Aminocarbene Complexes of Chromium in Heterocyclic Synthesis, XII[+]

One-Pot Formation of Functionalized Pyrrolinones and 2-Oxohexahydroindoles from Aminocarbene Complexes of Chromium

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Aminocarbene complexes of chromium **1b-d** react successively with diphenylacetylene, XH (X = PhS, PhSe, OAc) and finally with pyridine to give a series of functionalized pyrrolinones **7** via N-ylide complexes **2**. The X-ray structure of **7b** originating from a ring-opening reaction could be established. When this sequence was applied to the aminocarbene complex **8** bearing a tethered triple bond, synthesis of functionalized 2-oxohexahydroindole **11** was achieved. In the case of acetic acid, products resulting from a formal protonation/hydride addition reaction together with a carbon–nitrogen bond rupture were also observed besides protonation/dealkylation products.

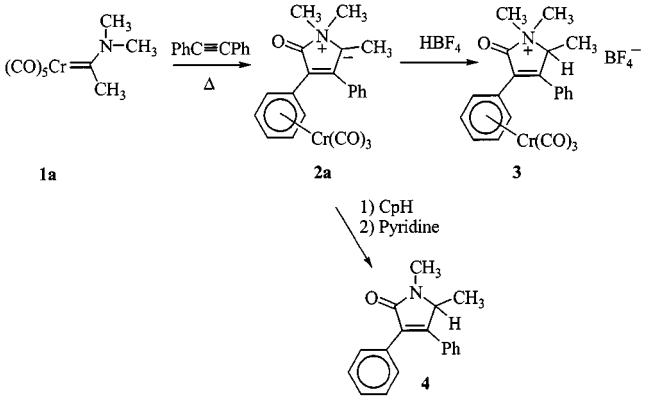
Introduction

Aminocarbene complexes of chromium have emerged as interesting starting material for the synthesis of a broad spectrum of heterocyclic compounds.[2] Our interest in this type of complexes arose when we discovered that they can be precursors of tricarbonylchromium complexes of a new type of nitrogen ylides.[3] These ylid complexes could in turn be thermally rearranged into a large array of polycyclic nitrogen-containing compounds. In order to even expand the scope of application of these complexes, we undertook a study aimed at using the intermediate N-ylides as starting material for new transformations.

This paper describes successful attempts to introduce, in one-pot reaction sequences new functionalities remote from the nitrogen atom by taking into advantage their easy protonation to alkylammonium derivatives and the reaction of the latter with nucleophiles. This led finally to highly functionalized pyrrolinones and hexahydroindoles, the biological properties of which are well established.[4][5]

Results and Discussion

In previous papers we demonstrated that the ylide **2a** obtained upon diphenylacetylene insertion into the carbene complex **1a** underwent *C*-protonation with strong acids, e.g. HBF_4, to give acyltrialkylammonium tetrafluoroborate **3**.[3a] Moreover, acids as weak as cyclopentadiene led in the case of the same complex **2a**, to the pyrrolinone **4** as the result of a *C*-protonation followed by demethylation at the nitrogen atom[6] (Scheme 1). It was therefore clear that due to their acidity, thiols (or selenols) should also be able to protonate such complexes and to generate ammonium thiolates. Conversely, it is also known that quaternary ammonium salts can be dealkylated by thiolates.[7] Taken together, and depending on the nature of the substituents on the nitrogen atom and on the site of reaction of the thiolate, these two successive reactions might indeed provide a way for further transformations of the ylide complexes into valuable products.



Scheme 1

Reaction of Thiophenol with Complex 2a

In order to demonstrate that thiols could act successively as protonation/dealkylation agents, we first attempted the reaction of thiophenol with complex **2a**. Thus, when **2a** was refluxed in benzene in the presence of an excess of thiophenol (4 equiv.) for 5 h, complete consumption of the starting material with formation of a new complex was observed by TLC. Treatment of the reaction residue in boiling

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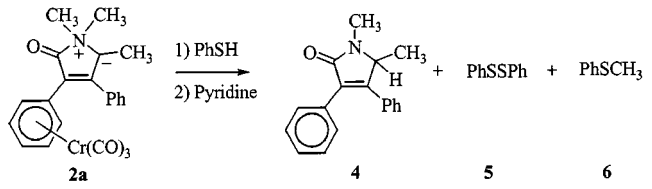
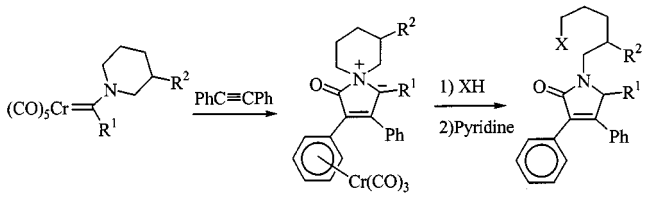


Scheme 2



Scheme 3

pyridine to remove the metal from the complexed organic products left a mixture of three compounds which were separated by silica gel chromatography and isolated in the following order of elution: first diphenyl disulfide (**5**) as a white crystalline solid and a stench product (7%) the NMR data of which corresponded to those of thioanisole (**6**). Finally, elution with petroleum ether/ethyl acetate gave a white solid (31%) the physical data of which agree fully with those of the known compound **4**, the signal for the hydrogen atom α to the nitrogen atom appearing as a quadruplet at δ = 4.40 and that of the methyl group as a doublet at δ = 1.18.[3c] The fate of the abstracted methyl group being thus clearly established by the isolation of thioanisole **6**, it appeared that protonation followed by dealkylation occurred indeed.

Reaction of Complexes 1b−d with Thiophenol and Selenophenol

That this protonation-dealkylation reaction was not limited to *N*-methyl-substituted ylide complexes and was of a general scope was demonstrated by the following reactions of complexes **2b−d**. Thus, under the same experimental conditions as for **1a**, cleavage of a carbon−nitrogen bond was also established in the case of complex **1b** which led to two compounds: diphenyl disulfide (**5**) (25%) and a more polar white solid (72%). Its ^{1}H-NMR spectrum confirmed again the protonation at the carbon atom α to the nitrogen atom with a singlet at δ = 5.38 and the presence of two multiplets at δ = 3.82 and 2.87 due to two diastereotopic

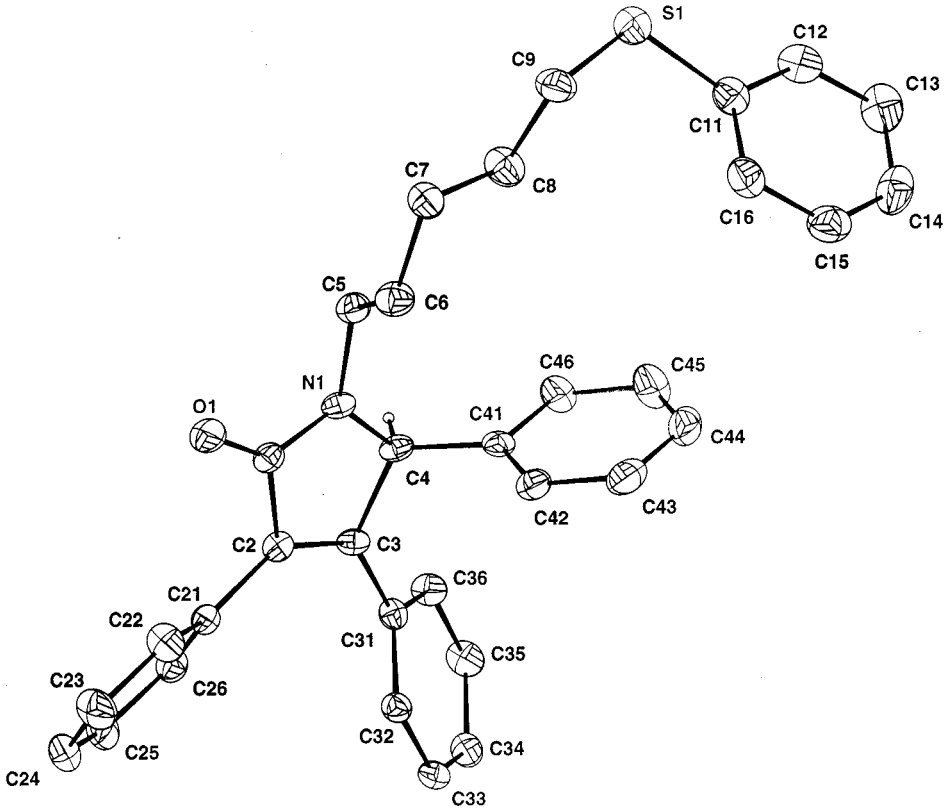


Figure 1. CAMERON projection of compound **7b** with selected atom distances [Å]: O(1)−C(1) 1.226(5), N(1)−C(4) 1.463(5), N(1)−C(1) 1.339(5), C(1)−C(2) 1.494(6), C(2)−C(3) 1.338(5), C(3)−C(4) 1.514(5), C(9)−S(1) 1.791(5)

hydrogen atoms of only one NCH_2 group, together with a triplet for a methylene group linked to the sulfur atom [$\delta(CH_2SPh) = 2.87$]. Confirmation of the six-membered ring opening with addition of the elements of PhSH came finally from an X-ray structure determination on this compound. As shown in the Cameron projection of Figure 1, protonation at C-5, cleavage of the piperidine ring at the nitrogen atom and formation of a carbon−sulfur bond leading to a pyrrolinone **7b** took indeed place.

The same transformation leading to the same mixture of products could also be conducted at room temperature, the reaction time being however much longer (2 d). On the other hand, **1c** led to **7c** in 61% yield. The ylide **2d**, which according to its NMR data exists as a 1:1 mixture of isomers, gave a 1:1 mixture of diastereomeric pyrrolinones **7d**. The regioselectivity of the ring-opening reaction was confirmed by ^{1}H-NMR spectroscopy: Both isomers gave indeed a doublet of doublets for the NCH_2 protons at δ = 3.60 and 3.68, the nitrogen−carbon bond cleavage taking thus place at the least-hindered position of the piperidinium group.

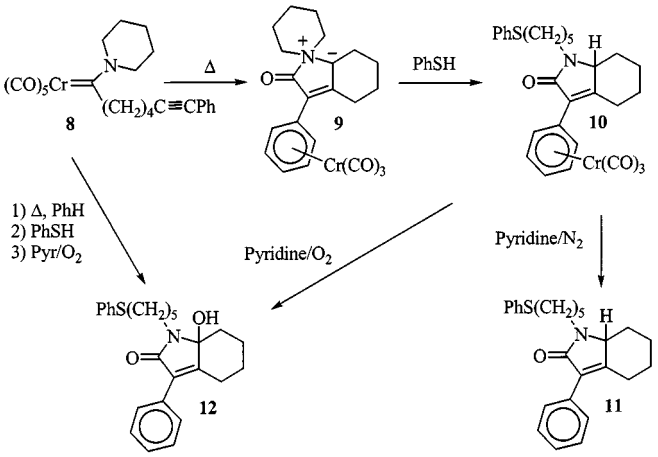
Phenylselenol behaved similarly: After 3 h, under the same conditions as above, a 87% yield of the complexed selenopyrrolinone was obtained from **2b**. It could be transformed into the metal-free pyrrolinone **7e** in 73% yield. Its NMR data very similar to those of the sulfur analog **7b**, the disubstituted carbon atom of the CH_2SePh group giving rise to a signal at δ = 29.62 instead of 33.43 for the CH_2SPh group of **7b**.

Reaction of Complex 8 with Thiophenol

Carbene complexes of the type **8**, bearing a tethered triple bond, are interesting starting material for the synthesis of tricyclic, nitrogen-containing compounds. Their transformation, which occurs smoothly on thermolysis, takes also place via N-ylide complexes, which could in several instances be isolated.[3b] In the light of the above results, a similar reactivity pattern towards acids and nucleophiles was expected. When complex **9**, obtained from **8**, was heated with thiophenol, then with pyridine, a new pyrrolinone **11** was isolated in 38% yield. Its NMR data are fully in agreement with this structure showing a typical signal at δ = 2.93 as a triplet for the CH_2SPh group, two signals at δ = 3.74 and 3.22 as multiplets for the NCH_2 and NCH protons, respectively, and a signal at δ = 170.33 as for the pyrrolinones **4** and **7**.

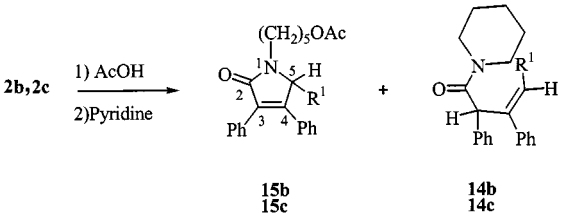
Reaction of Complexes 2b, c and 9 with Acetic Acid

In order to obtain more insight into the mechanism and the factors which govern these formal additions of XH to the N-ylide complexes, acetic acid was also used for that purpose.[8] Since the acetate ion is a much weaker nucleophile than PhS^- and $PhSe^-$, but a harder base, a different reactivity towards the ylide complexes was expected. And this proved to be the case.



Scheme 4

Thus, when complex **2b** was heated in benzene in the presence of an excess of acetic acid for 24 h, then with pyridine, two products could be isolated after chromatography. The less polar product (12%) was assigned structure **14b**. The ^{1}H-NMR spectrum confirmed the presence of the intact piperidine ring with a multiplet for two NCH_2 groups at δ = 3.60. Moreover, singlets for an olefinic proton at δ = 6.51 and for a benzylic proton at δ = 4.89 appeared also in the ^{1}H-NMR spectrum.

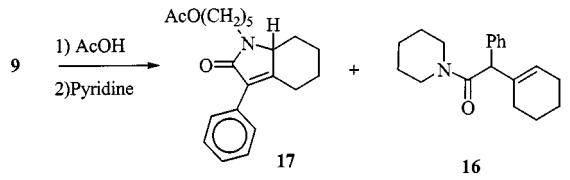


Scheme 5

The presence of an amide group [δ(CO) = 169.47] and of two tertiary carbon atoms, but the absence of a second carbonyl group agreed finally with a structure such as **14**. Confirmation of this structure came also from the reaction of **2c** ($R^1 = CH_3$) with acetic acid: Indeed, the methyl group signal of **14c** appeared as a doublet at δ = 1.58 and the olefinic proton as a quadruplet at δ = 5.53. Thus, cleavage of the C(5)−N(1) bond took place, however without addition of the acetoxy group.

To the more polar compound (42%) was assigned structure **15b**, the expected acetate: Indeed, signals of two carbonyl groups were present in the ^{13}C-NMR spectrum at δ(CO) = 171.27 and 170.31 which confirm the presence of a pyrrolinone and of an ester group, the presence of the latter being also confirmed by a triplet at δ = 4.50 in the ^{1}H-NMR spectrum attributable to the methylene protons of the CH_2OAc group. A much lower yield of **15c** (3.6%) was obtained from **2c**. Complex **9** behaved similary and led to two compounds in 24 and 19% yield. As in the previous case, a product **16** due to the five-membered ring cleavage, formation of a carbon−carbon double bond with a vinylic proton (δ = 5.42 as a multiplet) and of an amide [δ(CO) =

170.33] was isolated together with the expected protonation/substitution product **17** [δ(CO) = 171.29 and 170.29].

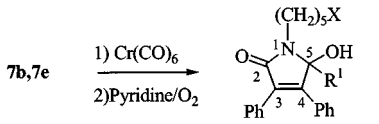


Scheme 6

Remark: Direct Formation of Hydroxypyrrolinones by Air Oxidation of the Pyrrolinones

During the transformation of the ylid complex **9** into the pyrrolinone **11**, a second, more polar compound was isolated in low yield (6%) as a white solid (m.p. 123°C). Its elemental analysis agrees with the presence of an extra oxygen atom in a molecule such as **11** (Scheme 4). A striking difference between this new compound and pyrrolinone **11** appeared also in the ^{13}C-NMR spectrum: The signal for the carbon atom α to the nitrogen atom appears now at δ = 87.77 instead of δ = 60.52 in **11**; thus, a second heteroatom must be attached to this carbon atom. This was confirmed by a DEPT experiment which established its quaternary nature. All these data are in agreement with a structure such as **12**: This pyrrolinone is thus an oxidation product of **11**.

We could confirm that under our reaction conditions [pyridine, $Cr(CO)_6$] and in the presence of air, the simplest pyrrolinones **7b** and **7e** were quantitatively oxidized to 5-hydroxy-3-pyrrolin-2-ones **13b** and **13e**. The mass spectrum as well as the NMR data confirm these structures: Of significance are the chemical shift of the quaternary C(5) carbon atoms bearing now two heteroatoms [δ(^{13}C) = 92.32 in **13b**, and 92.26 in **13e**]. Similarly, when the reactions with thiophenol were carried out directly in the presence of oxygen, substancial amounts of oxidized pyrrolinones were formed.



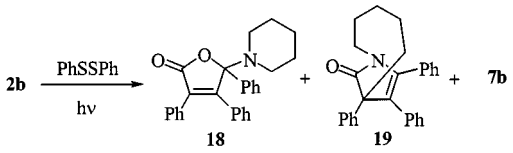
13b X=SPh
13e X=SePh

Scheme 7

The formation of this oxidation product is due to the presence during the reaction of residual oxygen: It is indeed known from the literature that 3-pyrrolin-2-ones are easily oxidized to hydroxypyrrolinones by atmospheric oxygen in the presence of a strong base (KOH, acetone).[4] It should, however, be noticed that in the absence of $Cr(CO)_6$ the formation of **13b**, **e** from **7b**, **e** was not observed.

Photolytic Reaction of Diphenyl Disulfide with Complex 2b

Since it was known that thiophenate dealkylations of quaternary ammonium salts could also occur along radicalar pathways,[7e] we checked whether radicals were able to induce the cleavage of the nitrogen−carbon bond of the ylid complex **2b**. For that purpose, diphenyl disulfide was irradiated in benzene solutions at room temperature in the presence of this complex. This photochemical reaction is indeed known to induce the formation of thiyl radicals.[9] After 15 h, the reaction went to completion. Three products could be separated by silica gel chromatography and fully characterized as the known amino lactone **18**, resulting from the oxidation of the starting ylid complex by residual oxygen in 15% yield; the product of the thermal rearrangement of the ylid complex, the known lactam **19** in 13% yield; and finally the ring-opened, sulfur-containing pyrrolinone **7b** in 60% yield.[6]



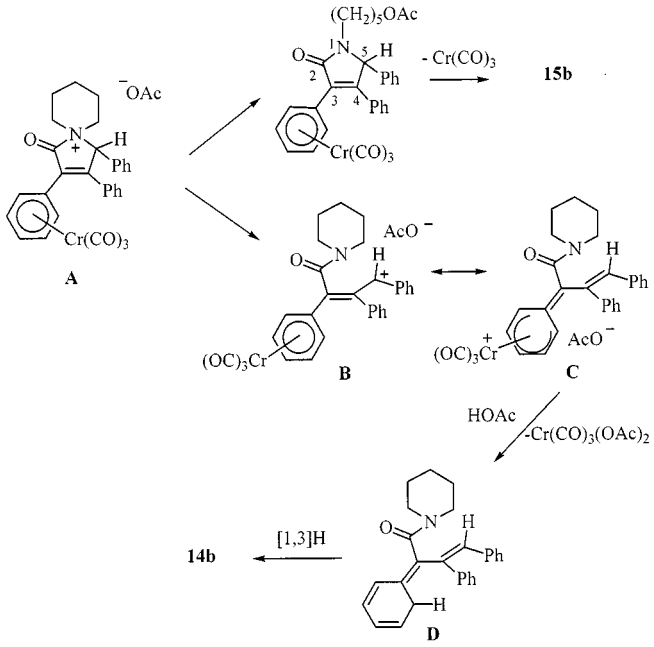
Scheme 8

Discussion

The transformations described herein are based on two chemical properties of thiophenol and selenophenol: their relatively high acidity and the high nucleophilicity of their conjugated bases, the thiophenate and selenophenate, the latter reacting in general five to ten times faster than the former. These nucleophiles have indeed been used for the selective dealkylation of quarternary ammonium salts to amines, a methyl group being more easily removed than a larger alkyl group, whereas pyrrolidines but not piperidines underwent ring-opening/dealkylation reactions.[7c] As far as the reactions of the different N-ylide complexes with acids are concerned, their protonation, followed by a nucleophilic dealkylation of the so-formed new ammonium salts, clearly can account for the formation of compounds **4**, **7**, **11**, **15**, and **17**.

However, acetic acid appeared to be a special case since two types of products were observed. The nucleophilicity of its conjugate base is much lower than that of PhS^- or $PhSe^-$, yet the expected products **15** and **17**, resulting from a protonation/nucleophilic nitrogen-to-carbon bond cleavage, were nevertheless observed.[7b] However, the formation of **14** and **16** cannot be explained by a direct interaction of the nucleophile with the organic ligand: Protonation together with a formal hydride transfer must occur since an overall reduction is observed. A mechanism which could account for this result would involve, after a *C*-protonation to give **A** as in the previous cases, cleavage of a carbon−nitrogen bond with formation of carbonylchromium acetate

via the tricarbonylchromium-stabilized carbocation (**B** ↔ **C**). Cleavage of the carbon−chromium bond followed by a 1,3-hydride shift in **D** would then lead to the observed unsaturated amides **14** or **16** and to $(CO)_3Cr(OAc)_2$ (Scheme 9). Support for such a mechanism came from two observations: First, the unsaturated amides **14** and **16** were present as metal-free products before the pyridine treatment; second, formation of a green insoluble complex (probably chromium acetate) which was, however, not further characterized, was also observed.



Scheme 9

Although most of the results could be explained by a protonation/nucleophilic dealkylation reaction, the detection of variable amounts of diphenyl disulfide during the reaction of the ylide complexes with thiophenol, might be indicative for the involvement of radical (or organometallic) pathways. According to the literature data, such dealkylation reactions can indeed occur either by means of a direct S_N2 substitution reaction, or by a single electron transfer (SET) between the thiophenate and the ammonium salt.[7d,7e] This might lead to thiyl radicals, which could either give diphenyl disulfide or react with the cleaved intermediate with formation of the observed pyrrolinone **7b**. Similarly, the photolytic cleavage of PhSSPh, which leads to phenylthiyl radicals, can react with the ylide complex according to a radical chain process, to give the same sulfur-containing pyrrolinone **7b**.

Conclusion

Regardless of the mechanistic aspects, the transformations described herein constitute a direct access to highly functionalized pyrrolinones since all the described reactions could also be carried out directly with the starting aminocarbene complexes without isolation of the intermediate ylide complexes.

Experimental Section

General Remarks: All reactions were carried out under argon in a previously dried and evacuated apparatus. The solvents were dried by standard procedures by distillation from Na/benzophenone ketyl (diethyl ether, tetrahydrofuran) and saturated with argon. Silica gel (Merck, type 60, 0.063−0.200 mm) was used for column chromatography. ^{1}H NMR: Bruker AC-200 (^{1}H, 200 MHz; ^{13}C, 50 MHz) and Bruker ARX-400 (^{1}H, 400 MHz; ^{13}C, 100 MHz). All NMR spectra were recorded in $CDCl_3$ unless otherwise specified with $CHCl_3$ at $\delta_H = 7.26$ as internal standard. IR spectra: Perkin-Elmer 1420. MS: ZAB HSQ (Fison) (EI, 70 eV). Complexes **2a**, **b** and **9** were prepared according to the literature.[3a,3b]

Pentacarbonyl[α-(3-methylpiperidinyl)benzylidene]chromium (1d): To a solution of 6.3 g (13.3 mmol) of pentacarbonyl(α-ethoxybenzylidene)chromium in 40 ml of diethyl ether 3-methylpiperidine (4 ml, 25.6 mmol) was added. The reaction mixture was stirred for 15 min at room temperature; then the solvent was evaporated under vacuum for 1 h. The residue was chromatographed on silica gel using petroleum ether/dichloromethane (95:5) as eluent to give 4.32 g (11.4 mmol, 86%) of **1d** as a yellow brownish oil. − ^{1}H NMR (200 MHz) (mixture of two isomers): δ = 7.38−6.68 (m, 10 H, ArH), 5.10−4.95 (m, 2 H, NCH), 3.90−3.75 (m, 2H, NCH), 3.70−3.55 (m, 1 H, NCH), 3.45−3.35 (m, 1 H, NCH), 3.05−2.90 (m, 1 H, NCH), 2.90−2.60 (m, 1 H, NCH), 2.20−1.20 (m, 10 H), 1.11 (d, ^3J = 6.5 H_2, 3H, CH_3), 0.73 (d, ^3J = 6.5 H_2, 3H, CH_3). − ^{13}C NMR (100 MHz): δ = 269.63 (Cr=C), 224.14 (*trans*-CO), 217.35 (*cis*-CO), 152.09 (*ipso*-Ar-C), 129.46−118.86 (Ar-C), 67.50 (NCH_2), 61.52, 61.09 (2 NCH_2), 55.26 (NCH_2), 34.47 (CH), 33.85 (CH), 32.71 (CH_2), 32.48 (CH_2), 27.50 (CH_2),, 26.90 (CH_2), 18.67 (CH_3). − MS (EI, 70 eV); *m*/*z* (%): 379 [M^+].

N-Ylid Complex (2d): A solution of 3.52 g (9.3 mmol) of carbene complex **1d** in 80 ml of cyclohexane and diphenylacetylene (2.09 g, 11 mmol) was heated at reflux temperature for 12 h after which time a yellow solid had precipitated. Filtration gave 2.2 g (4.2 mmol, 45%) of a yellow solid, m.p. 153°C. − ^{1}H NMR (400 MHz) (mixture of two isomers); δ = 7.35−7.21 (m, 20 H, ArH), 5.46−4.91 (m, 10 H, ArCr), 3.66−2.70 (m, 8 H, 4 NCH_2), 1.94−1.00 (m, 10 H), 0.90 (d, ^3J = 4 Hz, 6 H, 2 CH_3). − ^{13}C NMR (50 MHz): δ = 235.10 (Cr=C), 172.01 (NCO), 168.70 (C=C), 143.61−113.61 (C=C, Ar), 95.95, 95.50, 88.57, 88.29, 87.05, 86.45 (Ar−Cr), 62.04, 61.01, 55.86, 54.63 (4 NCH_2), 29.72, 26.99, 23.68, 21.51 (4 CH_2), 19.47, 18.99 (2 CH_3). − $C_{27}H_{25}NO_4Cr$ (479): calcd. C 70.32, H 5.10, N 2.64; found C 70.32, H 5.10, N 2.51.

General Procedure for the Reaction of N-Ylides 2b-d with Thiophenol, Selenophenol and Acetic Acid: A solution of 1 mmol of ylide complex and 2 mmol of XH in 30 ml of benzene was heated at reflux for 15 h. After evaporation of the solvent under vacuum, the residue was heated in 10 ml of pyridine for 5 h. Evaporation of the solvent gave a residue which was chromatographed on silica gel.

Thioanisole (6) and 1,5-Dimethyl-3,4-diphenyl-1,5-dihydropyrrol-2-one (4): Prepared from **2a** in 7 and 31% yield. Elution with petroleum ether gave **6** (33 mg, 0.27 mmol) as a stench oil. − ^{1}H NMR (200 MHz): δ = 7.56−7.26 (m, 5 H, ArH), 2.52 (s, 3 H, SCH_3). − ^{13}C NMR (50 MHz): δ = 138.0−125.08 (Ar), 1.59 (SCH_3). − Elution with petroleum ether/ethyl acetate (1:1) gave **4** (300 mg, 1.14 mmol); m.p. 93−94°C. − IR ($CHCl_3$): $\tilde{\nu}$ = 1670, 1600. − ^{1}H NMR (200 MHz): δ = 7.40−7.10 (m, 5 H, ArH), 4.40 (q, ^3J = 6.8 Hz, 1

H, C*H*CH_3), 3.08 (s, 3 H, NCH_3), 1.18 (d, ^3J = 6.8 Hz, 3 H, CHCH_3). − ^{13}C NMR (100 MHz): δ = 169.68 (CO), 153.61 (C=C), 132.89−127.80 (Ar, C=C), 59.24 (CH), 27.31 (NCH_3) 16.85 (CH_3). − HRMS: calcd. for $C_{18}H_{17}NO$ [M^+] 263.1310; found 263.1311.

$Cr(CO)_3$ Complex of 3,4,5-Triphenyl-1-[5(-phenylsulfanyl)pentyl]-1,5-dihydropyrrol-2-one (7b): Prepared from complex **2b** in 57% yield (1.78 g, 2.85 mmol) as a yellow oil. − ^{1}H NMR (200 MHz): δ = 7.44−6.95 (m, 15 H, ArH), 5.76 (m, 1 H, ArCr), 5.36−5.17 (m, 5 H, ArCr, CHPh), 3.81 (m, 1 H, NCH), 2.89−2.73 (m, 3 H, NCH, SCH_2), 1.62−1.39 (m, 6 H, $3CH_2$).

Pyrrolinone 7b: Prepared from the above complex in 72% yield (1.75 g, 3.6 mmol) as white solid, m.p. 110°C. − ^{1}H NMR (400 MHz): δ = 7.29−7.04 (m, 20 H, ArH), 5.40 (s, 1 H, CHPh), 3.86−3.79 (m, 1 H, NCH), 2.92-2.81 (m, 3 H, NCH, SCH_2), 1.68−1.41 (m, 6 H, 3 CH_2). − ^{13}C NMR (100 MHz): δ = 170.34 (CO), 152.28 (C-4), 135.66−125.88 (C-3, Ar), 66.99 (C-5), 40.50 (NC), 33.43 (CS), 28.82, 28.15, 26.11 (3 CH_2). − $C_{33}H_{31}NOS$ (489.2): calcd. C 80.98, H 6.33, N 2.86; found C 80.89, H 6.44, N 2.95.

5-Methyl-1-[2-methyl-5-(phenylsulfanyl)pentyl]-3,4-diphenyl-1,5-dihydropyrrol-2-one (7c): Prepared from **2c** in 61% yield (0.86 g, 3.6 mmol) as an oil. − ^{1}H NMR (400 MHz): δ = 7.48−7.12 (m, 15 H, ArH), 4.58 (q, ^3J = 6.8 Hz, 1 H, 4-H), 3.9 (td, ^2J = 13.6 Hz, ^3J = 9.8 Hz, NCH), 3.25 (td, ^2J = 13.6 Hz, ^3J = 6.2 Hz, NCH), 2.96 (t, ^3J = 7.3 Hz, 2 H, CH_2S), 1.8−1.5 (m, 6 H, 3 CH_2), 1.22 (d, ^3J = 6.8 Hz, 3 H, CH_3) − ^{13}C NMR (50 MHz): δ = 169.69 (CO), 153.89 (C-4), 136.82−125.84 (C-3, Ar), 57.38 (C-5), 40.16 (NC), 33.45 (CS), 28.85, 28.33, 26.18 (3 CH_2), 17.18 (CH_3). − MS (EI, 70 eV); *m*/*z*: 427 [M^+].

1-[2-Methyl-5-(phenylsulfanyl)pentyl]-3,4,5-triphenyl-1,5-dihydropyrrol-2-one (7d): A mixture of two isomers was prepared from complex **2d** in 61% yield (0.57 g, 1.13 mmol) as a viscous oil. − ^{1}H NMR (400 MHz): δ(isomer 1) = 7.51−7.00 (m, 20 H, ArH), 5.45 (s, 1 H, 5-H), 3.70 (dt, ^2J = 13.6 Hz, ^3J = 8.5 Hz, 1 H, NCH), 2.91 (t, ^{3}J = 7.2 Hz, CH_2S), 2.60(dt, ^2J = 13.6 Hz, ^3J = 5.5 Hz, 1 H, NCH), 1.77−1.30 (m, 5 H), 0.77 (d, ^3J = 6.6 Hz, 3 H, CH_3); δ(isomer 2) = 7.51−7.00 (m, 20 H, ArH), 5.39 (s, 1 H, 5-H), 3.64 (dt, ^2J = 13.6 Hz, ^3J = 8.5 Hz, NCH), 2.85 (m, 2 H, CH_2S), 3.68 (dt, ^2J = 13.8 Hz, ^3J = 5.5 Hz, NCH), 1.77−1.30 (m, 5 H), 0.91 (d, ^3J = 6.6 Hz, CH_3). − ^{13}C NMR (50 MHz) (2 isomers): δ = 170.64 (CO), 152.66 (C-4), 137.10−125.82 (C-3, Ar), 67.17 (C-5), 67.50 (C-5), 46.76 (NC), 46.46 (NC), 33.57 (CS), 32.82, 32.39, 32.12, 26.55, 26.11 (6 CH_2), 17.72 (CH_3), 17.60 (CH_3). − $C_{34}H_{33}NOS$ (503): calcd. C 81.11, H 6.56, N 2.78; found C 80.92, H 6.70, N 2.60.

$Cr(CO)_3$ Complex of 1-[2-Methyl-5-(phenylselanyl)pentyl]-3,4,5-triphenyl-1,5-dihydropyrrol-2-one (7e): Obtained from complex **2b** in 87% yield (2.90 g, 4.36 mmol) as an orange solid, m.p. 65°C. − ^{1}H NMR (200 MHz): δ = 7.46-6.95 (m, 15 H, ArH), 5.83−5.71 (m, 2 H, ArCr), 5.36−5.16 (m, 4 H, ArCr and 5-H), 3.95−3.68 (m, 1 H, NCH), 2.83−2.68 (m, 3 H, $NCHCH_2S$), 1.69−1.23 (m, 6 H, 3 CH_2). − ^{13}C NMR (100 MHz): δ = 168.12 (CO), 155.51 (C-4), 132.45−126.77 (C-3, Ar), 98.89−91.24 (ArCr), 67.73 (C-5), 40.32 (CN), 29.77 (CS), 27.91, 27.64, 26.97 (3 CH_2). − $C_{36}H_{31}CrNO_4Se$ (672): calcd. C 64.28, H 4.61, N 2.08; found C 64.18, H 4.66, N 2.04.

Pyrrolinone 7e: Obtained in 73% yield (256 mg, 0.4 mmol) as a white solid, m.p. 105°C from methanol/dichloromethane. − ^{1}H NMR (400 MHz): δ = 7.51−7.04 (m, 20 H, ArH), 5.39 (s, 1 H 5-H), 3.90−3.70 (m, 1 H, NCH), 2.91−2.76 (m, 3 H, NCH, CH_2S), 1.92−1.35 (m, 6 H, 3 CH_2). − ^{13}C NMR (50 MHz): δ = 170.15 (CO), 152.36 (C-4), 135.42−126.62 (C-3, Ar), 66.77 (C-5), 40.26 (NC), 29.62 (CS), 27.88, 27.52, 26.91 (3 CH_2). − $C_{33}H_{31}NOSe$ (536): calcd. C 73.88, H 5.78, N 2.61; found 73.26, H 5.80, N 2.55.

3-Phenyl-1-[5-(phenylsulfanyl)pentyl]-1,4,5,6,7,7a-hexahydroindol-2-one (11): Obtained from complex **9** in 38% yield (732 mg, 1.85 mmol) as an oil. − ^{1}H NMR (400 MHz): δ = 7.39−7.04 (m, 10 H, ArH), 3.82−3.77 (m, 1 H, 7a-H), 3.75−372 (m, 1 H, NCH), 3.30−3.15 (m, 1 H, NCH), 3.06 (m, 1 H, 4-H), 2.93 (t, ^3J = 7 Hz, 2 H, CH_2S), 2.5 (m, 1 H, 7-H), 2.28 (m, 1 H, 4-H), 2.05−1.90 (m, 2 H, 5-H, 6-H), 1.75−1.45 (m, 7 H), 1.40−1.25 (m, 1 H, 5-H), 1.20−1.08 (m, 1 H, 7-H). − ^{13}C NMR (100 MHz): δ = 170.33 (CO), 154.49 (C-4), 136.88, 133.00 (C-3, Ar), 129.38−126.5 (Ar), 60.52 (C-7a), 40.06 (NC), 33.50 (C-5), 33.41 (C-7), 28.96, 27.46, 26.25, 23.46, 21.16 (5 CH_2). − $C_{25}H_{29}ONS$ (391): calcd. C 76.73, H 7.42, N 3; found 76.89, H 7.35, N 3.51.

7α-Hydroxy-3-phenyl-1-[5-(phenylsulfanyl)pentyl]-1,4,5,6,7,7a-hexahydroindol-2-one (12): Obtained in 6% yield (118 mg, 0.3 mmol) as a white solid, m.p. 123°C. − ^{1}H NMR (400 MHz): δ = 7.69−7.40 (m, 10 H, ArH), 3.58−3.54 (m, 2 H, NCH_2), 3.17−3.14 (m, 3 H, 4-H, CH_2S), 2.77 (s, 1 H, OH), 2.66−2.63 (m, 2 H, 4-H, 7-H), 2.20 (m, 1 H, 6-H), 2.01−1.84 (m, 6 H, 3 CH_2), 1.78−1.68 (m, 2 H, CH_2), 1.65−1.50 (m, 2 H, 6-H, 7-H). − ^{13}C NMR (100 MHz): δ = 169.33 (CO), 155.37 (C-4), 137.16, 131.14 (C-3, C_q Ar), 129.64−126.11 (Ar), 87.77 (C-7a), 38.88 (C-7), 33.81 (CS), 29.20, 27.80, 26.80, 24.90, 21.94 (CH_2). − $C_{25}H_{29}O_2NS$ (407): calcd. C 73.71, H 7.12, N 3.44; found C 73.61, H 7.00, N 3.31.

5-Hydroxy-5-methyl-3,4-diphenyl-1-[5-(phenylsulfanyl)pentyl]-1,5-dihydropyrrol-2-one (13b): Obtained quantitatively upon heating of **7b** (200 mg, 0.41 mmol) and $Cr(CO)_6$ (90 mg, 0.41 mmol) in pyridine (20 ml) for 15 h in the presence of air. After evaporation of the solvent, followed by silica gel chromatography, elution with petroleum ether/ethyl acetate (70:30) gave **13b** (207 mg, 0.41 mmol) as a white solid, m.p. 48°C. − ^{1}H NMR (400 MHz): δ = 7.49−7.00 (m, 20 H, ArH), 3.43 (s, 1 H, NCH), 3.04−2.97 (m, 2 H, OH, NCH), 2.84 (t, ^3J = 7 Hz, 2 H, CH_2S) 1.65−1.28 (m, 6 H, 3 CH_2). − ^{13}C NMR (100 MHz): δ = 169.58 (CO), 153.95 (C-3), 137.52−125.79 (C-2, Ar), 92.32 (C-4), 39.70 (CN), 33.37 (CS), 28.71, 28.20, 26.73 (3 CH_2). − $C_{33}H_{31}NO_2S$ + 1/2 H_2O (514): calcd. C 77.04, H 6.03, N 2.72; found C 76.99, H 6.00, N 2.72. − MS (70 eV); *m*/*z*: 489 [M^+].

5-Hydroxy-5-methyl-3,4-diphenyl-1-[5-(phenylselanyl)pentyl]-1,5-dihydropyrrol-2-one (13e): Prepared from pyrrolinone **7c** in 33% yield (300 mg, 0.54 mmol) as a white solid, m.p. 46°C. − ^{1}H NMR (200 MHz): δ = 7.45−6.96 (m, 20 H, ArH), 4.13 (s, 1 H, OH), 3.45−3.22 (m, 1 H, NCH), 3.15−2.85 (m, 1 H, NCH), 2.77 (t, ^3J = 7 Hz, 2 H, CH_2S), 1.75−1.25 (m, 6 H, 3 CH_2). − ^{13}C NMR (50 MHz): δ = 169.59 (CO), 153.98 (C-3), 137.57−126.38 (C-3, Ar), 92.26 (NC), 29.66 (SC), 28.05, 27.69, 27.37 (3 CH_2). − $C_{33}H_{31}NO_2Se$ (552): calcd. C 71.74, H 5.61, N 2.54; found C 71.59, H 5.73, N 2.36.

2,3,4-Triphenyl-1-(piperidin-1-yl)but-3-en-1-one (14b) and 5-(5-Oxo-2,3,4-triphenyl-2,5-dihydropyrrol-1-yl)pentyl Acetate (15b): Prepared in 12% and 42% yield, respectively, from complex **2b**. − **14b:** Oil (90 mg, 0.23 mmol). − ^{1}H NMR (400 MHz): δ = 7.43−6.92 (m, 15 H, ArH), 6.51 (s, 1 H, 4-H), 4.89 (s, 1 H, 2-H), 3.84−3.38 (m, 4 H, NCH_2), 1.65−1.41 (m, 6 H, 3 CH_2). − ^{13}C NMR (100 MHz): δ = 169.47 (CO), 141.19−127.95 (C-4, C-3, Ar), 58.42 (C-2), 47.26, 43.46 (NC), 2633, 25.78, 24.68 (3 CH_2). − $C_{27}H_{27}ON$ (381): calcd. C 85.04, H 7.09, N 3.67; found C 84.93, H 7.11, N 3.64. − **15b:** Yellow oil (360 mg, 42%). − ^{1}H NMR (200 MHz): δ = 7.48−7.01 (m, 15 H, ArH), 5.39 (s, 1 H, 2-H), 4.00 (t, ^3J =

6.5 Hz, 2 H, SCH_2), 3.81 (dt, ^2J = 13.9 Hz, ^3J = 7 Hz, 1 H, NCH), 2.82 (dt, ^2J = 13.9 Hz, ^3J = 7 Hz, 1 H, NCH), 201 (s, 3 H CH_3), 1.63−1.20 (m, 6 H, 3 CH_2). − ^{13}C NMR (100 MHz): δ = 171.27, 170.31 (2 CO), 152.57 (C-3), 135.60−128.30 (C-4, Ar), 66.86 (C-2), 64.29 (CH_2O), 40.36 (CN), 28.31, 28.20, 23.32 (3 CH_2), 21.12 (CH_3). − MS (EI, 70 eV); *m*/*z*: 439 [M^+].

2,3-Diphenyl-1-(piperidin-1-yl)pent-3-en-1-one (14c) and 5-(2-Methyl-5-oxo-3,4-diphenyl-2,5-dihydropyrrol-1-yl)pentyl Acetate (15c): Prepared from complex **2c** in 34 and 36% yield, respectively. − **14c:** Oil (860 mg, 3.6 mmol). − ^{1}H NMR (200 MHz): δ = 7.31−7.07 (m, 10 H, ArH), 5.53 (q, ^3J = 6.9 Hz, 1 H, 4-H), 4.76 (s, 1 H, 2-H), 3.70−3.23 (m, 4 H, 2 NCH_2), 1.58 (d, ^3J = 6.9 H, CH_3), 1.54−1.25 (m, 6 H, CH_2). − ^{13}C NMR (100 MHz): δ = 168.65 (CO), 129.75−125.64 (C-3, C-4, Ar), 56.00 (C-2), 46.00, 42.17 (2 NCH_2), 25.10, 24.52, 23.51 (3 CH_2), 13.90 (CH_3). − MS (EI, 70 eV); *m*/*z*: 319 [M^+]. − **15c:** Oil (30 mg, 3.6%) − ^{1}H NMR (200 MHz): δ = 7.50−7.10 (m, 10 H, ArH), 4.55 (q, ^3J = 6.3 Hz, 1H, H-2) 4.10 (t, ^3J = 6.3 Hz, 2H,CH_2O), 3.9 (dt, ^2J = 15 Hz, ^3J = 6.8 Hz, 1H, NCH), 3.25 (dt, ^2J = 15 Hz, ^3J = 6.8 Hz, 1 H, NCH), 2.10 (s, 3 H, CH_3), 1.80−1.30 (m, 6 H, 3 CH_2), 1.2 (d, ^3J = 6.3 Hz, 3 H, CH_3). − ^{13}C NMR (200 MHz): δ = 171.37, 169.72 (2 CO), 152.84 (C-3), 133.08−128.23 (C-4, Ar), 64.35 (CH_2O), 57.33 (C-2), 40.09 (CN), 28.40, 23.44, 21.13 (4 CH_2), 17.19 (CH_3). − MS (EI, 70 eV); *m*/*z*: 377 [M^+].

2-(Cyclohex-1-enyl)-2-phenyl-1-(piperidin-1-yl)ethanone (16) and 5-(2-Oxo-3-phenyl-2,4,5,6,7,7a-hexahydroindol-1-yl)pentyl Acetate (17): Prepared from complex **9** in 24 and 18% yield, respectively. − **16:** Oil (155 mg, 0.55 mmol). − ^{1}H NMR (200 MHz): δ = 7.28−7.16 (m, 5 H, ArH), 5.42 (s, 1 H, =CH), 4.32 (s, 1 H, 2-H), 3.60−3.45 (m, 2 H, NCH_2), 3.45−3.20 (m, 2 H, NCH_2), 2.10−1.20 (m, 14 H, 7 CH_2). − ^{13}C NMR (50 MHz): δ = 170.23 (CO), 138.55−136.49 (=C, Ar), 129.29−125.08 (=CH, Ar), 56.72 (C-2), 47.02, 43.05 (2 NC), 28.36, 26.24, 25.66, 25.40, 2463, 23.02, 22.32, (7 CH_2). − MS (EI, 70 eV); *m*/*z*: 283 [M^+]. − **17:** Oil (148 mg, 0.43 mmol). − ^{1}H NMR (200 MHz): δ = 7.40−7.23 (m, 5 H, ArH), 3.98 (t, ^3J = 8 Hz, 2 H, CH_2O), 3.75 (m, 1 H, 7a-H), 3.70−3.65 (m, 1 H, NCH), 3.20−3.10 (m, 1 H, NCH), 3.05−2.95 (m, 1 H, 4-H), 2.45−2.40 (m, 1 H, 7-H), 2.25−2.15 (m, 1 H, 4-H), 1.96 (s, 3 H, CH_3), 1.98−1.85 (m, 2 H, 5-H, 6-H), 1.70−1.30 (m, 7 H), 1.30−1.20 (m, 1 H, 5-H), 1.15−1.05 (m, 1 H, 7-H). − ^{13} C NMR (50 MHz): δ = 171.29, 170.29 (2 CO), 154.44 (C-3a), 131.68, 127.60 (C-3, Ar), 64.35 (CH_2O), 60.42 (C-7a), 39.91 (C-7), 28.60, 28.38 (2 CH_2), 27.41 (C-6), 26.66 (C-4), 23.38 (C-5, C-6), 21.07 (CH_3). − $C_{21}H_{27}O_3N$ (341): calcd. C 73.90, H 7.92, N 4.10; found C 73.05, H 8.18, N 4.00.

Crystal-Structure Analysis of 7b: X-ray quality crystals were obtained by recrystallization of compound **7b** in acetone at −20°C. Data were collected at 193 K with a Nonius MACH3 diffractometer. Empirical absorption correction using DIFABS was applied. Anomalous dispersion terms and correction of secondary extinction were applied. The structure was solved by SHELXS[10] and refined by least-squares using anisotropic thermal parameters for all non-hydrogen atoms. H atoms were located in a difference Fourier map, and their coordinates were introduced in the last refinement with an overall isotropic thermal parameter. 2187 reflections with $F_o > 3\sigma(F_o)$ were used to solve and refine the structure to $R = 0.0489$ and $R_w = 0.0474$, 326 least-squares parameters. The programs used were CRYSTALS and CAMERON.[11][12] Crystal data: $C_{33}H_{31}ONS$, M = 489.7, monoclinic, space group $P2_1/n$, a = 10.951(3), b = 11.080(3), c = 21.938(11) Å, β = 90.36(3)°, V = 2662(2) Å^3, D_c = 1.22 g cm^{-3}. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-112084. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: int. code + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

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