Novel aspects of the chemistry of tosylmethyl isocyanide

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CHAPTER 5

Novel Synthesis of 3-Nitroindoles and 3-Cyanoindoles

via Electrocyclization of

4-Substituted 2,3-(Dialk-1-enyl)pyrroles[1]

Abstract : *3-Nitroindoles 5.10 are prepared in good yields via a thermal 6π-electrocyclization of 2,3-(dialkenyl)-4-nitropyrroles 5.4 in nitrobenzene, a solvent which causes in situ aromatization of the initially formed dihydroindoles 5.8. The corresponding reaction of 2-alkenyl-3-alkadienyl-4-nitropyrroles 5.5 also leads to 3-nitroindoles 5.11, however, now together with 3-nitrotetrahydroindole derivatives 5.12. The latter compounds are formed by a tandem 6π-electrocyclization - intramolecular Diels-Alder reaction, and are the predominant (or only) products when nitrobenzene is replaced by triglyme. The same was found for 2-alkenyl-3-alkadienyl-4-cyanopyrroles 5.18. 3-Cyanoindoles are prepared by refluxing 2,3-(dialkenyl)-4-cyanopyrroles 5.16 in nitrobenzene. 3-Formyl-indoles 5.20 are prepared from 3-cyanoindoles by reduction with DIBAL-H.*

5.1   Introduction

In Chapter 3, the history of the development of pyrrole chemistry was described briefly. In this section, we will describe in a similar fashion the historical development of indole chemistry. Both histories appeared, in general, more or less comparable. First, a compound is discovered which leads to intensive research activities centered on that particular compound and related compounds. Secondly, increased research activities continued to the beginning of the twentieth century at which point activity decreased. Finally, the research again intensified when biologically activities of the compounds were discovered.

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Research on indoles began in the mid-nineteenth century with the investgations of indigo. Since ancient times indigo has been used as a dye. In 1841, this dye was oxidized to isatin[2] and later, in 1866, isatin was reduced to oxindole.[3] The latter served as starting material for the synthesis of indole, which in 1866, was prepared by zinc dust pyrolysis of oxindole.[4] Three years later the chemical formula of the parent compound was proposed.[5] Indole chemistry continued to be important for the dyestuff industry until the beginning of the twentieth century. Newer dyes were discovered that replaced the indoles. From that time, the interest in indole chemistry started to decrease.

The revival of the research in indole chemistry took place in the 1930s when it was discovered that many indole alkaloids contain the indole ring system.[6] Research was further stimulated by the discovery of the biological activities of indoles. Well known indoles are: tryptophan, tryptamine, serotonin, melatonin, sumatriptan, and gramine. Other compounds with a more complicated indole structure are: strychnine, lysergic acid diethylamide (LSD), reserpine, and teleocydin B.

Tryptophan   Serotonin   Strychnine
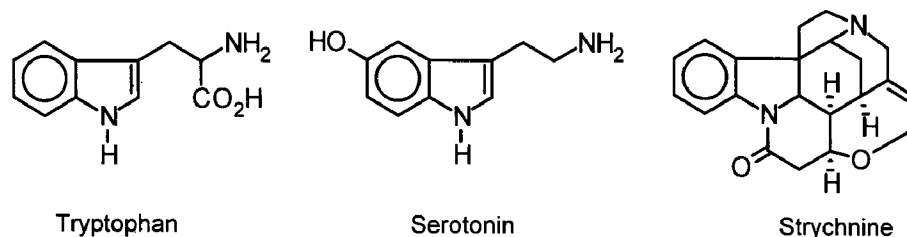
Scheme 5.1 : *Three Examples of Natural Indoles*

Since the investigation of the dye indigo, a variety of synthetic methods have been developed for the preparation of indoles. Most of these methods are based on a benzene nucleus carrying two *ortho* substituents or one *ortho* substituent and one free position. Examples of this approach are the Fischer,[7] the Bischler,[8] the Reissert,[9] the Madelung,[10] and the Nenitzescu[11] indole syntheses. The most versatile and widely used method is the Fischer indole synthesis.

In 1986,[12] our research group introduced a new synthesis of indoles. This method was not based on the general concept of building a pyrrole ring on to a benzene nucleus,[13] but on constructing a benzene ring on to a pyrrole nucleus. The indole ring, in this approach can be obtained via an electrocyclization reaction of 2,3-(dialkenyl)-pyrroles in triglyme, followed by dehydrogenation with DDQ.

In Chapter 3, we have described a simple method for the synthesis of 3(4)-nitropyrroles and 3(4)-cyanopyrroles.[14] This method offers the possibility to synthesize various 2,3-(dialkenyl)-4-nitropyrroles and 2,3-(dialkenyl)-4-cyanopyrroles. These pyr-

roles were obtained in one operation by reaction of conjugated dienes or trienes with 1-isocyano-1-tosyl-1-alkenes. In the next section, after a brief introduction, the electrocyclization of 2,3-(dialkenyl)-4-nitropyrroles wil be discussed.

## 5.2 Thermal Electrocyclization of 2,3-(Dialk-1-enyl)-4-nitropyrroles

5.2.1 Introduction

In this section, we will show that 2,3-(dialkenyl)-4-nitropyrroles **5.4** and **5.5** are ideal precursors for the synthesis of 3-nitroindoles **5.10** and **5.11** (Scheme 5.1). At present there is no reliable, generally applicable method for the preparation of 3-nitroindoles. Although the 3-position of indoles is the prime reaction site for electrophilic substitutions, nitration may well lead to indoles with nitro groups at C-4, C-5 and/or C-6, in addition to (or instead of) C-3. The results are strongly dependent on the presence of substituents and on the acidity of the nitrating medium. Furthermore, the nitration of indoles may be complicated by oxidation and dimerization reactions.[15] The best results so far, were obtained in certain *ipso* nitrations. One of the better examples of that approach is given by the preparation of 1-ethyl-3-nitro-2-phenylindole by replacement of a 3-phenylazo substituent (in 90 % yield, using 70 % HNO_3 in AcOH at rt for 50 h).[16] This approach, however, has severe limitations and, for example, does not appear to work for 2-unsubstituted indoles.[17]

5.2.2 Synthesis of 3-Nitroindoles and 3-Nitrotetrahydroindoles

The electrocyclization reaction of 2-alkenyl-1-methyl-4-nitro-3-(2-phenylethenyl)-pyrroles **5.4** takes place in a straightforward manner. 3-Nitroindoles **5.10** are formed in one operation when these *N*-methylated 4-nitropyrroles **5.4** are heated in refluxing nitrobenzene (bp 211 °C) (Scheme 5.2, Table 5.1, entries 1-3). In analogy to previous results,[12, 18] the reaction is assumed to proceed via the primary electrocyclization products **5.6** and their 1,5-hydrogen shifted isomers **5.8**, which are dehydrogenated *in situ* by nitrobenzene. Similar dehydrogenations by nitrobenzene are well known, for example, from the Skraup quinoline synthesis.[19]

The corresponding reaction of *N*-unsubstituted nitropyrrole **5.4d** was not successful (Table 5.1, entry 4). Under the conditions of entry 1, pyrrole **5.4d** gave a complex, tarry reaction mixture in which according to ¹H NMR neither starting material **5.4d** nor the desired nitroindole **5.10d** were present. Somewhat unexpectedly, the same was found for *N*-tosyl protected nitropyrrole **5.4e** (entry 5).
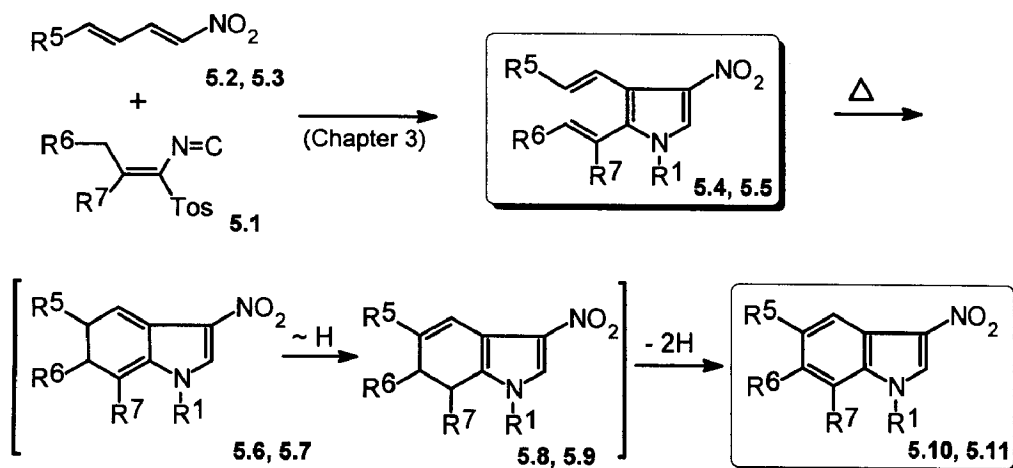
R^5 = Ph in even numbered compounds, (E)-PhCH=CH in odd numbered compounds

For **5.4** and **5.10**, see Table 5.1; for **5.5** and **5.11** Table 5.2

Scheme 5.2 : *Electrocyclization of 4-Nitropyrroles 5.4 and 5.5 to the Corresponding 3-Nitroindoles 5.10 and 5.11*

Electrocyclization of 2-alkenyl-4-nitro-3-(4-phenyl-1,3-butadienyl)pyrroles **5.5** (homologs of pyrroles **5.4**, with an additional double bond in the C-3 substituent) in nitrobenzene did not give (E)-5-(2-phenylethenyl)nitroindoles **5.11** as the only product (Scheme 5.2, Table 5.2). In addition to the 3-nitroindoles **5.11**, a second 3-nitroindole

Table 5.1 : *3-Nitroindoles 5.10 (R^5 = Ph) Prepared from Nitropyrroles 5.4 in Refluxing Nitrobenzene According to Scheme 5.2*

Entry	R^1	R^6	R^7	Product	React. Time (h)	Yield (%)	Mp (°C)
1	Me	H	Me	**5.10a**	2½	75	173-174
2	Me	Me	Ph	**5.10b**	5	85	267-268
3	Me	$-(CH_2)_4-$		**5.10c**	2½	69	271-272
4	H	H	Me	**5.10d**	2	a	
5	Tos	$-(CH_2)_4-$		**5.10e**	1	a	

(a) Nitroindole not identified, see text

derivative **5.12** was formed frequently, occasionally even as the main product (Table 5.2). Evidently, compounds **5.12** are formed by an intramolecular Diels-Alder reaction[20] of the primary formed electrocyclization products **7** (Scheme 5.3). This Diels-Alder reaction apparently can compete with the supposedly fast 1,5 H-shift[12] of **5.7** to **5.9**. The structure of **5.12a** was established unambiguously by X-ray analysis,[1b] thus ruling out the alternative structure **5.13a**, which would have resulted from a reversed Diels-Alder cycloaddition of **5.7a**.

Table 5.2 : *3-Nitroindoles* **5.11** *(R^5 = (E)-PhCH=CH) and* **5.12** *Prepared from Nitropyrroles* **5.5** *in Refluxing Nitrobenzene or Triglyme According to Schemes 5.2 and 5.3*

Entry	R^6	R^7	R^1	Solvent	React. Time (h)	Product	Yield (%) 5.11	Yield (%) 5.12
1	-(CH$_2$)$_4$-		Me	PhNO$_2$	3½	a	21	50
2	-(CH$_2$)$_4$-		Me	Triglyme	2	a	<1	75
3	-(CH$_2$)$_4$-		H	Triglyme	2	b		78
4	H	Me	Me	PhNO$_2$	2	c	68	12
5	H	Me	Me	Triglyme	2	c	10	70
6	H	Me	H	Triglyme	1½	d	46	
7	Me	Ph	Me	PhNO$_2$	2	e	90	
8	Me	Ph	Me	Triglyme	2	e	38[a]	
9	Me	Ph	H	Triglyme	2	f	b	

(a) Compound **5.11e** was identified by ^{1}H NMR in a mixture of two products. (b) This reaction, unexpectedly, gave a compound which was tentatively ascribed to **5.9f**.

The first electrocyclization experiments of Table 5.2 - with pyrrole **5.5a** - were carried out in refluxing nitrobenzene, following the procedure used for the reactions of Table 5.1. This reaction gave a mixture of two indole derivatives: 3-nitroindole **5.11a** (21 %) and 3-nitrotetrahydroindole **5.12a** (50 % yield, Table 5.2, entry 1). When the same reaction was repeated in refluxing triglyme (triethylene glycol dimethyl ether, bp 216 °C), 3-nitrotetrahydroindole **5.12a** was the only product (75 % yield, entry 2). Thus, nitrobenzene is likely to be involved in the formation of **5.11a** (entry 1), as well as the 3-nitropyr-

roles **5.10a, b,** and **c** of Table 5.1. As a matter of fact **5.12c** is partially converted to **5.11c** in refluxing nitrobenzene; the ratio **5.11c:5.12c** obtained after 2½ h was *ca.* 1.8 :1.0. The formation of **5.11c** in this experiment must be the result of the retro-Diels-Alder of **5.12c** to **5.7c**, followed by dehydrogenation (possible via **5.9c**) by nitrobenzene (Scheme 5.3).

For R^1, R^6, and R^7, see Table 5.2
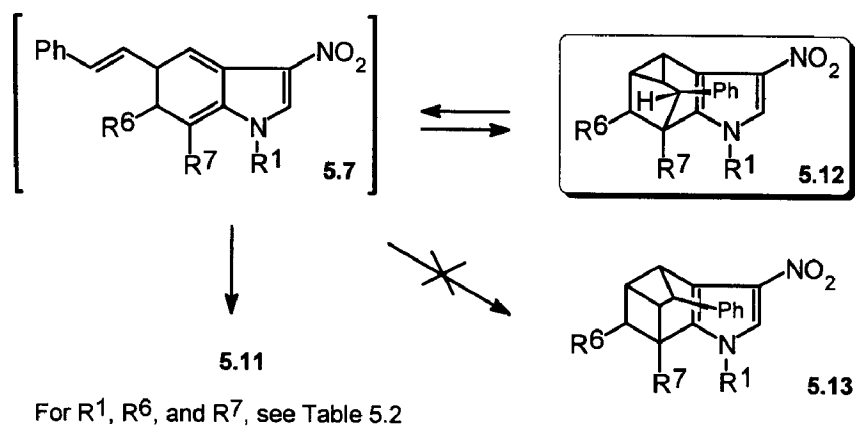
Scheme 5.3 : *Rationale of Formation of 3-Nitrotetrahydroindoles* **5.12**

The electrocyclization of pyrrole **5.5b** in triglyme also gave a 3-nitrotetrahydroindole derivative, **5.12b**, as the only product (78 %, entry 3). This experiment shows that electrocyclization of *N*-H unprotected pyrrole is successful when carried out in triglyme, unlike the reaction of **5.4d** in nitrobenzene (Table 5.1, entry 4).[21]

3-Nitroindoles **5.11c** and **5.11e** were the major and the sole products of entries 4 and 7 (Table 5.2), respectively, when the electrocyclizations were carried out in nitrobenzene. Entry 5, in triglyme, gave **5.12c** as the main product, as expected. The results of entries 6, 8, and 9 are less clear cut. In case of entry 6 the low yield, possibly, can be explained by an intermolecular dehydrogenation. Dihydroindole **5.9d** oxidizes another
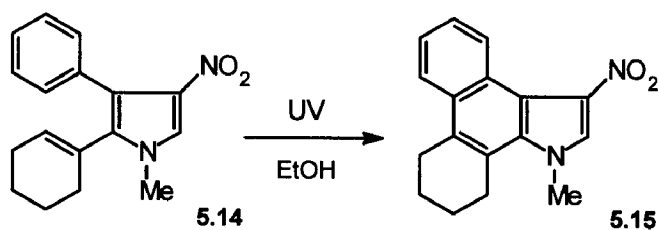
Scheme 5.4 : *Photochemical Electrocyclization of Pyrrole* **5.14** *to Nitroindole* **5.15.**

dihydroindole **5.9d** to the indole **5.11d** (like the *in situ* dehydrogenation with nitroben-zene). Possibly, nitro groups of other intermediates in the electrocyclization reaction can do the same. The intermolecular dehydrogenation can also be used to explain the low yield in case of entry 8.

Finally, the electrocyclization (and dehydrogenation) of **5.14**, which bears an aromatic side chain at C-3, was achieved photochemically in ethanol to give 3-nitrobenzindole **5.15** in 18 % yield (Scheme 5.4).

5.2.3 Structure Elucidation of Pyrrole 5.12a by X-Ray Analysis

It was not possible to establish the exact structure of **5.12a**, prepared via thermal ring closure and a subsequent intramolecular Diels-Alder reaction of (*E,E*)-2-(Cyclohex-1-enyl)-1-methyl-4-nitro-3-(4-phenylbuta-1,3-dienyl)pyrrole, by ^{1}H NMR and ^{13}C NMR.
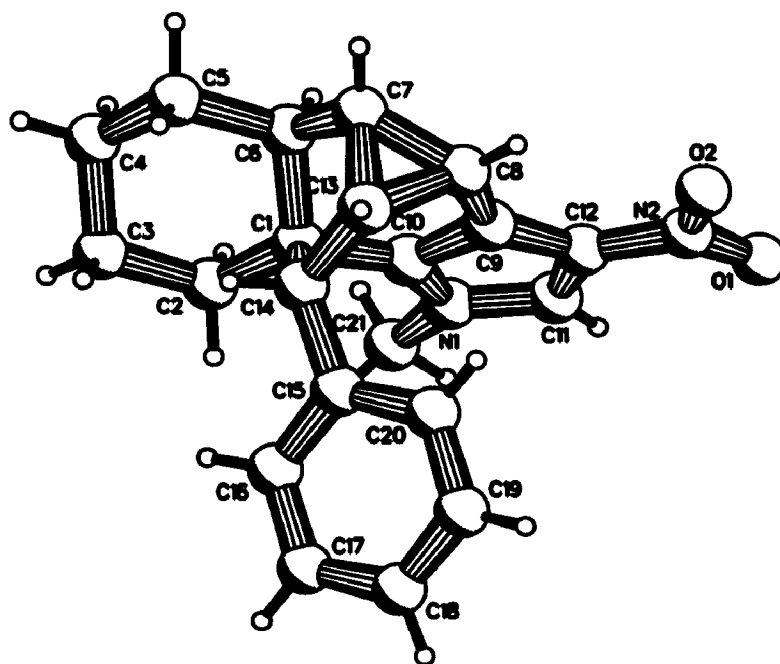

Figure 5.1 : *Pluto Representation of 5.12a. Bond Lengths and Bond Angles are Listed in Table 5.5 (Experimental Section)*

Therefore a single crystal X-ray analysis of **5.12a** was carried out. The X-ray analysis excludes the alternate pyrrole structure **5.13a** (Scheme 5.3).

Compound **5.12a** contains six rings. These are the two five membered rings, the pyrrole ring (C9C10N1C11C12) and a ring C1C6C7C13C14, which is a part of a tricyclic unit, and, furthermore, three six membered rings: (1) the phenyl ring; (2) the cyclohexyl ring; (3) the ring C1C6C7C8-C9C10 within the tricyclic unit. The remaining ring is a three membered ring (C7C8C10) which also is a part of the tricyclic unit. The bond lengths and angles of the pyrrole are in general agreement with other pyrrole units in 4,5,6,7-tetrahydroindoles.[22] The nitro group is coplanar with the pyrrole ring, the relevant torsion angle being 179.8(2)°. The structure most closely related to that of the tricyclic octene unit was found in the C ring of staphisine; the bond lengths and angles are in good agreement with those of this tricyclic structure.[23]

5.3 Thermal Electrocyclization of 4-Cyano-2,3-(dialk-1-enyl)pyrroles

5.3.1 Introduction

Not only 3-nitroindoles are compounds of interest with regard to their potential biological behaviour, the same holds for 3-cyanoindoles. Furthermore, the cyano group of the indole can be converted into an aldehyde group. The 3-formylindoles so obtained can be used as starting materials for other compounds of interest, for example trypta-mine derivatives. The conversion of 3-formylindoles into tryptamine derivatives was earlier described and is based on a condensation with nitromethane and subsequent reduction of the nitroethenyl moiety.[24] In the next section we will describe the electrocyclization of 2,3-(dialkenyl)-4-cyanopyrroles.

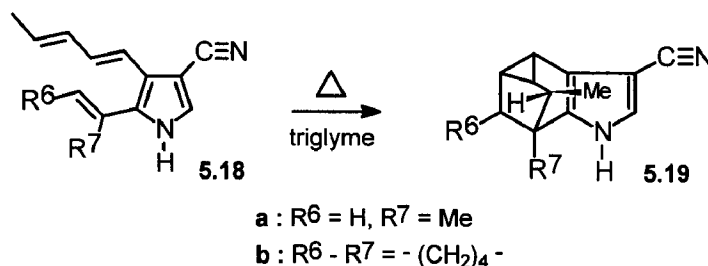### 5.3.2 Synthesis of 3-Cyanoindoles and 3-Cyanotetrahydroindoles
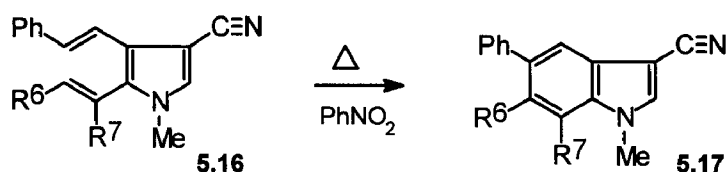
Scheme 5.5 : *Electrocyclization of 2,3-(Dialkenyl)-4-cyano-pyrroles* **5.16**

In Chapter 3, we described the synthesis of 2,3-(dialkenyl)-4-cyanopyrroles **5.16** by the base-induced cycloaddition of 1-isocyano-1-tosyl-1-alkenes to cyanodienes (Section

Table 5.3 : *3-Cyanoindoles 5.17 (R^5 = Ph) Prepared from 3-Cyanopyrroles 5.16 in Refluxing Nitrobenzene According to Scheme 5.5*

Entry	R^6	R^7	Product	React. Time (h)	Yield (%)	Mp (°C)
1	H	Me	**5.17a**	11	80	148-150
2	Me	Ph	**5.17b**	19	75	137-139
3	-(CH$_2$)$_5$-		**5.17c**	19	73	209-211
4	-(CH$_2$)$_4$-		**5.17d**	7	60	193-195

3.3.3) and cyanotrienes (Section 3.3.4). In Section 5.2.2 the thermal electrocyclization of 2,3-(dialkenyl)-4-nitropyrroles was discussed (Table 5.1). For the electrocylization of pyrroles **5.16** we have applied the same conditions as were used in the case of the corresponding nitropyrroles, that is refluxing nitrobenzene. The results of the thermal electrocyclization of **5.16** are collected in Table 5.3.

a : R^6 = H, R^7 = Me

b : R^6 - R^7 = - (CH$_2$)$_4$ -

Scheme 5.6 : *Synthesis of 4-Cyanotetrahydroindoles 5.19*

As already has been mentioned, 2-alkenyl-3-(butadien-1,3-yl)-4-cyanopyrroles have been prepared from 1-isocyano-1-tosyl-1-alkenes and (*E,E,E*)-ethyl 2-cyanooctatrienoate (Section 3.3.4). Refluxing of **5.18** under non-oxidizing conditions (triglyme) gave the 4-cyanotetrahydroindoles **5.19a** and **5.19b** in 68 % and 55 % yield, respectively. The structures were determined with ^{1}H NMR and compared to the ^{1}H NMR spectra obtained in the series of the nitrotetrahydroindoles (Table 5.2).

5.3.3 Synthesis of 3-Formylindoles

3-Formylindoles are important starting materials for the synthesis of a whole range of 3-substituted indoles, includes for example, tryptamine, tryptophan, melatonin,

serotonin derivatives. Tryptamine derivatives can easily be prepared from nitromethane and subsequent reduction of the condensation products (Section 5.3.1). Another way to prepare tryptamine derivatives was shown by Merour *et al.*[25] They used the reductive cyanation procedure of aldehydes which was developed in our research group.[26] Reaction of TosMIC anion to 3-formylindoles gave the corresponding 3-cyanomethyl-indoles, which were hydrogenated with Raney nickel to give tryptamine derivatives.

Scheme 5.7 : *Conversion of 5.17 to 5.20 with DIBAL-H*

The conversion of the cyano moiety to a formyl moiety can easily be achieved by reduction with DIBAL-H, as in the case of the 3-cyanopyrroles (Section 3.5.1). Reduction of 3-cyanoindoles **5.17** with DIBAL-H resulted in 3-formylindoles **5.20** (Scheme 5.7). The results are collected in Table 5.4.

Table 5.4 : *Reduction of 3-Cyanoindoles 5.17 with DIBAL-H*
According to Scheme 5.7

Entry	R⁶	R⁷	Product	Yield (%)	Mp (°C)
1	H	Me	**5.20a**	96	161-162
2	Me	Ph	**5.20b**	83	202-205
3	-(CH$_2$)$_5$-		**5.20c**	89	188-190

5.4 Experimental Section (for General Remarks, see Chapter Two)

All experiments were carried out in a dry nitrogen atmosphere. 2,3-(Dialkenyl)-4-nitropyrroles **5.4** and **5. 5** were prepared as reported in Chapter 3. Triglyme and nitrobenzene were distilled prior to use. The photoelectrocyclization was performed with a high-pressure pyrex immersion mercury UV lamp.

5.4.1 Synthesis of 3-Nitroindoles and 3-Nitrotetrahydroindoles

1,7-Dimethyl-3-nitro-5-phenylindole (5.10a), (Typical Procedure) :
(*E*)-1-Methyl-2-(1-methylethenyl)-4-nitro-3-(2-phenylethenyl)pyrrole (**4a**, 0.54 g, 2.0 mmol) was

refluxed in nitrobenzene (20 mL) for 2½ h. The solvent was removed in a bulb-to-bulb destillation unit, and the black residue was filtered through a short column of Al_2O_3 (CH_2Cl_2). The eluent was concentrated to give, after washing with pentane, **5.10a** as a yellow solid (0.40 g, 75 %), pure according to ^1H NMR. Crystallization from MeOH gave analytically pure **5.10a**, as yellow crystals: mp 173-174 °C; ^1H NMR ($CDCl_3$, 200 MHz): δ = 2.80 (s, 3H), 4.10 (s, 3H), 7.27-7.52 (m, 4H), 7.67-7.71 (m, 2H), 7.93 (s, 1H), 8.36 (s, 1H); ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 19.58 (q), 38.27 (q), 116.91 (d), 122.53 (s), 122.81 (s), 126.83 (d), 127.24 (d), 127.35 (d), 128.78 (d), 131.59 (s), 133.15 (d), 134.02 (s), 137.66 (s), 140.80 (s); MS (relative intensity, %): m/z = 28 (7.24), 102 (3.44), 108 (3.19), 133 (4.66), 165 (4.17), 178 (4.42), 218 (4.66), 220 (6.50), 236 (6.75), 266 (M⁺, 100); HRMS: m/z calc. for $C_{16}H_{14}N_2O_2$: 266.106, found 266.106; Anal. calc. for $C_{16}H_{14}N_2O_2$: C, 72.15; H, 5.30; N, 10.52; found C, 71.82; H, 5.17; N, 10.40.

1,6-Dimethyl-5,7-diphenyl-3-nitroindole (5.10b) :

Following the procedure described for **5.10a**, (E,E)-1-methyl-4-nitro-3-(2-phenylethenyl)-2-(1-phenylprop-1-enyl)pyrrole (**5.4b**, 0.69 g, 2.0 mmol) was refluxed for 5 h. After workup, **5.10b** was obtained as a yellow solid (0.58 g, 85 %), pure according to ^1H NMR. Crystallization from MeOH gave analytically pure **5.10b**, as yellow crystals: mp 267-268 °C; ^1H NMR ($CDCl_3$, 200 MHz): δ = 1.98 (s, 3H), 3.16 (s, 3H), 7.34-7.51 (m, 10 H), 7.92 (s, 1H), 8.21 (s, 1H); 13C NMR ($CDCl_3$, 75.4 MHz): δ = 18.29 (q), 37.67 (q), 119.39 (s), 120.65 (d), 126.79 (d), 127.16 (s), 127.84 (s), 127.97 (d), 128.03 (d), 128.37 (d), 129.47 (d), 130.30 (d), 131.14 (s), 133.08 (s), 133.19 (d), 137.47 (s), 139.46 (s), 142.23 (s); MS (relative intensity, %): m/z = 28 (18.38), 280 (6.80), 281 (6.60), 294 (7.12), 312 (10.15), 342 (M⁺, 100); HRMS: m/z calc. for $C_{22}H_{18}N_2O_2$: 342.137, found 342.137; Anal. calc. for $C_{22}H_{18}N_2O_2$: C, 77.16; H, 5.30; N, 8.19; found C, 76.98; H, 5.46; N, 8.26.

1-Methyl-3-nitro-5-phenyl-6,7,8,9-tetrahydrobenz[g]indole (5.10c) :

Following the procedure described for **5.10a**, (E)-2-(cyclohex-1-enyl)-1-methyl-4-nitro-3-(2-phenylethenyl)pyrrole (**5.4c**, 0.62 g, 2.0 mmol) gave, after washing with pentane, **5.10c** as a yellow solid (0.43 g, 69 %), pure according to ^1H NMR. Crystallization from MeOH gave analytically pure **5.10c**, as yellow crystals: mp 272-273 °C; ^1H NMR ($CDCl_3$, 200 MHz): δ = 1.68-1.95 (m, 4H), 2.65 (t, J = 5.8 Hz, 2H), 3.35 (t, J = 6.1 Hz, 2H), 4.15 (s, 3H), 7.27-7.52 (m, 5H), 7.89 (s, 1H), 7.99 (s, 1H); ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 22.27 (t), 22.38 (t), 26.11 (t), 29.14 (t), 39.33 (q), 118.94 (d), 119.45 (s), 122.45 (s), 126.72 (d), 127.90 (d), 129.28 (d), 132.10 (s), 132.87 (d), 133.95 (s), 139.84 (s), 141.92 (s); MS (relative intensity, %): m/z = 28 (10.08), 115 (4.88), 189 (5.67), 230 (6.14), 231 (6.14), 230 (6.14), 261 (6.93), 278 (10.55), 289 (7.72), 306 (M⁺, 100); HRMS: m/z calc. for $C_{19}H_{18}N_2O_2$: 306.137, found 306.136; Anal. calc. for $C_{19}H_{18}N_2O_2$: C, 74.49; H, 5.92; N, 9.14; found C, 74.12; H, 5.99; N, 9.10.

(E)-1-Methyl-3-nitro-5-(2-phenylethenyl)-6,7,8,9-tetrahydrobenz[g]indole (5.11a) :

(E,E)-2-(Cyclohex-1-enyl)-1-methyl-4-nitro-3-(4-phenylbuta-1,3-dienyl)pyrrole (**5.5a**, 0.40 g, 1.2 mmol) was refluxed in nitrobenzene (25 mL) for 3½ h. After cooling, the solvent was removed in a bulb-to-bulb destillation unit, and the solid residue was filtered through a short column of Al_2O_3 (CH_2Cl_2) to give a mixture of two compounds. These were separated by column chromatography on Al_2O_3. The first fraction was obtained with CH_2Cl_2/pentane (1:1) and consisted of **5.12a** (0.20 g, 50 %), this compound was identical by ^1H NMR with the material described below. The second fraction, eluted with CH_2Cl_2 gave **5.11a** as a yellow solid (84 mg, 21 %), pure according to ^1H NMR. Crystallization from EtOH (96 %) gave analytically pure **5.11a**, as yellow crystals: mp 241-242 °C; ^1H NMR ($CDCl_3$, 200 MHz): δ = 1.86-1.91 (m, 4H), 2.94 (m, 2H), 3.30 (m, 2H), 4.14 (s,

3H), 7.05-7.59 (m, 7H), 7.91 (s, 1H), 8.36 (s, 1H); ^{13}C NMR (CDCl$_3$, 50.3 MHz): δ = 22.22 (t), 22.29 (t), 26.33 (t), 27.74 (t), 39.38 (q), 115.06 (d), 119.79 (s), 122.40 (s), 126.47 (d), 126.54 (d), 127.43 (d), 127.70 (s), 128.53 (d), 130.60 (d), 132.03 (s), 132.91 (d), 134.20 (s), 134.42 (s), 137.51 (s); MS (relative intensity, %): m/z = 28 (19.74), 77 (6.58), 91 (6.91), 128 (11.84), 213 (7.57), 241 (6.25), 304 (10.53), 332 (M⁺, 100); HRMS: m/z calc. for C$_{21}$H$_{20}$N$_2$O$_2$: 332.152, found 332.152; Anal. calc. for C$_{21}$H$_{20}$N$_2$O$_2$: C, 75.87; H, 6.07; N, 8.43; found C, 76.02; H, 6.01; N, 8.35.

(*E*)-1,7-Dimethyl-3-nitro-5-(2-phenylethenyl)indole (5.11c) :

(*E,E*)-1-Methyl -2-(1-methylethenyl)-4-nitro-3-(4-phenylbuta-1,3-dienyl)pyrrole (5.5c, 0.29 g, 1.0 mmol) was refluxed in nitrobenzene (20 mL) for 2 h. After cooling, the solvent was removed in a bulb-to-bulb destillation unit, and the solid residue was filtered through a short column of silicagel (CH$_2$Cl$_2$). After concentration, a orange solid was obtained which consisted of a mixture of two compounds, which were separated by column chromatography (Al$_2$O$_3$, CH$_2$Cl$_2$). The first fraction gave 5.12c (described below) as a yellow solid (35 mg, 12 %), and the second fraction gave 5.11c also as a yellow solid (0.20 g, 68 %), both compounds were pure according to ^{1}H NMR. Crystallization of 5.11c, from EtOH (96 %), gave analytically pure 5.11c, as yellow crystals: mp 191-192 °C; ^{1}H NMR (CDCl$_3$, 200 MHz): δ = 2.79 (s, 3H), 4.12 (s, 3H), 7.20-7.57 (m, 8H), 7.96 (s, 1H), 8.28 (d, J = 1.5 Hz, 1H); ^{13}C NMR (CDCl$_3$, 75.4 MHz): δ = 19.47 (q), 38.18 (q), 116.93 (d), 122.45 (s), 122.58 (s), 125.59 (d), 126.37 (d), 127.49 (d), 128.17 (s), 128.31 (d), 128.49 (d), 128.60 (d), 132.89 (d), 133.81 (s), 134.09 (s), 137.32 (s), 192.15 (s); MS (relative intensity,%): m/z = 115 (8.80), 129 (6.49), 202 (7.51), 203 (7.00), 228 (9.61), 243 (8.88), 244 (8.75), 245 (6.49), 257 (13.75), 292 (M⁺, 100); HRMS: m/z calc. for C$_{18}$H$_{16}$N$_2$O$_2$: 292.121, found 292.121; Anal. calc. for C$_{18}$H$_{16}$N$_2$O$_2$: C, 73.94; H, 5.52; N, 9.59; found C, 73.51; H, 5.55; N, 9.42. The same indole 5.11c was formed when indole 5.12c (50 mg, 0.17 mmol) was refluxed in nitrobenzene (10 mL) for 2½ h. After cooling, the solvent was removed in a bulb-to-bulb destillation unit. The dark solid was filtered through a short column of Al$_2$O$_3$ (CH$_2$Cl$_2$). After concentrating the eluent, the remaining oil was washed with hexane to give a yellow oil (35 mg), which consisted of a mixture of two compounds : 5.11c and 5.12c. The ratio 1.8 : 1 (5.11c : 5.12c) was determined by ^{1}H NMR.

(*E*)-7-Methyl-3-nitro-5-(2-phenylethenyl)indole (5.11d)

(*E,E*)-2-(1-Methylethenyl)-4-nitro-3-(4-phenylbuta-1,3-dienyl)pyrrole (5.5d, 0.40 g, 1.43 mmol) was refluxed in triglyme (20 mL) for 1½ h. After cooling, the solvent was removed in a bulb-to-bulb destillation unit, and the solid residue was purified by crystallization from CHCl$_3$/pentane to give 5.11d, as a orange solid (0.18 g, 46 %): mp > 300 °C; ^{1}H NMR (DMSO.d$_6$, 200 MHz): δ = 2.54 (s, 3H), 7.20-7.65 (m, 8H), 8.08 (s, 1H), 8.63 (s, 1H), 12.7 (br, 1H); ^{13}C NMR (DMSO.d$_6$, 50.3 MHz): δ = 16.41 (q), 115.88 (d), 120.19 (s), 122.74 (d), 123.31 (s), 126.36 (d), 127.37 (d), 127.45 (d), 128.64 (d), 128.80 (s), 128.98 (d), 130.43 (d), 133.14 (s), 134.26 (s), 137.22 (s); MS (relative intensity) : m/z = 28 (68.1), 77 (7.90), 101 (7.8), 109 (9.3), 115 (8.7), 122 (8.8), 176 (17.5), 189 (11.0), 217 (11.6), 230 (13.6), 243 (10.4), 248 (10.7), 278 (M⁺, 100); HRMS m/z calc. for C$_{17}$H$_{14}$N$_2$O$_2$: 278.106, found 278.106.

(*E*)-1,6-Dimethyl-3-nitro-7-phenyl-5-(2-phenylethenyl)indole (5.11e) :

(*E,E,E*)-1-Methyl-4-nitro-3-(4-phenylbuta-1,3-dienyl)-2-(1-phenylprop-1-enyl)pyrrole (5.5e, 0.37 g, 1.0 mmol) was refluxed in nitrobenzene for 2 h. After cooling, the solvent was removed in a bulb-to-bulb destillation unit, the solid residue was washed with Et$_2$O to give 5.11e, as a yellow solid (0.33 g, 90 %), pure according to ^{1}H NMR. Crystallization from MeOH gave analytically pure

5.11e, as yellow crystals: mp 289-290 °C; ^{1}H NMR(CDCl$_3$, 200 MHz): δ = 2.17 (s, 3H), 3.12 (s, 3H), 7.11-7.60 (m, 12H), 7.89 (s, 1H), 8.54 (s, 1H); ^{13}C NMR (CDCl$_3$, 75.4 MHz): δ = 16.85 (q), 37.65 (q), 116.84 (d), 119.93 (s), 126.56 (d), 126.99 (s), 127.18 (d), 127.55 (d), 127.97 (s), 128.09 (d), 128.34 (d), 128.60 (d), 130.39 (d), 131.16 (d), 131.52 (s), 133.22 (d), 133.34 (s), 134.30 (s), 137.41 (s), 137.57 (s); MS (relative intensity, %): m/z = 28 (79.87), 146 (5.19), 306 (5.11), 320 (5.03), 333 (7.06), 338 (6.98), 368 (M$^+$, 100); HRMS: m/z calc. for C$_{24}$H$_{20}$N$_2$O$_2$: 368.152, found 368.152; Anal. calc. for C$_{24}$H$_{20}$N$_2$O$_2$: C, 78.23; H, 5.48; N, 7.61; found C, 77.63; H, 5.57; N, 7.55.

In another experiment, pyrrole **5.5e** (0.37 g, 1.0 mmol) was refluxed in triglyme (20 mL) for 2 h. After cooling, the solvent was removed in a bulb-to-bulb destillation unit, and the solid residue was filtered through a short column of Al$_2$O$_3$ (EtOAc). After concentrating the eluent, the remaining oil was crystallized twice from Et$_2$O to give a yellow solid (0.18 g), which consisted of a mixture of two compounds. One of these was identified as indole **5.11e** by ^{1}H NMR in a yield of ca. 0.14 g (38 %).

rac-1-Methyl-4-nitro-{(1R,6S,8S)-6-phenyl-5,8-(tetramethylene)tricyclo[3.2.1.0$^{2.7}$]oct-3-eno}[4,3-b]pyrrole[27] (5.12a) :

Pyrrole **5.5a** (0.33 g, 1.0 mmol) was refluxed in triglyme (20 mL) for 2 h. After cooling, the solvent was removed in a bulb-to-bulb destillation unit, and the residue was filtered through a short column of Al$_2$O$_3$ (CH$_2$Cl$_2$) to give a yellow solid, which contained, according to ^{1}H NMR, about 1 % of indole **5.11a**. One crystallization from MeOH gave **5.12a**, as a yellow solid (0.25 g, 75 %): mp 190-191 °C; ^{1}H NMR (CDCl$_3$, 200 MHz): δ = 1.30-2.22 (m, 11H), 3.12 (t, J = 7.2 Hz, 1H), 3.19 (s, 3H), 3.55 (d, J = 2.0 Hz, 1H), 6.73-6.78 (m, 2H), 7.00 (s, 1H), 7.07-7.28 (m, 3H); ^{13}C NMR (CDCl$_3$, 50.3 MHz): δ = 13.49 (d), 21.52 (t), 22.11 (d), 25.33 (t), 26.50 (t), 28.35 (t), 37.42 (q), 41.27 (d), 44.18 (d), 47.62 (s), 115.51 (s), 122.41 (d), 126.34 (d), 127.65 (d), 127.67 (d), 127.74 (d),127.92 (d), 130.75 (d), 138.58 (s); MS (relative intensity, %): m/z = 28 (72.54), 32 (16.73), 42 (13.15), 77 (7.09), 91 (9.32), 115 (9.96), 117 (7.73), 230 (29.63), 243 (31.35), 288 (10.47), 317 (32.25), 334 (M$^+$, 100); HRMS: m/z calc. for C$_{21}$H$_{22}$N$_2$O$_2$ 334.168, found 334.168; Anal. calc. for C$_{21}$H$_{22}$N$_2$O$_2$: C, 75.48; H, 6.64; N, 8.38; found C, 75.46; H, 6.56; N, 8.67.

rac-4-Nitro-{(1R,6S,8S)-6-phenyl-5,8-(tetramethylene)tricyclo[3.2.1.0$^{2.7}$]oct-3-eno}[4,3-b]pyrrole[7] (5.12b) :

(E,E)-2-(Cyclohex-1-enyl)-4-nitro-3-(4-phenylbuta-1,3-dienyl)pyrrole (**5.5b**, 0.50 g, 1.6 mmol) was refluxed in triglyme (20 mL) for 2 h. After cooling, the solvent was removed in a bulb-to-bulb destillation unit, the solid residue was filtered through a short column of silicagel (CH$_2$Cl$_2$) and was purified by crystallization from CHCl$_3$/pentane, to give **5.12b** as a yellow solid (0.38 g, 78 %), pure according to ^{1}H NMR: 254-255 °C; ^{1}H NMR (DMSO.d$_6$, 200 MHz): δ = 1.11-1.83 (m, 12H), 2.86 (t, J = 7.2 Hz, 1H), 3.51 (s, 1H), 6.67-6.71 (m, 2H), 7.04-7.06 (m, 3H), 7.38 (s, 1H); ^{13}C NMR (CDCl$_3$, 50.3 MHz): δ = 13.16 (d), 20.46 (t), 21.10 (d), 21.44 (d), 24.97 (t), 25.00 (t), 26.86 (t), 40.02 (d), 43.34 (d), 44.03 (s), 111.50 (s), 117.70 (d), 126.06 (d), 127.47 (d), 127.88 (d), 131.80 (s), 133.40 (s), 138.67 (s); MS (relative intensity, %): m/z = 28 (100), 32 (22.15), 216 (25.87), 229 (22.90), 303 (9.09), 320 (M$^+$, 100); HRMS: m/z calc. for C$_{20}$H$_{20}$N$_2$O$_2$: 320.152, found 320.152; Anal. Calc. for C$_{20}$H$_{20}$N$_2$O$_2$: C, 74.96; H, 6.30; N, 8.75; found C, 73.31; H, 6.21; N, 8.53.

rac-1-Methyl-4-nitro-{(1R,6S)-5-methyl-6-phenyltricyclo[3.2.1.0$^{2.7}$]oct-3-eno}[4,3-b]pyrrole[7] (5.12c) :

Pyrrole **5.5c** (0.29 g, 1.0 mmol) was refluxed in triglyme (15 mL) for 2 h. Following the procedure

described for **5.11c**, compound **5.12c** (0.20 g, 70 %) and compound **5.11c** (30 mg, 10 %), were obtained as yellow solids, both pure according to ^{1}H NMR. Crystallization of the first fraction from MeOH gave **5.12c**, as yellow crystals: mp 134-135 °C; ^{1}H NMR (CDCl$_3$, 200 MHz): δ = 1.30 (d, J = 11.7 Hz, 1H), 1.58 (s, 3H), 1.78-1.94 (m, 3H), 2.90 (s, 1H), 3.15 (t, J = 7.1 Hz, 1H), 3.23 (s, 3H), 6.73-6.78 (m, 2H), 7.07-7.1 (m, 4H); ^{13}C NMR (CDCl$_3$, 75.4 MHz): δ = 13.69 (d), 16.20 (d), 19.76 (d), 23.79 (q), 36.71 (q), 40. 54 (t), 43.78 (s), 51.68 (d), 114.96 (s), 122.03 (d), 126.48 (s), 127.62 (d), 127.76 (d), 129.54 (s), 132.29 (s), 138.40 (s); MS (relative intensity): m/z = 28 (29.80), 77 (14.97), 91 (14.24), 115 (16.57), 117 (18.02), 144 (16.57), 174 (15.41), 196 (85.17), 203 (M$^+$, 100), 232 (11.05), 233 (13.35), 262 (34.59), 277 (62.35), 279 (57.12), 294 (M$^+$, 68.90); HRMS: m/z calc.for C$_{18}$H$_{18}$N$_2$O$_2$: 294.137, found 294.137; Anal. calc. for C$_{18}$H$_{18}$N$_2$O$_2$: C, 73.44; H, 6.17; N, 9.52; found C, 73.40; H, 6.21; N, 9.49.

1-Methyl-3-nitro-8,9,10,11-tetrahydrodibenzo[e,g]indole (5.15) :
EtOH (75 mL) was added to a solution of 2-(cyclohex-1-enyl)-1-methyl-4-nitro-3-phenylpyrrole (**5.14**, 0.28 g, 1.0 mmol) in CH$_2$Cl$_2$ (2 mL). The stirred reaction mixture was irradiated with a high-pressure pyrex immersion mercury UV lamp at rt for 45 h. The solvent was removed and the residue was filtered through a short column of Al$_2$O$_3$ (CH$_2$Cl$_2$). After washing with pentane, a yellow solid (0.12 g) was obtained, which consisted of a mixture of starting material and indole **5.15** (ca. 1:1.3). Two crystallizations from EtOH (96 %) gave **5.15**, as yellow crystals (50 mg, 18 %), pure according to ^{1}H NMR: mp 215-216 °C; ^{1}H NMR(CDCl$_3$, 300 MHz): δ = 1.89-1.98 (m, 4H), 3.16-3.18 (m, 2H), 3.27-3.29 (m, 2H), 4.16 (s, 3H), 7.54-7.58 (m, 2H), 7.96 (s, 1H), 8.02-8.04 (m, 1H), 9.25-9.27 (m, 1H); ^{13}C NMR (CDCl$_3$, 125.7 MHz): δ = 22.30 (t), 22.56 (t), 26.92 (t), 27.45 (t), 40.08 (q), 114.39 (s), 122.17 (s), 123.01 (d), 125.21 (s), 125.27 (d), 125.36 (d), 126.45 (s), 130.45 (d), 130.49 (s), 131.59 (s), 132.91 (d), 132.94 (d); MS (relative intensity, %): m/z = 28 (90.6), 32 (21.6), 77 (1.9), 115 (3.4), 152 (8.9), 165 (17.3), 178 (8.4), 204 (8.8), 235 (11.7), 280 (M$^+$, 100); HRMS: m/z calc. for C$_{17}$H$_{16}$N$_2$O$_2$: 280.121, found 280.121.

5.4.2 Synthesis of 3-Cyanoindoles and 3-Cyanotetrahydroindoles

3-Cyano-1,7-dimethyl-5-phenylindole (5.17a):
Following the procedure described for **5.10a**, (E)-4-cyano-1-methyl-2-(1-methylethenyl)-3-(2-phenylethenyl)pyrrole (**5.16a**, 1.0 g, 4.0 mmol) was refluxed in nitrobenzene (50 mL) for 11 h. Filtration through a short column of Al$_2$O$_3$ (CH$_2$Cl$_2$) and washing with Et$_2$O/hexane (1:1) gave **5.17a**, as a white solid (0.8 g, 80 %), pure according to ^{1}H NMR: mp 148-150 °C; ^{1}H NMR (CDCl$_3$, 300 MHz): δ = 2.80 (s, 3H), 4.08 (s, 3H), 7.26-7.49 (m, 5H), 7.63-7.66 (m, 2H), 7.78 (s, 1H); ^{13}C NMR (CDCl$_3$, 125.7 MHz): δ = 19.40 (q), 37.50 (q), 85.54 (s), 115.71 (s), 115.89 (d), 122.48 (s), 126.04 (d), 126.90 (d), 127.12 (d), 128.64 (d), 129.45 (s), 134.10 (s), 135.61 (s), 137.03 (d), 140.82 (s); MS (relative intensity, %): m/z = 28 (13.5), 77 (1.5), 115 (3.0), 123 (8.7), 169 (2.7), 203 (2.3), 229 (6.1), 246 (M$^+$, 100); HRMS: m/z calc. for C$_{17}$H$_{14}$N$_2$: 246.116, found 246.116; Anal. calc. for C$_{17}$H$_{14}$N$_2$: C, 82.90; H, 5.73; N, 11.37; found C, 83.00; H, 5.76; N, 11.28.

3-Cyano-1,6-dimethyl-5,7-diphenylindole (5.17b) :
Following the procedure described for **5.10a**, (E,E)-4-cyano-1-methyl-3-(4-phenylethenyl)-2-(1-phenylprop-1-enyl)pyrrole (**5.16b**, 0.65 g, 2.0 mmol) was refluxed in nitrobenzene (30 mL) for 19 h. Filtration through a short column of Al$_2$O$_3$ (CH$_2$Cl$_2$) and washing with Et$_2$O/hexane (1:1) gave **5.17b**, as a pale brown solid (0.48 g, 75 %), pure according to ^{1}H NMR: mp 137-139 °C; ^{1}H NMR (CDCl$_3$, 300 MHz): δ = 2.00 (s, 3H), 3.14 (s, 3H), 7.35-7.49 (m, 11H), 7.65 (s, 1H); ^{13}C NMR

(CDCl$_3$, 125.7 MHz): δ = 18.24 (q), 37.00 (q), 84.94 (s), 99.05 (s), 115.76 (s), 119.76 (d), 126.34 (s), 126.67 (d), 126.90 (s), 127.79 (d), 127.94 (d), 128.21 (d), 129.49 (d), 130.27 (s), 130.33 (d), 133.27 (s), 137.22 (d), 137.42 (s), 137.91 (s), 142.31 (s); MS (relative intensity, %): m/z = 243 (6.2), 245 (10.6), 305 (5.7), 306 (5.0), 322 (M⁺, 100); HRMS: m/z calc. for C$_{23}$H$_{18}$N$_2$: 322.147, found 322.146.

3-Cyano-1-methyl-5-phenyl-pentahydrobenz[g]indole (5.17c) :

Following the procedure described for **5.10a**, (*E*)-4-Cyano-2-(cyclohepta-1-enyl)-1-methyl-3-(2-phenylethenyl)pyrrole (**5.16c**, 0.60 g, 2.0 mmol) was refluxed in nitobenzene (30 mL) for 19 h. Filtration through a short column of Al$_2$O$_3$ (CH$_2$Cl$_2$) and washing with Et$_2$O/hexane (1:1) gave **5.17c**, as a yellow solid (0.44 g, 73 %), pure according to ¹H NMR Crystallization from cyclohexane-isopropanol gave **5.17c** as pale yellow solid: mp 209-211 °C; ¹H NMR (CDCl$_3$, 300 MHz): δ = 1.62-1.64 (m, 2H), 1.79-1.86 (m, 4H), 2.86-2.89 (m, 2H), 3.32-3.35 (m, 2H), 4.08 (s, 3H), 7.26-7.46 (m, 7H); ¹³C NMR (CDCl$_3$, 125.7 MHz): δ = 27.08 (t), 27.65 (t), 30.49 (t), 31.13 (t), 38.89 (q), 84.97 (s), 115.77 (s), 118.37 (d), 126.45 (d), 127.03 (s), 127.83 (d), 127.98 (s), 129.50 (d), 133.64 (s), 137.21 (s), 137.97 (d), 138.18 (s), 142.73 (s); MS (relative intensity, %): m/z = 243 (15.6), 245 (12.1), 257 (11.9), 271 (21.9), 300 (M⁺, 100); HRMS: m/z calc. for C$_{21}$H$_{20}$N$_2$: 300.162, found 300.165; Anal. calc. for C$_{21}$H$_{20}$N$_2$: C, 83.96; H, 6.71; N, 9.33; found C, 83.90; H, 6.69; N, 9.29.

3-Cyano-1-methyl-5-phenyl-6,7,8,9-tetrahydrobenz[g]indole (5.17d) :

Following the procedure described for **5.10a**, (*E*)-4-Cyano-2-(cyclohex-1-enyl)-1-methyl-3-(2-phenylethenyl)pyrrole (**5.16d**, 0.57 g, 2.0 mmol) was refluxed in nitrobenzene (30 mL) for 7 h. Filtration through a short column of silica gel (CH$_2$Cl$_2$) and washing with Et$_2$O/hexane (1:1) gave **5.17d**, as a yellow solid (0.34 g, 60 %). Crystallization from EtOH (96 %) gave **5.17d** as pale yellow crystals: mp 193-195 °C; ¹H NMR (CDCl$_3$, 300 MHz): δ = 1.61-1.65 (m, 2H), 1.77-1.81 (m, 2H), 2.54-2.58 (m, 2H), 3.25-3.29 (m, 2H), 4.04 (s, 3H), 7.17-7.33 (m, 7H); ¹³C NMR (CDCl$_3$, 75.4 MHz): δ = 22.58 (t), 22.62 (t), 26.34 (t), 29.28 (t), 38.67 (q), 85.07 (s), 115.82 (s), 118.24 (d), 122.22 (s), 126.45 (s), 126.66 (d), 127.91 (d), 129.36 (d), 131.29 (s), 134.12 (s), 136.97 (d), 137.87 (s), 142.00 (s); MS (relative intensity, %): m/z = 243 (12.0), 257 (21.5), 258 (25.5) 286 (M⁺, 100); HRMS: m/z calc. for C$_{20}$H$_{18}$N$_2$ 286.147, found 286, 149.

rac-4-Cyano-{(1R,6S,8S)-6-methyl-5,8-(tetramethylene)tricyclo[3.2.1.0²·⁷]oct-3-eno}[4,3-b]pyrrole²⁷ (5.19a) :

(*E,E*)-4-Cyano-2-(1-methylethenyl)-3-(pent-2,4-enyl)pyrrole (**5.18a**, 0.33 g, 1.0 mmol) was refluxed in triglyme (30 mL) for 7 h. After cooling, the solvent was removed in a bulb-to-bulb destillation unit, and the residue was filtered through a short column of Al$_2$O$_3$ (CH$_2$Cl$_2$) to give **5.19a** as a pink solid (0.34 g, 68 %). ¹H NMR (CDCl$_3$, 300 MHz): δ = 0.23 (d, J = 6.8 Hz, 3H), 0.96 (d, J = 11.5 Hz, 1H), 1.35 (s, 3H), 1.41-1.79 (m, 4H), 2.17 (t, J = 7.0 Hz, 1H), 7.00 (d, J = 2.9 Hz, 1H), 8.72 (br, 1H); ¹³C NMR (CDCl$_3$, 75.4 MHz): δ = 11.16 (q), 12.57 (d), 16.08 (d), 16.16 (q), 22.87 (d), 37.46 (t), 40.43 (d), 89.86 (s), 117.01 (s), 117.30 (s), 121.51 (d), 131.21 (s); MS (relative intensity, %): m/z = 77 (6.8), 142 (21.2), 143 (17.9), 155 (50.6), 156 (61.5), 157 (42.8), 169 (82.6), 183 (100), 198 (M⁺, 93.4); HRMS: m/z calc. for C$_{13}$H$_{14}$N$_2$: 198.116, found 198.119.

rac-4-Cyano-{(1R,6S,8S)-6-methyl-5,8-(tetramethylene)tricyclo[3.2.1.0²·⁷]oct-3-eno}[4,3-b]pyrrole²⁷ (5.19b) :

Following the procedure described for **5.19a**, (*E,E*)-4-cyano-2-(cyclohex-1-enyl)-3-(pent-2,4-

enyl)pyrrole (**5.18b**, 0.48 g, 2.0 mmol)) was refluxed in triglyme (25 mL) for 8 h. After cooling and workup, **5.19b** was obtained as a pink solid (0.26, 55 %). ^{1}H NMR (CDCl$_3$, 300 MHz): δ = 0.11 (d, J = 7.0 Hz, 3H), 0.97-2.23 (m, 13 H), 6.88 (d, J = 2.9 Hz, 1H), 8.33 (br, 1H); ^{13}C NMR (CDCl$_3$, 75.4 MHz): δ = 10.46 (q), 12.65 (d), 21.11 (t), 21.33 (d), 21.94 (d), 23.59 (t), 25.32 (t), 27.24 (t), 30.95 (d), 42.31 (t), 42.53 (d), 90.18 (s), 91.01 (s), 117.19 (s), 117.27 (s), 121.14 (d), 132.55 (s). MS (relative intensity, %): m/z = 57 (12.0), 71 (8.5), 85 (6.5), 155 (32.2), 168 (13.3), 169 (11.1), 181 (18.4), 183 (10.9), 195 (39.7), 196 (31.5), 209 (54.2), 223 (17.7), 238 (M$^+$, 100); HRMS: m/z calc. for C$_{16}$H$_{18}$N$_2$ 238.147, found 238.149.

5.4.3 Synthesis of 3-Formylindoles

1,7-Dimethyl-3-formyl-5-phenylindole (5.20a) :

DIBAL-H (1 M solution in CH$_2$Cl$_2$, 2.0 mL, 2.0 mmol) was added dropwise to a stirred solution of 3-cyano-1,7-dimethyl-5-phenylindole (**5.17a**, 0.25 g, 1.0 mmol) in CH$_2$Cl$_2$ (40 mL) at -30 °C. After stirring for 75 min while the temperature was allowed to rise to 0 °C, water (1 mL) was added and stirring was continued for another 30 min. Then MgSO$_4$ was added and the mixture was stirred for 30 min. The solid was removed and thoroughly extracted with CH$_2$Cl$_2$. The organic layer was filtered through a short column of (Al$_2$O$_3$) and concentrated to give **5.20a** as an off-white solid (0.24 g, 96 %),pure according to ^{1}H NMR. Crystallization from EtOH (96 %) gave **5.20a** as pale orange needles: 161-162 °C; ^{1}H NMR (CDCl$_3$, 200 MHz): δ = 2.80 (s, 3H), 4.11 (s, 3H), 7.27-7.50 (m, 6H), 7.56 (s, 1H), 7.67-7.72 (m, 2H), 8.43 (s, 1H), 9.98 (s, 1H); ^{13}C NMR (CDCl$_3$, 125.7 MHz): δ =19.44 (q), 37.69 (q), 117.64 (s), 118.11 (d), 121.84 (s), 126.17 (d), 126.69 (d), 126.82 (s), 127.21 (d), 128.50 (d), 135.88 (s), 136.29 (s), 141.11 (d), 141.16 (s), 184.06 (d); MS (relative intensity, %): m/z = 83 (10.9), 124 (9.7), 178 (5.9), 204 (8.8), 220 (7.7), 249 (M$^+$, 100); HRMS: m/z calc. for C$_{17}$H$_{15}$NO: 249.115, found 249.116.

1,6-Dimethyl-3-formyl-5,7-diphenylindole (5.20b) :

Following the procedure described for **5.20a**, 3-cyano-1,6-dimethyl-5,7-diphenylindole (**5.17b**, 0.32 g, 1.0 mmol) gave after 90 min, as pale orange foam (0.27 mg, 83 %), pure according to ^{1}H NMR. Crystallization from EtOH (96 %) gave **5.20b** as pale orange crystals: mp 202-205 °C; ^{1}H NMR (CDCl$_3$, 200 MHz): δ = 2.00 (s, 3H), 3.16 (s, 3H0, 7.33-7.52 (m, 11H), 8.24 (s, 1H), 9.97 (s, 1H); ^{13}C NMR (CDCl$_3$, 75.4 MHz): δ = 18.26 (q), 37.23 (q), 117.19 (s), 121.93 (d), 123.71 (s), 127.45 (d), 127.81 (d), 128.15 (d), 129.59 (d), 130.30 (s), 130.41 (d), 135.04 (s), 138.15 (s), 141.22 (d), 142.66 (s), 184.04 (d); MS (relative intensity, %): m/z = 281 (8.2), 296 (8.1), 325 (M$^+$, 100); HRMS: m/z calc. for C$_{23}$H$_{19}$NO: 325.147, found 325.146.

3-Formyl-1-methyl-5-phenyl-pentahydrocyclohept[g]indole (5.20c) :

Following the procedure described for **5.20a**, 3-cyano-1-methyl-5-phenyl-6,7,8,9-tetrahydro-benz[g]indole (**5.17d**, 0.30 g, 1.0 mmol) gave **5.20c** as a red solid (0.27 g, 89 %), pure according to ^{1}H NMR. Crystallization from EtOH (96 %) gave **5.20c** as red crystals: mp 188-190 °C; ^{1}H NMR (CDCl$_3$, 200 MHz): δ = 1.59-1.62 (m, 2H), 1.78-1.83 (m, 4H), 2.84- 2.88 (m, 2H), 3.30-3.33 (m, 2H), 4/09 (s, 3H), 7.24-7.40 (m, 5H), 7.55 (s, 1H), 8.04 (s, 1H), 9.92 (s, 1H); ^{13}C NMR (CDCl$_3$, 75.4 MHz): δ = 27.11 (t), 27.49 (t), 27.65 (t), 30.50 (t), 31.05 (t), 39.07 (q), 117.08 (s), 120.43 (d), 124.41 (s), 126.22 (d), 127.45 (s), 127.66 (d), 129.57 (d), 135.40 (s), 137.87 (s), 138.21 (s), 142.23 (d), 143.10 (s), 183.90 (d); MS (relative intensity, %): m/z = 218 (8.4), 246 (9.7), 274 (21.9), 303 (M$^+$, 100); HRMS: m/z calc. for C$_{21}$H$_{21}$NO: 303.162, found 303.162.

X-Ray crystal structure of rac-1-Methyl-4-nitro-{(1R,6S,8S)-6-phenyl-5,8-(tetramethylene)-tricyclo[3.2.1.0²·⁷]oct-3-eno}[4,3-b]pyrrole (5.12a) :

Crystal data : Formula: $C_{21}H_{22}N_2O_2$: M = 334.42, crystal color and habit: yellow parallelepiped, crystal size: 0.50 x 0.40 x 0.38 mm; triclinic; space group: P1; a = 7.799(1) Å, b = 9.872 (1) Å, c = 11.770 (1) Å; V = 820.77(15) Å³; α = 109.638(4)°; β = 100.339 (6)°; γ = 97.756(6)°; Z = 2, ρ = 1.353 g/cm³; μ = 0.82 mm⁻¹. *Data collection* : The data were collected on an Enraf-Nonius CAD-4F diffractometer (Mo tube, 50 kV, 40 mA, monochromated Mo-Kα radiation (λ = 0.71073 Å), Δω = 1.05 + 0.34 tg θ), interfaced to a MS-DOS computer; T = 130 K; θ range 15.54-18.97°; reflections collected: 4098; independent reflections: 3569. *Solution and refinement*²⁸: The structure was solved by direct method (SHELXS) and refined anisotropically by full-matrix least squares (Xtal CRYLSQ) based on $F_o^2 > 0$; data/parameters 3265/315; data-to-parameter ratio: 10.4:1; R₁ = 0.048 [F₀>4.0 σ(F₀)], wR₂ = 0.058 [I>0]; absolute-stucture parameter; maximal residual electron density 0.443 e/Å³. The program PLUTO has been used for graphical representation of the crystal structure.

Table 5.5 : *Bond Lengths and Bond Angles for Compound 5.11a (Excluding H-Atoms)*

Interatomic Distances (Å)							
O(1)-N(2)	1.235(3)	C(1)-C(10)	1.503(3)	C(7)-C(13)	1.505(3)	C(14)-C(15)	1.518(3)
O(2)-N(2)	1.248(3)	C(1)-C(14)	1.588(3)	C(8)-C(9)	1.469(3)	C(15)-C(16)	1.396(3)
N(1)-C(10)	1.395(3)	C(2)-C(3)	1.527(3)	C(8)-C(13)	1.536(3)	C(15)-C(20)	1.398(3)
N(1)-C(11)	1.355(3)	C(3)-C(4)	1.524(3)	C(9)-C(10)	1.369(3)	C(16)-C(17)	1.388(3)
N(1)-C(21)	1.461(3)	C(4)-C(5)	1.525(3)	C(9)-C(12)	1.416(3)	C(17)-C(18)	1.393(3)
N(2)-C(12)	1.414(3)	C(5)-C(6)	1.539(3)	C(11)-C(12)	1.382(3)	C(18)-C(19)	1.387(3)
C(1)-C(2)	1.525(3)	C(6)-C(7)	1.512(3)	C(13)-C(14)	1.516(3)	C(19)-C(20)	1.390(4)
C(1)-C(6)	1.563(3)	C(7)-C(8)	1.530(3)				

Bond Angles (deg)					
C(10)-N(1)-C(11)	108.97(17)	C(6)-C(7)-C(8)	116.84(18)	N(1)-C(11)-C(12)	107.50(18)
C(2)-C(1)-C(6)	112.05(16)	C(6)-C(7)-C(13)	106.64(18)	N(2)-C(12)C(9)	127.8(2)
C(2)-C(1)-C(10)	116.16(17)	C(8)-C(7)-C13	60.80(14)	N(2)-C(12)C(11)	123.44(19)
C(2)-C(1)-C(14)	115.82(17)	C(7)-C(8)-C(9)	115.3(2)	C(9)-C(12)-C(11)	108.8(2)
C(6)-C(1)-C(10)	105.20(16)	C(7)-C(8)-C(13)	58.79(14)	C(7)-C(13)-C(8)	60.41(14)
C(6)-C(1)-C(14)	100.58(15)	C(9)-C(8)-C(13)	115.76(18)	C(7)-C(13)-C(14)	108.68(19)
C(10)-C(1)-C(14)	105.39(15)	C(8)-C(9)-C(10)	117.65(19)	C(8)-C(13)-C(14)	115.60(18)
C(1)-C(6)-C(5)	112.55(17)	C(8)-C(9)-C(12)	136.3(2)	C(1)-C(14)-C(13)	102.76(16)
C(1)-C(6)-C(7)	104.03(17)	N(1)-C(10)-C(1)	133.52(19)	C(1)-C(14)-C(15)	116.83(17)
C(5)-C(6)-C(7)	108.93(18)	C(1)-C(10)-C(9)	117.72(18)	C(13)-C(14)-C(15)	115.23(19)

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