alkyl) lead to the production of isomeric enamines due to possibility of a tautomeric shift of the C=N double bond [13, 14].

Some time ago, we reported on the syntheses of various heterocyclic and polycyclic compounds *via* cycloaddition reactions of aromatic diimines [15], azomethine compounds having [2.2]paracyclophane [16], ethenyl-[2.2]paracyclophane [17], and 4-arylidene-2-phenyl-5(4*H*)-1,3-oxazolones [18] with some chosen dienophiles. Recently, we have succeeded to synthesize many classes of heterophanes derived from [2.2]paracyclophane [19, 20], in addition to the synthesis of heterocyclic compounds with pharmaceutical and biological interest [21, 22].

Fused imidazoles are described to have antibacterial, current antiviral therapy for chronic hepatitis C, antifungal and perspectives of drug design that targets RNA [23]. Moreover, the structural features of these compounds are found in nature and are incorporated as key structural fragments in many biological and chemical systems [24]. Therefore, our aim is extended to the synthesis of fused-imidazoles from the reactions between *N*-vinyl-1*H*-imidazole (**1**) and various selected $\pi$-deficient compounds.

## 2. Results and Discussion

On reaction of **1** with 1,1,2,2-tetracyanoethylene (**TCNE**, **2**) in acetonitrile at room temperature, the reaction failed to give any product. On refluxing the two starting materials in toluene, the reaction worked and gave the cycloadduct **3** in 65% yield (Scheme 1). The structure of **3** was established on the basis of mass,




*Reagents and conditions*: i) **2**, toluene, reflux, 20 h; ii) **2**, dioxane, $Et_3N$, $-15$ °C; 1 h, r. t., 1 h, reflux, 4 h; iii) **5**, EtOH, $Et_3N$, $-15$ °C, 1 h, r. t., 1 h, reflux, 24 h; iv) **7, 9, 11, 13, 15** or **17**, $CH_3COOEt$, $Et_3N$, $-15$ °C, 1 h, r. t., 1 h, reflux, 1 – 3 d.

Scheme 1: Reactions of **1** with $\pi$-deficient compounds.

IR, $^1$H NMR, $^{13}$C NMR spectra as well as elemental analysis. Elemental analysis and the mass spectrum of **3** established its molecular formula as $C_7H_4N_4$. The $^1$H NMR spectrum of **3** revealed only four protons, two doublets at $\delta = 7.40$, 7.60 ($J_{H,H} = 1.3$ Hz) and others singlets at $\delta = 8.00$ and 8.50. The $^{13}$C NMR spectrum of **3** was in accordance with its $^1$H NMR spectrum and showed two very close signals of nitrile carbons at $\delta = 115.30$ and 115.40. Five distinguished carbon signals resonated in the $^{13}$C NMR spectrum of **3** at $\delta = 80.50$, 129.40, 130.00, 136.30 and 142.00 (Fig. 1, see also Section 3). Compound **3** was unequivocally identified as 2-imidazolo-1-ylmethylenemalononitrile. The mechanism of the formation of **3** is probably based on a $[2\pi + 2\pi]$cycloaddition reaction followed by elimination of 2-methylenemalononitrile (Scheme 1).

Previously it was mentioned that the addition of a base to vinylimidazoles catalyzes nucleophilic reactions. Thus, we treated a solution of **1** in dioxane together with few drops of triethylamine at $-15$ °C. Subsequently, compound **2** was added and the reaction was completed at refluxing temperature (see Section 3). We succeeded, within 4 h, to obtain compound **4** in 70% yield (Scheme 1). Mass spectral and elemental analysis of **4** confirmed its molecular formula as $C_{11}H_8N_6O$. The $^1$H NMR spectrum of **4** indicated the presence of the vinylic double bond protons at $\delta = 5.50$ (dd, 1 H, $J_{H,H} = 11.0$, 1.4 Hz, vinyl-$H_{trans}$), 5.64 (dd, 1 H, $J_{H,H} = 17.0$, 1.4 Hz, vinyl-$H_{cis}$) and 6.70 (dd, 1 H, $J_{H,H} = 17.5$, 10.5 Hz, vinyl-$H_{gem}$). The $^1$H NMR spectrum of **4** also showed two broad singlets at $\delta = 7.10$ and 7.30 corresponding to H-2 and H-3 protons of the imidazole ring. Besides, the $^1$H NMR spectrum of **4** revealed another two singlets resonated at $\delta$ = 4.50 and 3.60 assigned to the hydroxyl and amino protons, respectively. The $^{13}$C NMR spectrum of **4** revealed the two vinylic-carbons at $\delta = 106.20$ and 128.40 (Fig. 1, see Section 3). The two signals of imidazole-carbons (*C*-3 and *C*-2) resonated in the $^{13}$C NMR spectrum of **4** at $\delta = 129.10$ and 128.90, respectively. The signals of *C*-5, *C*-7a and *C*-6 carbons appeared in the $^{13}$C NMR spectrum of **4** at $\delta = 149.80$, 90.50 and 110.30, respectively (Fig. 1). COSY H-H spectrum of compound **4** showed long-range coupling between the vinylic-HC proton and H-2 of the imidazole ring. From NMR spec-

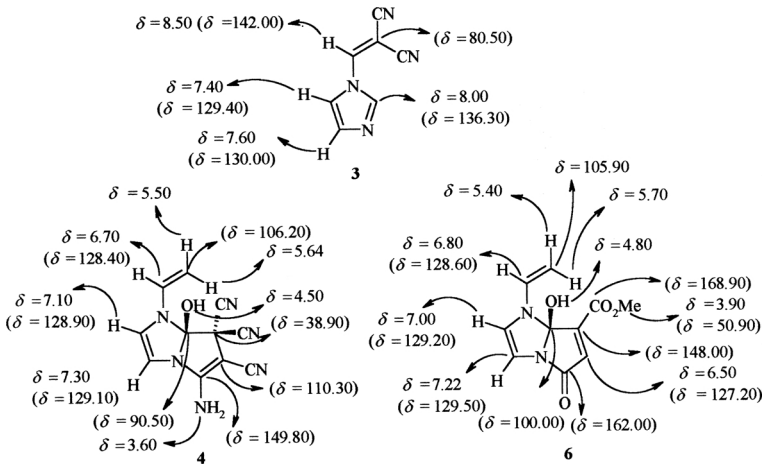



Fig. 1. Distinctive $\delta'$s values of compounds **3, 4** and **6**.

tra of **4**, some $\delta$'s values were distinguished as given in Fig. 1. According to semi-empirical calculations using the MM2 level of theory [25], the stereoview of compound **4**, in the case of minimization the steric energy value ($\Delta$E = 40.80 Kcal/mol), is as suggested in Scheme 1.

Reaction of **1** with diemethyl acetylenedicarboxylate (**5**) in refluxing toluene failed to give any cycloadduct. In ethanol solution, on the other hand, the reaction of **1** with **5** under basic conditions afforded compound **6** in 75% yield (Scheme 1). The IR spectrum of **6** showed distinguished absorption bands at $\lambda_{max}$ 3490, 1720 and 1685 cm$^{-1}$ arising from to the absorption of the OH, carbonyl-ester and $\alpha,\beta$-unsaturated carbonyl. The $^1$H NMR spectrum of **6** revealed, in addition to the vinylic- and imidazole-protons, two singlets at $\delta$ = 6.50 and 3.90 assigned to H-6 and the *Me*-ester protons, respectively. The $^{13}$C NMR spectrum of **6** showed five peculiar signals at $\delta$ = 162.00, 127.20, 148.00, 168.90 and 50.90 related to *C*-5, *C*-6, *C*-7, CO-ester and *Me*-ester carbons, respectively. The COSY H-H and C-H spectra of **6** revealed some distinctive $\delta$'s values as given in Fig. 1. According to semi-empirical calculations using the MM2 level of theory [25], the stereoview of **6**, in case of minimization the steric energy value ($\Delta$E = 24.80 Kcal/mol), is as suggested in Scheme 1.

The p$K_a$ of imidazole is 14.4, which means that in most instances it binds through *N*-3, with the *N*-1 remaining protonated. Imidazole is a weak acid and, consequently, deprotonation at *C*-2 occurs in small percentage. Interestingly, the action of base on **1** will directly increase the direction towards the anion formation at *C*-2 (**1-II**). Therefore, under basic condition, the reaction of the intermediate **1-II** with either **2** or **5** can explain the formation of **4** or **6** (Fig. 2).

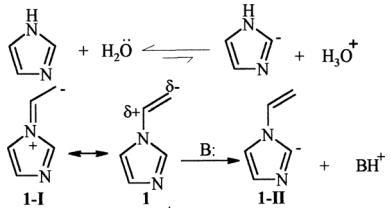



Fig. 2. Base catalyzes anion formation at C-2 of **1**.

We decided to investigate the basic catalytic reaction of **1** with 2-dicyanomethyleneindane-1,3-dione (**7**) [26], 2,3-dicyano-1,4-naphthoquinone (**9**) [27], 2,3,5,6-tetrachloro-1,4-benzoquinone (**11**), 2,3-dichloro-1,4-naphthoquinone (**13**), 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (**15**) and 3,4,5,6-tetrachloro-1,2-benzoquinone (**17**). Particularly interesting, the reaction of **1** with either **7** or **9** proceeded to afford products **8** and **10**, respectively (Scheme 1). Elemental analysis and mass spectrometry of either **8** or **10** confirmed the same molecular formula $C_{16}H_9N_3O$. The IR spectra of both **8** and **10** showed absorptions of cyano groups at $\lambda_{max}$ 2215 – 2221 cm$^{-1}$, whereas the phenolic-hydroxy groups absorbed at $\lambda_{max}$ 3480 – 3500 cm$^{-1}$. The phenolic- and the cyano-carbons appeared in the $^{13}$C NMR spectra of both **8** and **10** at $\delta$ = 150.00 – 150.86 and 113.60 – 113.80, respectively. The COSY H-H and C-H spectra helped to distinguish some of the $\delta$'s values of both **8** and **10** as shown in Fig. 3.

In the same manner, **1** reacted with **11** and **13** to yield the imidazoloisoquinoline **12** and imida-

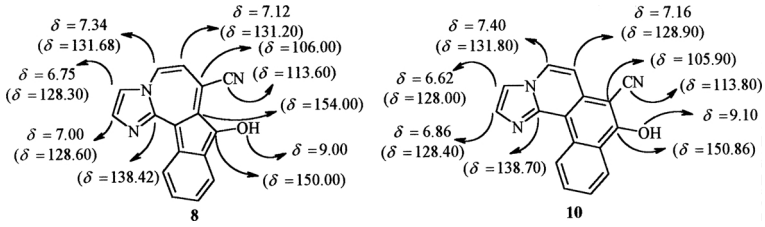



Fig. 3. Distinctive $\delta'$s values of compounds **8** and **10**.

zolobenzo[g]isoquinoline **14**, respectively (Scheme 1). In continuation to this strategy we carried out the reaction between **1** and **15** under the same reaction conditions. The reaction afforded another derivative of imidazoloisoquinoline **16** (Scheme 1). Elemental analysis and mass spectrometry confirmed the molecular formula of **16** as $C_{12}H_5Cl_2N_3O$. The IR spectroscopy of **16** did not show any absorption of a carbonyl group, whereas a peak appeared at $\lambda_{max}$ 3500 $cm^{-1}$ caused by a phenolic-hydroxy group. Additionaly, a characteristic cyano absorption peak was noted in the IR spectrum of **16** at $\lambda_{max}$ 2220 $cm^{-1}$. The phenolic- and the cyano-carbons appeared in the $^{13}C$ NMR of **16** at $\delta = 150.98$ and 113.70, respectively (see Section 3). However, on reaction of **1** with another $\pi$-acceptor namely, 3,4,5,6-tetrachloro-1,2-benzoquinone (***o*-CHL**, **17**), the tetrachloroimidazoloisoquinoline **18** was obtained in 75% yield (Scheme 1). Analogously, the behavior of the exocyclic-methylene carbons, attached directly to the nitrogen hetero-atoms [7, 28, 29] or those exocyclic-methylene carbons exist in conjugation with these heteroatoms [30, 31], indicated nucleophilic cycloaddition reactions under thermal or basic conditions. It is also worth mentioning that reactions of **1** with the aforementioned quinones failed to give any cycloadducts under direct thermal conditions.

In conclusion, our results demonstrate an extraordinary reactivity of **1** toward $\pi$-deficient compounds.

## 3. Experimental Section

Melting points are uncorrected values. $^1H$ NMR and $^{13}C$ NMR spectra were carried out in $CDCl_3$, or DMSO-$d_6$. The chemical shifts relative to the internal standard TMS, Bruker AM 400 (400.134 MHz and 100.60 MHz). Coupling constants are expressed in Hz. For preparative thin layer chromatography (PLC), glass plates (20 × 48 cm) were covered with slurry of silica gel Merck $PF_{254}$ and air-dried using the solvents listed for development. Zones are detected by quenching of indicator fluorescence upon exposure to 254 nm UV light. Elemental analyses were carried in Assuit Microanalysis center of Assuit University. Mass spectroscopy was performed by Finnigan MAT 8430 spectrometer at 70 eV. IR spectra were run using KBr on Schimadzu 470 spectrometer.

### *3.1. Starting materials*

*N*-Vinyl-1*H*-imidazole (**1**) and $\pi$-deficient compounds, under investigation, were bought from Fluka and Aldrich. 1,1,1,2-Tetracyanoethylene (**TCNE**, **2**, Merck) was purified by crystallization from chlorobenzene and sublimed, m. p. 198 – 199 °C. 2-Dicyanomethyleneindane-1,3-dione (**7**), and 2,3-dicyano-1,4-naphthoquinone (**9**) were prepared following the procedure mentioned in references [26] and [27], respectively.

### *3.2. Reaction of* **1** *with 1,1,2,2-tetracyanoethylene (***2***)*

#### 3.2.1. 2-Imidazolo-1-ylmethylene-malononitrile (**3**)

In 250 $cm^3$ two-necked round bottom flask was flame-dried under $N_2$ atmosphere and then cooled to room temperature. In this flask, toluene (100 $cm^3$) contained a mixture (0.20 g, 2 mmol) of **1** and (0.26 g, 2 mmol) of **2**. The mixture was refluxed with stirring for 20 h. The solvent was evaporated under vacuum and the residue was applied on PLC using toluene as eluent to afford product **3**. The title compound **3** (0.15 g, 65%) was obtained as yellowish-green crystals ($R_f$ 0.6, $CH_2Cl_2$), m. p. 140 °C (acetone). – IR (KBr): $\tilde{\nu} = 3010 - 2980$ (Ar-CH), 2220 (CN), 1590 (C=N) $cm^{-1}$. – UV($CH_3CN$) $\lambda_{max}$ (log $\varepsilon$) 410 (4.05). – $^1H$ NMR (400.134 MHz, $CDCl_3$): $\delta = 7.40$ (d, 1 H, $J_{H,H}$ = 1.3 Hz, H-5), 7.60 (d, 1 H, $J_{H,H}$ = 1.3 Hz, H-4), 8.00 (s, 1 H, H-2), 8.50 (s, 1 H, *H*C=C). – $^{13}C$ NMR (100.6 MHz, $CDCl_3$): $\delta = 80.50$ (*C*$(CN)_2$), 115.30, 115.40 (CN), 129.40 (*C*-5), 130.00 (*C*-4), 136.30 (*C*-2), 142.00 [*C*H=C$(CN)_2$]. – MS (EI, 70 eV): *m/z* (%) 144 (100) [$M^+$], 118 (40), 92 (24), 78 (22), 50 (14), 24 (18). – $C_7H_4N_4$ (144.134): calcd. C 58.33, H 2.80, N 38.87; found C 58.20, H 2.70, N 39.00.

#### 3.2.2. 5-Amino-7a-hydroxy-1-vinyl-1,5,6,7a-tetrahydro-1*H*-pyrrolo[1,2-*a*]-imidazole-6,7,7-tricarbonitrile (**4**)

A 250 $cm^3$ two-necked round bottom flask was flame-dried under $N_2$ atmosphere and then cooled to room tem-

perature. In this flask, dioxane (100 ml) contained **1** (0.20 g, 2 mmol) and few drops of triethylamine was placed and stirred in an ice cold bath (−15 °C) under a stream of $N_2$ atmosphere for 1 h. To the latter intense yellow, a solution of **2** (0.26 g, 2 mmol) in dioxane (30 ml) was added dropwise. The reaction mixture was then stirred at room temperature under $N_2$ for another 1 h. The reaction mixture was refluxed for 4 h. The solvent was evaporated in vacuum, and the residue was dissolved in acetone (30 ml) and then subjected to PLC using toluene as eluent to give **4**. The title compound **4** (0.24 g, 70%) was obtained as pale yellow crystals ($R_f$ 0.4, $CH_2Cl_2$), m. p. 240 – 242 °C (acetone). – IR (KBr): $\tilde{\nu} = 3490$ (OH), 3230 ($NH_2$), 2985 – 2870 (Ali.-CH), 2222 – 2210 (CN), 1590 (C=N), 990, 970 $cm^{-1}$. – UV($CH_3CN$) $\lambda_{max}$ ($\log\varepsilon$) 398 (3.90). – $^1$H NMR (400.134 MHz, $CDCl_3$): $\delta = 3.60$ (br s, 2 H, $NH_2$), 4.50 (br s, 1 H, OH), 5.50 (dd, 1 H, $J_{H,H} = 11.0$, 1.4 Hz, vinyl-H*trans*), 5.64 (dd, 1 H, $J_{H,H} = 17.0$, 1.4 Hz, vinyl-H*cis*), 6.70 (dd, 1 H, $J_{H,H} = 17.5$, 10.5 Hz, vinyl-H*gem*), 7.10 (s, 1 H, H-2), 7.30 (s, 1 H, H-3). – $^{13}$C NMR (100.6 MHz, $CDCl_3$): $\delta = 38.90$ (C-7), 90.50 (*C*-7a), 106.20 (CH= *C*$H_2$), 110.30 (C-6), 113.40, 113.60, 114.00 (CN), 128.40 (*C*H=$CH_2$), 128.90 (*C*-2), 129.10 (*C*-3), 159.80 (*C*-5). – MS (EI, 70 eV): *m/z* (%) 240 (100) [$M^+$], 224 (40), 206 (22), 198 (18), 172 (16), 156 (24), 144 (20), 104 (22), 92 (34), 78 (16), 50 (12), 24 (14). – $C_{11}H_8N_6O$ (240.221): calcd. C 55.00, H 3.36, N 34.96; found C 55.17, H 3.30, N 35.00.

### *3.3. Reactions of* **1** *with dimethyl acetylenedicarboxylate (***5***)*

#### Methyl 7a-hydroxy-5-oxo-1-vinyl-5,7a-dihydro-1*H*-pyrrolo[1,2-*a*]imidazole-7-carboxylate (**6**)

On applying the same procedure mentioned before, as a mixture of **1** (0.19 g, 2 mmol) and **5** (0.29 g, 2 mmol) in ethanol (200 ml) together with few drops of triethyl amine. The mixture was refluxed for 24 h. The solvent was evaporated in vacuum, and the residue was dissolved in acetone (40 ml) and then subjected to PLC using toluene: ethyl acetate as (10:1) eluent to give **6**. The title compound **6** (0.24 g, 75%) was obtained as pale yellow crystals ($R_f$ 0.4, $CH_2Cl_2$), m. p. 160 – 162 °C (ethanol). – IR (KBr): $\tilde{\nu} = 3490$ (OH), 2990 – 2860 (Ali.-CH), 1720 (CO-ester), 1685 ($\alpha,\beta$-CO), 1585 (C=N), 992, 978 $cm^{-1}$. – UV($CH_3CN$) $\lambda_{max}$($\log\varepsilon$) 398 (3.90). – $^1$H NMR (400.134 MHz, $CDCl_3$): $\delta = 3.90$ (s, 3 H, *Me*-ester), 4.80 (br s, 1 H, OH), 5.40 (dd, 1 H, $J_{H,H} = 11.0$, 1.4 Hz, vinyl-H*trans*), 5.70 (dd, 1 H, $J_{H,H} = 17.0$, 1.4 Hz, vinyl-H*cis*), 6.50 (s, 1 H, H-6), 6.80 (dd, 1 H, dd, $J_{H,H} = 17.5$, 10.5 Hz, vinyl-H*gem*), 7.00 (s, 1 H, H-2), 7.22 (s, 1 H, H-3). – $^{13}$C NMR (100.6 MHz, $CDCl_3$): $\delta = 50.90$ (*Me*-ester), 100.00 (*C*-7a), 105.90 (CH=$CH_2$), 127.20 (*C*-6), 128.60 (*C*H=$CH_2$), 129.20 (*C*-2), 129.50 (*C*-3), 148.00 (*C*-7), 162.00 (*C*-5), 168.90 (CO-ester). – MS (EI, 70 eV): *m/z* (%) 222 (100) [$M^+$], 206 (28), 190 (20), 174 (14), 146 (16), 120 (30), 92 (34), 78 (16), 50 (12), 24 (14). – $C_{10}H_{10}N_2O_4$ (222.197): calcd. C 54.05, H 4.54, N 12.61; found C 54.12, H 4.50, N 12.54.

### *3.4. Reaction of* **1** *with* **7**, **9**, **11**, **13**, **15** *and* **17***: General procedure*

To the intense yellow a solution (0.2 g, 2 mmol) of **1**, as shown before, either of **7, 9, 11, 13, 15** or **17** (2 mmol) was added dropwise in ethyl acetate (200 ml). The reaction mixture was further refluxed with stirring under $N_2$ atmosphere for 1 – 3 d (the reaction was followed up by TLC analysis). The solvent was evaporated in vacuum, and the residue was directly applied on column chromatography using dichloromethane as eluent to give the following compounds.

#### 3.4.1. 8-Hydroxy-indanyl[*c*]imidazolo[1,2-*a*]-azepine-7-carbonitrile (**8**)

Compound **8** (0.37 g, 70%) was obtained as purple crystals ($R_f$ 0.2, $CH_2Cl_2$), m. p. 220 – 224 °C (acetone). – IR (KBr): $\tilde{\nu} = 3480$ (OH), 3045 – 3008 (Ar-CH), 2215 (CN), 1590 (C=N) $cm^{-1}$. – UV($CH_3CN$) $\lambda_{max}$ ($\log\varepsilon$) 410 (4.20). – $^1$H NMR (400.134 MHz, $CDCl_3$): $\delta = 6.75$ (s, 1 H, H-3), 7.00 (s, 1 H, H-2), 7.12 (d, 1 H, $J_{H,H} = 8.2$ Hz, H-6), 7.20 – 7.48 (m, 5 H, H-5 and Ar-H), 9.00 (br s, 1 H, OH). – $^{13}$C NMR (100.6 MHz, $CDCl_3$): $\delta = 106.00$ (*C*-7), 113.60 (CN), 124.90, 127.90 (Ar-CH), 128.30 (*C*-3), 128.60 (*C*-2), 128.86, 129.30 (Ar-CH), 130.22, 130.80 (Ar-*C*), 131.20 (*C*-6), 131.68 (*C*-5), 134.82 (Ar-*C*), 138.42 (azomethine-*C*), 150.00 (*C*-8), 154.00 (*C*-7a). – MS (EI, 70 eV): *m/z* (%) 260 (30) [M + 1], 259 (100) [$M^+$], 242 (30), 216 (22), 204 (24), 190 (18), 166 (22), 132 (34), 128 (24), 116 (14), 104 (18), 90 (24), 76 (20). – $C_{16}H_9N_3O$ (259.262): calcd. C 74.12, H 3.50, N 16.21; found C 74.30, H 3.40, N 16.30.

#### 3.4.2. 8-Hydroxy-imidazolo[2,1-*a*]phenanthridine-7-carbonitrile (**10**)

Compound **10** (0.39 g, 72%) was obtained as buff crystals ($R_f$ 0.3, $CH_2Cl_2$), m. p. 242 – 244 °C (ethanol). – IR (KBr): $\tilde{\nu} = 3500$ (OH), 3060 – 3012 (Ar-CH), 2221 (CN), 1590 (C=N) $cm^{-1}$. – UV($CH_3CN$) $\lambda_{max}$ ($\log\varepsilon$) 400 (3.90). – $^1$H NMR (400.134 MHz, DMSO-$d_6$): $\delta = 6.62$ (s, 1 H, H-3), 6.86 (s, 1 H, H-2), 7.16 (d, 1 H, $J_{H,H} = 8.2$ Hz, H-6), 7.28 – 7.56 (m, 5 H, H-5 and Ar-H), 9.10 (br s, 1H, OH). – $^{13}$C NMR (DMSO-$d_6$, 100.6 MHz): $\delta = 105.90$ (*C*-7), 113.80 (CN), 126.40, 126.90, 127.80 (Ar-CH), 128.00 (*C*-3), 128.40 (*C*-2), 128.90 (*C*-6), 129.00 (Ar-CH), 130.42 (Ar-*C*), 131.80 (*C*-5), 132.00, 133.60, 136.20 (Ar-*C*), 138.70

(azomethine-*C*), 150.86 (*C*-8). – MS (EI, 70 eV): *m/z* (%) 260 (28) [M + 1], 259 (100) [$M^+$], 242 (24), 218 (20), 206 (18), 190 (22), 166 (24), 128 (30), 116 (18), 104 (14), 90 (20), 76 (18). – $C_{16}H_9N_3O$ (259.262): calcd. 74.12, H 3.50, N 16.21; found C 74.28, H 3.46, N 16.24.

3.4.3. 7,8,9-Trichloro-imidazolo[2,1-*a*]isoquinoline-10-ol (**12**)

Compound **12** (0.38 g, 65%) as yellow crystals ($R_f$ 0.2, $CH_2Cl_2$), m. p. 280 – 282 °C (acetone). IR (KBr): $\tilde{\nu}$ = 3480 (OH), 3048 – 3010 (Ar-CH), 1590 (C=N) $cm^{-1}$. – UV($CH_3CN$) $\lambda_{max}$ ($\log\varepsilon$) 380 (3.60). – $^1$H NMR (400.134 MHz, DMSO-$d_6$): $\delta$ = 6.46 (d, 1 H, d, $J_{H,H}$ = 8.2 Hz, H-6), 6.62 (d, 1 H, $J_{H,H}$ = 8.0 Hz, H-5), 6.74 (s, 1 H, H-3), 6.80 (s, 1H, H-2), 9.10 (br s, 1 H, OH). – $^{13}$C NMR (100.6 MHz, DMSO-$d_6$): $\delta$ = 123.80 (*C*-6), 124.60 (*C*-5), 125.20, 125.69 (*C*-Cl), 127.10 (*C*-3), 127.40 (*C*-2), 130.40 (*C*-Cl), 131.60, 132.10 (Ar-*C*), 138.40 (azomethine-*C*), 150.60 (*C*-9). – MS (EI, 70 eV): *m/z* (%) 290 (12) [M + 3], 288 (60) [M + 1], 287 (100) [$M^+$], 272 (22), 270 (26), 252 (28), 236 (24), 234 (30), 200 (18), 198 (24), 172 (30), 168 (24), 166 (22), 128 (26), 114 (18), 106 (16), 90 (22), 76 (14). – $C_{11}H_5Cl_3N_2O$ (287.528): calcd. C 45.95, H 1.75, Cl 36.99, N 9.74; found C 45.80, H 1.72, Cl 36.80, N 9.70.

3.4.4. 7-Chloro-imidazolo[2,1-*a*]phenanthridine-12-ol (**14**)

Compound **14** (0.41 g, 76%) as orange crystals ($R_f$ 0.35, $CH_2Cl_2$), m. p. > 300 °C (acetone). – IR (KBr): $\tilde{\nu}$ = 3500 (OH), 3080 – 3030 (Ar-CH), 1680 (CO), 1590 (C=N) $cm^{-1}$. – UV ($CH_3CN$) $\lambda_{max}$ ($\log\varepsilon$) 420 (4.10). – $^1$H NMR (400.134 MHz, DMSO-$d_6$): $\delta$ = 6.10 (d, 1 H, $J_{H,H}$ = 8.2 Hz, H-6), 6.30 (d, 1 H, $J_{H,H}$ = 8.2 Hz, H-5), 6.52 (s, 1 H, H-3), 6.68 (s, 1 H, H-2), 7.20 – 7.42 (3 H, m), 7.65 (dd, 1 H, $J_{H,H}$ = 8.4, 1.3 Hz), 8.10 (m, 1 H). – $^{13}$C NMR (100.6 MHz, DMSO-$d_6$): $\delta$ = 125.00 (*C*-6), 125.60 (*C*-5), 125.90 (*C*-7), 126.20 (*C*-3), 126.60 (*C*-2), 127.70, 128.80, 129.00, 130.00 (Ar-CH), 132.20, 133.00, 133.80, 134.80 (Ar-C), 136.20 (azomethine-*C*), 150.80 (*C*-12). – MS (EI, 70 eV): *m/z* (%) 269 (24) [M + 1], 268 (100) [$M^+$], 266 (20), 252 (18), 222 (24), 220 (20), 180 (32), 156 (24), 128 (30), 104 (26), 92 (26), 76 (16). – $C_{15}H_9ClN_2O$ (268.698): calcd. C 67.05, H 3.38, Cl 13.19, N 10.43; found C 67.18, H 3.30, Cl 13.00, N 10.34.

3.4.5. 7,8-Dichloro-9-hydroxy-imidazolo-[2,1-*a*]isoquinoline-10-carbonitrile (**16**)

Compound **16** (0.37 g, 65%) as orange crystals ($R_f$ 0.50, $CH_2Cl_2$), m. p. > 300 °C (ethyl acetate). – IR (KBr): $\tilde{\nu}$ = 3500 (OH), 3060 – 3020 (Ar-CH), 2220 (CN), 1590 (C=N) $cm^{-1}$. – UV($CH_3CN$) $\lambda_{max}$ ($\log\varepsilon$) 440 (4.60). – $^1$H NMR (400.134 MHz, DMSO-$d_6$): $\delta$ = 6.00 (d, 1 H, $J_{H,H}$ = 8.2 Hz, H-6), 6.20 (d, 1H, $J_{H,H}$ = 8.2 Hz, H-5), 6.40 (s, 1 H, H-3), 6.60 (s, 1 H, H-2), 9.20 (br s, 1 H, OH). – $^{13}$C NMR (100.6 MHz, DMSO-$d_6$): $\delta$ = 100.10 (C-10), 113.70 (CN), 124.80 (*C*-6), 125.40 (*C*-5), 126.40 (*C*-3), 126.80 (*C*-2), 127.40 (*C*-7), 128.90 (*C*-8), 130.40, 134.80, (Ar-*C*), 136.80 (azomethine-*C*), 150.98 (*C*-9). – MS (EI, 70 eV): *m/z* (%) 280 (50) [M + 2], 278 (100) [$M^+$], 262 (22), 244 (18), 242 (20), 228 (24), 226 (30), 202 (32), 200 (34), 164 (40), 162 (42), 128 (22), 114 (18), 94 (22), 67 (16), 52 (14). – $C_{12}H_5Cl_2N_3O$ (278.093): calcd. C 51.83, H 1.81, Cl 25.50, N 15.11; found C 51.70, H 1.80, Cl 25.56, N 15.10.

3.4.6. 7,8,9,10-Tetrachloro-imidazolo[2,1-*a*]isoquinoline (**18**)

Compound **18** (0.48 g, 75%) was obtained as yellow crystals ($R_f$ 0.6, $CH_2Cl_2$), m. p. > 300 °C (ethyl acetate). – IR (KBr): $\tilde{\nu}$ = 3055 – 3010 (Ar-CH), 1595 (C=N), 1580 (CH=CH) $cm^{-1}$. – UV($CH_3CN$) $\lambda_{max}$ ($\log\varepsilon$) 390 (4.00). – $^1$H NMR (400.134 MHz, DMSO-$d_6$): $\delta$ = 5.98 (d, 1 H, $J_{H,H}$ = 8.2 Hz, H-6), 6.24 (d, 1 H, $J_{H,H}$ = 8.4, 1.5 Hz, H-5), 6.84 (s, 1 H, H-3), 7.00 (s, 1 H, H-2). – $^{13}$C NMR (100.6 MHz, DMSO-$d_6$): $\delta$ = 124.60 (*C*-6), 126.50 (*C*-5), 127.50 (*C*-3), 128.20 (*C*-2), 129.40, 130.00, 131.67, 132.24, 132.40, 134.00 (Ar-*C*), 136.20 (azomethine-*C*). – MS (EI, 70 eV): *m/z* (%) 309 (20) [M + 4], 307 (50) [M + 2], 305 (100) [$M^+$], 303 (78), 250 (30), 270 (30), 268 (28), 234 (28), 232 (34), 202 (18), 200 (24), 166 (24), 164 (28), 128 (32), 104 (18), 90 (26), 76 (14). – $C_{11}H_4Cl_4N_2$ (305.974): calcd. C 43.18, H 1.32, Cl 46.35, N 9.16; found C 43.00, H 1.26, Cl 46.20, N 9.12.


[1] J. Sepúlveda-Arques, B. Abarca-González, M. Medio-Simón, Adv. Heterocyclc. Chem. **63**, 339 (1995).

[2] Y. Chen, V. Raika-Dias, C. J. Lovely, Tetrahedron Lett. **44**, 1379 (2003).

[3] K. H. Wu, T. C. Chang, Y. T. Wang, Y. S. Hong, T. S. Wu, Eur. Poly. J. **39**, 239 (2003).

[4] C. Luca, S. Mihailescu, M. Popa, Eur. Poly. J. **38**, 1501 (2002).

[5] C. Alexander, L. Davidson, W. Hayes, Tetrahedron **59**, 2025 (2003).

[6] a) N. Pekel, H. Savas, O. Guven, Colloid & Poly. Science **280**, 46 (2002); b) N. Pekel, B. Salih, O. Guven, J. Mol. Catalysis B. **21**, 273 (2003).

[7] C. J. Lovely, H. Du, H. V. Dias, Org. Lett. **3**, 1319 (2001).

[8] K. Choji, T. Atsushi, T. Tadakuni, J. Heterocycl. Chem. **21**, 201 (1984).
[9] D. Branowska, A. Rykowski, Synlett. **11**, 1892 (2002).
[10] B. A. Trofimov, L. V. Morozova, M. V. Sigalov, A. I. Mikhaleva, M. V. Markova, Makromol. Chem. **188**, 2251 (1987).
[11] K. W. Kottsieper, O. Stelzer, P. Wasserschei, J. Mol. Cat. A. **175**, 285 (2001).
[12] T. Itoh, M. Miyazaki, K. Negata, A. Ohswa, Tetrahedron **56**, 4383 (2000).
[13] a) J. Suwinski, W. Szczepankiewicz, Polish J. Chem. **65**, 515 (1991); b) J. Suwinski, W. Sczepankiewicz, Tetrahedron Asymm. **2**, 941 (1991); c) J. Suwinski, W. Szczepankiewicz, E. M. Holt, Tetrahedron **52**, 14905 (1996); d) W. Szczepankiewicz, J. Suwinski, Tetrahedron Lett. **39**, 1785 (1998); e) W. Szczepankiewicz, J. Suwinski, Tetrahedron **56**, 9343 (2000); f) S. Krompiec, M. Pigulla, W. Szczepankiewicz, T. Bieg, N. Kuznik, K. Leszczynska-Sejda, M. Kubicki, T. Borowiak, Tetrahedron Lett. **42**, 7095 (2001); g) J. Suwinski, W. Szczepankiewicz, K. Swierczek, P. Wagner, K. Walczak, Eur. J. Org. Chem. 1080 (2003).
[14] C. G. Frost, P. Mendonca, J. Chem. Soc. Perkin Trans. I 2615 (1998).
[15] A. A. Aly, N. K. Mohamed, A. A. Hassan, A. E. Mourad, Tetrahedron **55**, 1111 (1999).
[16] A. A. Aly, A. E. Mourad, K. M. El-Shaieb, H. Hopf, Synth. Commun. **31**, 637 (2001).
[17] A. A. Aly, H. Hopf, L. Ernst, Eur. J. Org. Chem. 3021 (2000).
[18] A. A. Aly, Tetrahedron **59**, 6067 (2003).
[19] A. A. Aly, Tetrahedron **59**, 1739 (2003).
[20] A. A. Aly, Org. Biomol. Chem. **1**, 756 (2003).
[21] A. A. Aly, A. E. Mourad, A. A. Hassan, N. K. Mohamed, B. A. Ali, M. M. El-Sayed, Arch. Pharm. Pharm. Med. Chem. **337**, 133 (2004).
[22] A. A. Aly, K. M. El-Shaieb, Tetrahedron **60**, 3797 (2004).
[23] K. Hanazaki, P. Gupta, S. K. Singh, T. Srinivasan, B. Kundu, Geir Hetland, Current Med. Chem.-Anti-Infective Agents **2**, 103 (2003).
[24] K. Bleicher, F. Gerber, Y. Wüthrich, A. Alanine, and A. Capretta, Tetrahedron Lett. **43**, 7687 (2002).
[25] N. L. Allinger, MM2 (91) force field Program, obtained from Quantum Chemistry Program, Indiana University; Molecular Mechanics PM3 Program (ACD/3D), Advanced Chemical Development Inc., Toronto, Canada (1988).
[26] Chatterjee, S. J. Chem. Soc. B. 725 (1969).
[27] M. L. Budni, E. S. Jayadevappa, Spectrochim. Acta. **44A**, 607 (1988).
[28] R. Grigg, T. Mongkolaussavaratana, J. Chem. Soc. Perkin Trans. I 541 (1988).
[29] Siberdt, J. Nasielski, Bull. Soc. Chim. Belg. **106**, 29 (1997).
[30] A. Diáz-Ortiz; J. R. Carrillo, E. Diez-Barra, A. De la Hoz, M. J. Gomez-Escalonilla, A. Moreno, F. Langa, Tetrahedron **52**, 9237 (1996).
[31] B. Dolensky, K. Kirk, J. Org. Chem. **66**, 4687 (2001).